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RESEARCH

Adiposity is associated with a higher number of thyroid nodules and worse fine-needle aspiration outcomes

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Abstract

Background: Adiposity may be associated with thyroid nodularity. However, its impact on the number of nodules and the risk of malignancy is unclear.

Aim: To evaluate the impact of adiposity on thyroid nodules using body mass index (BMI), ultrasonographic (US) data and cytological data.

Methods: A retrospective cohort study of 310 patients with thyroid nodules was performed. Patients were categorized based on their BMI, and grayscale US data and fine-needle aspiration cytology results were evaluated.

Results: Patients with BMI ≥ 25 kg/m^2 were found to have a higher number of thyroid nodules compared to those with BMI < 25 kg/m^2 (4.25 ± 2.42 vs 3.66 ± 1.93) (*P* value = 0.05). Patients with BMI ≥ 25 kg/m^2 had more suspicious and malignant cytology than those with BMI < 25 kg/m^2 (*P* value = 0.029). Patients with BMI ≥ 25 kg/m^2 had more nodules with intermediate and high suspicion sonographic patterns. However, this did not reach statistical significance.

Conclusion: Overweight and obese patients have a trend for more thyroid nodules and have a higher risk of being diagnosed with thyroid malignancy.

Keywords: thyroid nodules; obesity; BMI; thyroid ultrasound; FNA; adiposity

Introduction

Over the past few decades, the prevalence of thyroid nodules worldwide has been significantly increasing. This increased rate is primarily attributed to thyroid ultrasonography's high availability and use (1, 2). Nevertheless, although thyroid nodules are benign in their majority, there is a 7–15% risk of malignancy, highlighting the importance of early and accurate detection and proper investigation (3, 4).

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The global incidence of obesity has also spiked dramatically over the past few years, affecting people of all ages. BMI, the most cited method of assessing obesity, has been linked to an increased risk of various cancers, including thyroid cancer (5). Multiple studies suggest that higher body mass index (BMI) may be correlated with the prevalence of thyroid nodules. However, the association between adiposity and the number of thyroid nodules or the risk of thyroid malignancy remains elusive (6, 7, 8, 9, 10, 11, 12, 13, 14).

This study aims to assess the impact of adiposity on thyroid nodules by examining the relationship between BMI and ultrasonographic (US) and cytological characteristics of a cohort of 310 patients with thyroid nodules. We hypothesized that adiposity increases the number of thyroid nodules and the malignancy risk. Ultrasound and fine-needle aspiration (FNA) cytology results were evaluated to explore potential correlations between BMI and nodule features, including malignancy risk.

Materials and methods

Study design and participants

This is a retrospective cohort study of 310 consecutive patients diagnosed with thyroid nodules and evaluated at the Thyroid & Endocrinology Center between 2020 and 2021. The Thyroid & Endocrinology Center is a referral clinic and teaching affiliate of the European University Cyprus School of Medicine. Data recorded were gender, age, weight, height, thyroid-stimulating hormone (TSH) levels, the number of nodules and the maximal diameter of the largest nodule. In cases where FNA was performed, cytology results were recorded.

The sole inclusion criterion in the study was the diagnosis of thyroid nodules, solitary or multiple. Patients with no nodules, autoimmune thyroiditis and pregnant patients were excluded. All patients included were adults. Patients were divided into two groups according to their BMI: normal BMI < 25 kg/m^2 and overweight and obese patients with BMI ≥ 25 kg/m^2. BMI was calculated using weight and height measurements at the first appointment, and the formula used was weight (kg) divided by height (m) squared (5).

All patients underwent an initial comprehensive thyroid and neck ultrasound examination by an experienced endocrinologist. A GE Logiq E9 ultrasound system was used with an ML6-15 probe. Data regarding the size and the number of nodules in each patient were collected. A thyroid nodule was considered any discrete lesion compared to the surrounding normal thyroid gland parenchyma measuring a minimum of 0.2 cm. The sonographic patterns were classified based on the US features of the thyroid nodules, estimating the risk of malignancy according to 2015 ATA guidelines (15). One hundred seventy-one nodules underwent US-guided FNA. The cytological diagnosis was categorized based on the Royal College of Pathologists' reporting (16).

This study was approved by the Cyprus National Bioethics Committee (ΕΕΒΚ ΕΠ 2022.01.89). Data collection and analysis were anonymous, using codes for patients as a reference.

Statistical analysis

The following parameters were examined regarding the impact and association between BMI and thyroid nodules: the number of nodules, size of nodules and FNA cytology results. The data collected are presented as mean and SD for numerical variables. Categorical variables are presented with absolute values and percentages. To compare the values of a continuous variable between two independent groups, we performed an independent samples *t*-test. The Pearson chi-square test was used to compare categorical variables with multiple possible outcomes: gender, FNA results and the number of patients with solitary nodules. Differences in FNA cytology between group 1 and group 2 were further evaluated using multivariable analysis with multiple ordinal logistic regression, adjusting for gender and age. A two-sided P value <0.05 was considered statistically significant. The data were entered into an Excel worksheet, and the statistical analysis was done with the R software package (https://www.r-project.org/).

Results

Table 1 demonstrates the demographic and clinicopathological characteristics of the 310 patients with thyroid nodules according to BMI. The mean age in group 1 (BMI < 25) was 41.9 years ± 14.3, ranging from 18 to 86 years, whereas in group 2 (BMI ≥ 25), the mean age was 51.2 ± 12.6, ranging from 20 to 80 ($P < 0.01$). There were more male patients in group 2 than in group 1. The two groups had no statistically significant difference in TSH levels.

In group 1, 37 patients (29.37%) had a solitary nodule and 89 (70.63%) had multiple nodules. In group 2, 144 patients (78.26%) had multiple nodules and 40 (21.74%) had a solitary nodule. The mean number of nodules in group 1 was 3.66 ± 1.93, and it was 4.25 ± 2.42 in group 2 (P value = 0.05). There was no statistically significant difference in the maximal nodule diameter between the two groups. In group 1, 64 (50.79%) patients had very low to low suspicion nodules, 39 (30.95%) had intermediate suspicion, and 23 (18.25%) patients had high suspicion of malignancy. In group 2, 78 (42.39%) patients had low suspicion, 66 (35.87%) had intermediate suspicion nodules and 40 (21.74%) had high suspicion sonographic patterns.

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Table 1 Clinicopathological characteristics according to BMI. Continuous variables are expressed as mean ± SD, and categorical variables are expressed as *n* (%).

	Group 1: BMI < 25	Group 2: BMI ≥ 25	*P* value
n	126	184	
Gender			
Male	16 (12.70%)	81 (44.02%)	<0.01†
Female	110 (87.30%)	103 (55.98%)	
Age (years)	41.9 ± 14.3	51.2 ± 12.6	<0.01*
TSH (mU/L)	1.58 ± 0.93	1.69 ± 1.12	0.41*
Solitary nodule	37 (29.36%)	40 (21.74%)	0.16†
Multiple nodules	89 (70.36%)	144 (78.261%)	
Number of nodules	3.66 ± 1.93	4.25 ± 2.42	0.05*
Maximal nodule diameter (cm)	1.49 ± 1.12	1.47 ± 1.00	0.86*
2015 ATA			
Very low–low suspicion	64 (50.79%)	78 (42.39%)	0.35†
Intermediate suspicion	39 (30.95%)	66 (35.869%)	
High suspicion	23 (18.25%)	40 (21.739%)	

*Independent samples *t*-test; †Pearson's chi-square.
BMI, body mass index; TSH, thyroid-stimulating hormone.

Table 2 demonstrates the clinicopathological and cytological characteristics of the 171 nodules that underwent US-guided FNA. The mean age in group 1 was 43.82 ± 12.28, whereas in group 2, it was 49.93 ± 12.20 ($P < 0.01$). There were more male patients

Table 2 Clinicopathological characteristics and cytological results according to BMI. Categorical variables are expressed as *n* (%), and continuous variables are expressed as mean ± SD.

	Group 1: BMI < 25	Group 2: BMI ≥ 25	*P* value
n	61	110	
Gender			
Male	8 (13.11%)	47 (42.73%)	<0.01*
Female	53 (86.89%)	63 (57.27%)	
Age (years)	43.82 ± 12.28	49.93 ± 12.20	<0.01†
TSH (mU/L)	1.38 ± 0.69	1.66 ± 1.17	0.09†
Solitary nodule	11 (18.03%)	17 (15.45%)	0.83*
Multiple nodules	50 (81.97%)	93 (84.55%)	
Number of nodules	3.34 ± 2.17	3.94 ± 2.62	0.14†
Maximal nodule diameter (cm)	1.86 ± 1.15	1.77 ± 1.05	0.59†
2015 ATA			
Very low–low suspicion	16 (26.23%)	31 (28.18%)	0.96*
Intermediate suspicion	26 (42.62%)	46 (41.82%)	
High suspicion	19 (31.15%)	33 (30%)	
FNA results			
Thy2	55 (90.16%)	86 (78.18%)	
Thy3	5 (8.19%)	9 (8.18%)	
Thy4–Thy5	1 (1.63%)	15 (13.64%)	0.040*; 0.029‡

*Pearson's chi-square; *independent samples *t*-test; ‡multiple ordinal logistic regression adjusting for gender and age.
BMI, body mass index; FNA, fine-needle aspiration; TSH, thyroid-stimulating hormone.

in group 2 than in group 1. There were no statistically significant differences in TSH levels, the number of nodules, maximal nodule diameter or 2015 ATA sonographic patterns. In group 1, 55 nodules (90.16%) had Thy2 cytology, 5 (5.16%) nodules had Thy3 cytology, and one patient had Thy5 cytology (1.63%). In group 2, 86 nodules (78.18%) had Thy2 cytology, nine nodules (8.18%) had Thy3 cytology, and 15 nodules (13.645%) had Thy4–Thy5 cytology. A statistically significant difference was observed between the two groups in the FNA category Thy4–Thy5 ($P = 0.04$, Pearson's chi-square test). This difference remained statistically significant after adjusting for gender and age using an ordinal logistic regression model ($P = 0.029$).

Discussion

In this study, we evaluated data from 310 patients to investigate the possible association between obesity and thyroid nodules. Our results showed that overweight and obese individuals (BMI ≥ 25 kg/m^2) had a trend for more thyroid nodules compared to individuals with normal BMI. In addition, patients with BMI ≥ 25 kg/m^2 had worse FNA outcomes than patients with BMI < 25 kg/m^2, suggesting a positive correlation between obesity and the risk of developing thyroid malignancy.

Multiple studies suggest a relationship between a higher BMI and thyroid nodules (9, 17, 18, 19). A recent large-scale study by Xu *et al.* found that BMI was correlated with a higher risk of thyroid nodules and that overweight and individuals with higher central obesity were found to have a significantly higher prevalence of multiple nodules compared with solitary thyroid nodules (20). Hu *et al.* associated thyroid nodules with higher BMI and other components of the metabolic syndrome, such as insulin resistance; also, the prevalence of thyroid nodules increased with age and was significantly higher in women (21). Moon *et al.* unveiled a link between BMI and the occurrence of thyroid nodules, specifically in women (22). Song *et al.* had shown that women with a BMI of 25 or more had an elevated risk of thyroid nodules (23). Kim *et al.* showed the relationship between BMI and thyroid nodules in Korean women (24).

In our study, there were more patients with intermediate and high suspicion sonographic pattern nodules in the overweight and obese group compared to patients with normal weight; however, this was not statistically significant. Lai *et al.* found that a higher BMI exhibited an augmented risk of thyroid nodules with highly suspicious sonographic patterns (19). An association between obesity and a taller-than-wide nodule was also suggested in women (12). In another study, severely obese individuals presented with increased hypoechogenicity and more frequency of thyroid nodules during ultrasound evaluation, but no significant difference was seen in the 2015 ATA and TI-RADS criteria (10).

In addition, Zhao *et al.* found that overweight and obese individuals were at greater risk of multifocality than non-overweight individuals (25).

In our study, overweight and obese patients had more suspicious and malignant cytology. Our results agree with Zhao *et al.* who found a correlation between obesity and thyroid cancer, where the prevalence of obese patients was higher in the malignant population examined. However, Rotondi *et al.* and Ahmadi *et al.* found no association between obesity and differentiated thyroid carcinoma (7, 26).

There are several mechanisms that can explain the association between obesity, thyroid nodules and cancer (27). Obesity is a chronic, low-grade inflammatory disease characterized by increased systemic inflammatory markers with a nonspecific immune response. These inflammatory factors act as signal mediators in peritumoral tissue and the progression of tumor growth. The increase in adipose tissue leads to a rise in leptin synthesis, and this increase in chronic inflammation state augments the secretion of TNF and cytokine IL-6 which contribute to cancer development, progression and metastasis by decreasing tumor suppressor genes and increasing oncogene expression (7, 28, 29, 30).

Obesity and metabolic syndrome trigger the development of thyroid nodules by stimulating thyroid proliferation and angiogenesis due to hyperinsulinemia, hyperglycemia and dyslipidemia. Liu and coworkers suggested that insulin resistance is related to the distribution and structure of thyroid blood vessels, which may promote thyroid nodule generation. Furthermore, insulin and insulin growth factor-1 (IGF-1) regulate the expression of thyroid genes and the proliferation and differentiation of thyroid cells. Thyroid cells may synthesize IGF-1 and express the IGF-1 receptor, with the expression levels being higher in the thyroid cells of the nodules than in non-nodular thyroid cells. It was also observed that thyroid nodules decreased in volume after metformin administration (10, 23, 28, 31).

Our study's main limitation is its single-center retrospective design. Another limitation is that BMI was used to evaluate obesity, which is a good measurement of body fat but a weak indicator of adiposity distribution. In addition, the study did not include other parameters of the metabolic syndrome or examine other confounding factors, such as the duration of the obesity and other environmental differences. Moreover, in our study, there were more males in the overweight and obese group and they were also older compared to the normal weight group. The prevalence of thyroid nodules appears to increase with age (21), and gender can affect both the prevalence and the suspicious features of thyroid nodules (19).

In conclusion, our study demonstrated that patients with a higher BMI have a trend for more thyroid nodules and worse FNA outcomes. Further studies are required to clarify the mechanisms behind the observed association between obesity and thyroid nodules. There is also a need for further investigation of this association to uncover the potential ties between obesity, thyroid nodules and thyroid cancer. Future research should focus on the impact of weight loss on thyroid cancer among obese and overweight individuals, deepen our understanding of the disease and aim to create more efficient preventative and therapeutic strategies. Obesity is a modifiable risk factor and can become a crucial focus for public health initiatives aimed at reducing the occurrence of thyroid cancer and thyroid nodule development (32).

Declaration of interest

The authors declare that they have no competing interests regarding the publication of this work.

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Data availability

The data supporting the findings of this study are available on request from the corresponding author.

Author contribution statement

ED, AE and PE were involved in the conception, design and writing of the study, in the collection and interpretation of the data and in the drafting the manuscript. MF was involved in the process of the collection, analysis and interpretation of the data. DL was involved in the conception and design of the study, in the statistical analysis and in the drafting of the manuscript. SP was involved in the conception and design of the study and in the interpretation of the data. PP was involved in the conception of the study, in the analysis of the data and in the drafting of the paper. All authors have critically reviewed and approved the final version of the manuscript.

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