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ORIGINAL RESEARCH

Analysis of Body Mass Index and Clinicopathological Factors in Patients with Papillary Thyroid Carcinoma

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Objective: To analyze the correlation between body mass index (BMI) and clinicopathological factors of papillary thyroid cancer (PTC).

Methods: The clinical data of patients with PCT who were hospitalized in the Department of Thyroid Surgery of the Affiliated Hospital of Guizhou Medical University from March 2023 to September 2023 were retrospectively collected, including age, gender, height, weight, BMI, v-raf murine sarcoma viral oncogene homolog B (*BRAF*) gene mutation, tumor size, multifocus, Hashimoto's thyroiditis, lymph node metastasis and other clinicopathological factors. According to the World Health Organization (WHO) definition for Asian population, BMI≥25kg/m^2 was obese group, 23≤BMI≤24.9kg/m^2 was overweight group, 18.5≤BMI≤22.9kg/m^2 was normal weight group, and BMI≤18.5kg/m^2 was low weight group. The clinicopathological factors of overweight and obese patients with PTC were analyzed.

Results: A total of 164 PTC patients were included, with an average BMI of (24.44±3.57) kg/m^2. Age of overweight and obese PTC patients (Z=1.978, p=0.083); Gender of overweight and obese PTC patients (χ^2 value: 11.570, p=0.004); Tumor size in overweight and obese PTC patients (Z=0.894, p=0.411); *BRAF* gene mutation in overweight and obese PTC patients (χ^2 value: 1.452, p =0.623); Multifocal lesions were found in overweight and obese patients (χ^2 value: 1.653, p =0.201). Hashimoto's thyroiditis was found in overweight and obese PTC patients (χ^2 value: 1.147, p=0.298). Overweight and obese patients with PTC had lymph node metastasis (χ^2 value: 1.690, p =0.251).

Conclusion: Overweight and obesity in PTC patients are correlated with male, but not with age, tumor size, *BRAF* mutation, multifocality, Hashimoto's thyroiditis and lymph node metastasis.

Keywords: papillary thyroid carcinoma, body mass index, clinicopathological factors, correlation analysis

Introduction

The incidence of differentiated types thyroid Cancer (TC) has been increasing over the past few decades.[1,2] In addition to more widespread screening for thyroid nodules and more sensitive examination methods, the increasing incidence of thyroid cancer may also be related to environmental factors, lifestyle, dietary and nutritional habits, and the increased prevalence of individual risk factors such as obesity.[3,4]

Obesity has gradually become an important factor affecting health worldwide.[5,6] It is a risk factor for metabolic and cardiovascular diseases, and it is also gradually recognized as a risk factor for the increasing incidence of some malignant tumors.[7,8] The incidence of TC and the prevalence of obesity are both increasing, and the two are "synchronizing the epidemic". In some studies, overweight and obesity have been considered as risk factors for TC and are associated with TC through a variety of mechanisms.[9,10] However, there are still few studies on the clinical characteristics of overweight and obese PTC patients, and the conclusions are inconsistent. The purpose of this study was to evaluate the changes in weight among patients with papillary thyroid cancer (PTC) and to explore the relationship between these changes and various clinical pathological factors.

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Materials and Methods

Study Subjects

The clinical data of patients with PCT who were hospitalized in the Department of Thyroid Surgery, the Affiliated Hospital of Guizhou Medical University from March 2023 to September 2023 were retrospectively collected. Inclusion criteria: (1) All patients had complete data. (2) All patients only had PTC. (3) All patients >18 years old. Exclusion criteria: (1) Patients with other types of TC or other malignant tumors. (2) Patients were unconscious. (3) Without patient permission. (4) Patient has chronic disease. (5) Some patients have pre-existing conditions such as being overweight or obese since adolescence. (6) Some patients account for factors such as poor compliance with levothyroxine or improper medication use lead to high TSH levels and subsequent increase in BMI. The study was performed with the approval of the hospital ethics committee. All patients were informed and written informed consent was obtained.

Data Collection

The general information of the patients (including age, gender, height, weight, BMI,[11] v-raf murine sarcoma viral oncogene homolog B (*BRAF)* gene mutation, tumor size, multifocality, Hashimoto's thyroiditis, lymph node metastasis and other clinicopathological factors was collected. We defined BMI ≤ 18.5 kg/m^2 as underweight, between 18.5 and 22.9 kg/m^2 as normal weight, between 23 and 24.9 kg/m^2 as overweight and BMI >25 kg/m^2 as obese.

Evaluation Methods

① Using height and weight data, the body mass index (BMI) of each patient was calculated. The formula for calculating BMI is weight (in kilograms) divided by the square of height (in meters). ② *BRAF* Gene Mutation: PCR (Polymerase Chain Reaction) or other molecular biology techniques, such as sequencing or primer extension, were used to detect gene mutations in thyroid cancer tissue samples. The results of the detection were qualitatively or quantitatively analyzed to determine whether the *BRAF* gene was mutated, and the type of mutation was recorded. ③ Tumor Size: Imaging examinations (such as ultrasound, CT scans, or MRI) or surgical specimens were used to measure the maximum diameter or volume of thyroid cancer tumors. The measurement results were accurately recorded, usually in cubic centimeters (cm). ④ Multifocality: Imaging techniques such as ultrasound, CT scans, or MRI were used to examine the thyroid gland to determine whether multiple tumors were present. During surgery, an examination of the excised thyroid tissue determined whether multiple primary tumors were present. ⑤ Hashimoto's Thyroiditis: Diagnosis of Hashimoto's thyroiditis was based on the patient's clinical symptoms, thyroid function tests, and imaging characteristics. Histopathological examination of thyroid tissue biopsy or surgical specimens confirmed the histological inflammatory changes. ⑥Lymph Node Metastasis: Ultrasound, CT scans, MRI, and other imaging techniques were used to examine whether there was metastasis to the neck lymph nodes. During thyroid surgery, an anatomical examination of the neck lymph nodes determined whether lymph node metastasis was present. In data analysis, potential biases such as selection bias and information bias were considered, and corresponding measures were taken to minimize their impact on the results. Evaluation was conducted by two experienced physicians, and in case of assessment bias, a decision was made by a third senior attending physician.

Statistical Analysis

SPSS 22.0 statistical software was used to compare the clinicopathological factors of the two groups. The quantitative data conforming to normal distribution were analyzed by *t*-test analysis, and the quantitative data not conforming to normal distribution were analyzed by Wilcoxon rank sum test. Qualitative data were analyzed using the 2 test analysis. The confidence interval was calculated with 95% CI. Among them, age and tumor size were non-normal quantitative treatments, and Wilcoxon rank sum test was used.

Results

Demographic Parameters

A total of 164 patients were enrolled, with an average age of (41.7±10.5) years and an average BMI of (24.44±3.57) kg/m^2, including 5 patients with BMI<18.5kg/m^2 (3.0%), 73 patients 18.5≤BMI<22.9kg/m^2 (44.5%), 16 patients 23≤BMI<24.9kg/

m^2 (9.8%) and 70 patients BMI≥25kg/m^2 (42.7%). There were 129 (78.7%) females and 35 (21.3%) males. *BRAF* mutation was detected in 121 (73.8%) cases and wild type in 43 (26.2%) cases. The mean tumor size was (0.7±0.4) cm. 55 cases (33.5%) had multiple tumors and 109 cases (66.5%) had single tumors. 32 cases (19.5%) were complicated with Hashimoto's thyroiditis and 132 cases (80.5%) were not complicated. There were 55 cases (33.5%) with lymph node metastasis and 109 cases (66.5%) without lymph node metastasis. (See Table 1)

BMI-Based Analysis of Clinicopathological Factors Between Overweight and Obesity Group and Normal Weight and Weight Loss Group

A total of 164 patients were divided into overweight and obesity group and normal and reduced group. The clinico-pathological factors of the two groups were analyzed, including age, gender, tumor size, tumor multifocality, *BRAF* gene mutation, Hashimoto's thyroiditis and lymph node metastasis. The age of overweight and obese PTC patients (Z=1.978, p=0.083). Gender of overweight and obese PTC patients (χ^2 value: 11.570, p=0.004). Tumor size in overweight and obese PTC patients (Z=0.894, p=0.411). *BRAF* gene mutation in overweight and obese PTC patients (χ^2 value: 1.452, p =0.623). Multifocal lesions were found in overweight and obese patients (χ^2 value: 1.653, p =0.201). Hashimoto's thyroiditis was found in overweight and obese PTC patients (χ^2 value: 1.147, p=0.298). Overweight and obese PTC patients had lymph node metastasis (χ^2 value: 1.690, p =0.251), as shown in Table 2. The results showed that overweight and obesity in PTC patients were correlated with male, but not with age, tumor size, *BRAF* gene mutation, multifocality, Hashimoto's thyroiditis and lymph node metastasis.

Discussion

It has been reported that obesity is associated with a higher risk of TC in men, with the highest risk in obese men (HR =1.58, 95% CI =1.52–1.64), but not in women.[12] In the present study, overweight and obesity were also associated with male PTC patients (χ^2 value: 11.570, p=0.004). However, a meta-analysis of obesity and TC showed a different view.

Table 1 General Conditions of 164 Patients

General Conditions	Proportion/Average
BMI	(24.44±3.57) kg/ m^2
BMI < 18.5 kg/ m^2	5 (3.0%)
18.5 ≤ BMI ≤ 22.9 kg/ m^2	73 (44.5%)
23≤BMI≤ 24.9kg/m^2	16 (9.8%)
BMI≥25kg/m^2	70 (42.7%)
Age	(41.7±10.5) years
Gender	
Male	35 (21.3%)
Females	129 (78.7%)
BRAF gene mutation	
Mutations	121 (73.8%)
Wild type	43 (26.2%)
Tumor size	(0.7±0.4) cm
Whether multifocal	
Multifocal	55 (33.5%)
Single focus	109 (66.5%)
Hashimoto's thyroiditis or not	
Merge	32 (19.5%)
Not combined	132 (80.5%)
Lymph node metastasis or not	
Metastasis	55 (33.5%)
No metastasis	109 (66.5%)

Abbreviation: BMI, body mass index.

Table 2 Analysis of Clinicopathological Factors in Overweight and Obesity Group and Normal Weight and Weight Loss Group

Factors	BMI		$x^{2/}Z$ score	*p* value
	≥23kg/m²	< 23kg/m²		
Age	41.6±8.75	38.8±-11.31	1.978	0.083
Gender				
Male	24	11	11.570	0.004
Female	62	67		
Tumor size	0.7 ±0.2	0.7 ± 0.3	0.894	0.411
Whether multifocal				
Single focus	52	57	1.653	0.201
Multiple foci	34	21		
BRAF gene				
Mutations	60	61	1.452	0.623
Wild type	26	17		
Combined Hashimoto's thyroiditis				
Merge	17	15	1.147	0.298
Do not merge	69	63		
Lymph node metastasis				
Metastasis	34	21	1.690	0.251
Not transferred	52	57		

Abbreviation: BMI, body mass index.

Obesity was associated with a higher risk of TC in women (RR = 1.29, 95% CI = 1.14–1.46, $p < 0.001$), but not in men (RR = 1.25, 95% CI = 0.97–1.62, P = 0.001). $p = 0.08$). In addition, weight gain increased the risk of TC (RR = 1.18, 95% CI = 1.14–1.22, $p < 0.001$), while weight loss decreased the risk (RR = 0.89, 95% CI = 0.85–0.93, $p < 0.001$). In addition, it is suggested that BMI control strategies will help to reduce the risk of TC.[13] Other studies have found that obesity is related to tumor size and multifocality of TC, and the risk of TC in obese men is higher than that in obese women. However, obesity did not increase the risk of capsular invasion or tumor stage in male patients. However, the results of the current study were not identical.[14] In the present study, overweight and obese PTC patients had tumor size (Z=0.894, p =0.411), *BRAF* gene mutation (χ^2 value: 1.452, p=0.623), multifocality (χ^2 value: 1.653, p=0.201), and lymph node metastasis (χ^2 value: 1.690, p=0.251). There are still few studies on the clinical characteristics of overweight and obese PTC patients, and the conclusions are inconsistent. Larger randomized controlled trials may be needed to produce more convincing evidence in the future.

Does current obesity affect treatment strategies for patients with TC? It has been found that obese patients exhibit parenchymal hypoechogenicity and an increased frequency of thyroid nodules on ultrasound assessment. However, no significant difference in the risk of nodular malignancy was observed between obese and non-obese patients, although the incidence of thyroid nodules was higher in obese patients according to the American Thyroid Association 2015 guidelines and thyroid TI-RADS classification criteria. Therefore, there is no need for more frequent thyroid ultrasound screening in obese patients.[15] A study on obesity and TC in the United States also believes that although obesity is related to TC, obesity should not be considered as a risk factor for TC screening, and patients with thyroid nodules should not be screened because of obesity.[16] A study of obesity and Differentiated thyroid carcinoma (DTC) in Caucasians also found that there was no correlation between BMI and DTC aggressiveness either at the time of TC diagnosis or at the time of follow-up. Treatment strategies and follow-up of obese DTC patients with postoperative evaluation should be equivalent to those of the general population.[17] In a retrospective analysis with a mean follow-up of 3.4 years, obesity and DTC histopathological features, risk of recurrence, and iodine-131 therapy showed no additive effect of obesity on DTC aggressiveness or response to treatment. Obese patients with TC can be treated according to current guidelines without special measures.[18] However, in a Chinese study on obesity and TC, it was found that central obesity was still associated with a significantly increased risk of malignant thyroid nodules, and closer clinical observation is needed. It is suggested that waist circumference may be superior to BMI in evaluating the risk of thyroid nodule malignancy in Chinese population.[19] In a study of childhood obesity and TC, it was also found that obese children had a significantly increased risk of single and multiple thyroid nodules. It is also suggested that waist circumference measurement can be used to assess the degree of obesity in children.[20] Another study of the Fat Mass and Obesity Associated (FTO) gene and TC showed that Individuals carrying dominant rs17817288, rs9937053, rs12149832, rs1861867, rs7195539 and recessive rs8044769 FTO have an increased risk of TC malignancy, and more close clinical follow-up is needed.[21] In general, obesity does not affect the treatment strategy of TC patients, but many studies have suggested that obese TC patients should be more active clinical observation.

Is obesity associated with the risk of TC recurrence? Some studies have suggested that obesity increases the risk of TC only in papillary, follicular and anaplastic TC, while the risk of medullary thyroid cancer is decreased in obese patients, indicating that the effect of obesity on TC may be dependent on TC type and histological specificity.[22] In a study of obesity and PTC, it was found that the risk of minimal extrathyroidal extension (minimal ETE), multifocal, and bilateral PTC was higher in obese patients. Obesity is significantly associated with aggressiveness of PTC. Obesity should be considered as a risk factor for poor prognosis in the development of treatment options for PTC patients.[23] However, some studies have suggested that although obesity is related to the pathological factors of poor prognosis. However, they may not be associated with the risk of tumor recurrence in PTC.[24] The retrospective study by Zhao et al[25] analyzed the effect of high BMI on the prevalence and clinicopathological parameters of PTC. Obesity was associated with a high risk of TC. Obesity was an independent predictor of tumor size larger than 1 cm (OR = 1.562, P <0.001) and multifocus (OR = 1.616, P <0.001). However, there was no statistical significance between obesity and cervical lymph node metastasis. Cui et al[26] reported that obesity was associated with several unfavorable clinicopathological prognostic features, including older age, male sex, tumor size ≥1 cm, extrathyroidal extension, and multifocus. However, obesity was not associated with thyrotropin (TSH) level, vascular invasion, lymph node metastasis, distant metastasis, or recurrence. O'Neill et al[27] reported that obesity was associated with tumor size, multifocus, extrathyroidal extension invasion and lymph node metastasis, and the correlation was more obvious with the increase of BMI, but obesity was not associated with vascular invasion or patient prognosis. Feng et al[28] suggested that obesity was associated with extra-thyroidal invasion and vascular invasion in PTC patients. Although this study found that obesity was related to the aggressive clinicopathological characteristics of PTC, this study still suggested that obesity was not related to the risk of postoperative complications and local recurrence. However, Li et al[29] suggested that obesity was associated with lymph node metastasis and worse prognosis in PTC. Gąsior-Perczak et al[30] suggested that obesity was neither associated with the more aggressive clinicopathological features of TC, nor a risk factor for disease progression to more advanced stages, nor a prognostic factor for poor treatment response and clinical outcome. The study of Cao et al[31] on obesity and TC iodine-131 therapy suggested that although obesity may have an additive effect on the aggressiveness of PTC, there was no difference in the treatment response to iodine-131 therapy between obese patients and normal weight patients. In general, although many studies have found that obesity is related to the adverse pathological factors of TC, they do not believe that obesity is related to the risk of TC recurrence, and some studies have different opinions and are controversial.

However, limitations remain in this study. Firstly, it is a single-center study; however, future research will expand to include more cases and conduct a multi-center study to enhance the validity of the findings. Since this study is retrospective, this data cannot be collected such as (circumference and Body Fat (%)). In future studies, we will include more relevant indicators. Secondly, the follow-up period for patients was short, but extending the follow-up duration will allow for a more comprehensive observation of the impact of obesity and overweight on PTC patients. Finally, the potential correlation between BMI and post-surgery early complications and hospitalization might be a further study expansion.

Conclusion

In conclusion. The results obtained in this study may be independent of obesity and clinicopathological factors of TC, and may not affect the treatment strategy of TC patients.

Data Sharing Statement

All data generated or analyzed during this study are included in this published article.

Ethics Approval and Consent to Participate

This study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of Affiliated Hospital of Guizhou Medical University.

Written informed consent was obtained from the participant.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests in this work.

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