Original Article

Correlation between body mass index and lymph node metastasis in papillary thyroid carcinoma: a retrospective clinical study

Haoran Ding[1,2#], Fazhan Xu[1,2#], Wenxian Guan[1,2], Jianfeng Sang[1,2]

[1]Division of Thyroid Surgery, Department of General Surgery, Nanjing Drum Tower Hospital Clinical College of Nanjing Medical University, Nanjing, China; [2]Division of Thyroid Surgery, Department of General Surgery, Nanjing Drum Tower Hospital, the Affiliated Hospital of Medical School, Nanjing University, Nanjing, China

Contributions: (I) Conception and design: H Ding, F Xu, J Sang; (II) Administrative support: J Sang, W Guan; (III) Provision of study materials or patients: All authors; (IV) Collection and assembly of data: H Ding, F Xu; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Jianfeng Sang, MD. Division of Thyroid Surgery, Department of General Surgery, Nanjing Drum Tower Hospital Clinical College of Nanjing Medical University, 321 Zhongshan Road, Nanjing 210008, China; Division of Thyroid Surgery, Department of General Surgery, Nanjing Drum Tower Hospital, the Affiliated Hospital of Medical School, Nanjing University, Nanjing, China. Email: drsangjianfeng@163.com; Wenxian Guan, MD. Division of Thyroid Surgery, Department of General Surgery, Nanjing Drum Tower Hospital Clinical College of Nanjing Medical University, 321 Zhongshan Road, Nanjing 210008, China; Division of Thyroid Surgery, Department of General Surgery, Nanjing Drum Tower Hospital, the Affiliated Hospital of Medical School, Nanjing University, Nanjing, China. Email: guan_wenxian@sina.com.

Background: Papillary thyroid carcinoma (PTC) is the most common malignant tumor of the thyroid gland, with lymph node metastasis significantly affecting patient prognosis. In recent years, body mass index (BMI) has garnered widespread attention as a potential factor influencing cancer development. This study aimed to explore the relationship between BMI and lymph node metastasis in patients with PTC, particularly focusing on the risk of metastasis in the lateral and central neck compartments.

Methods: This retrospective study comprised 993 patients who underwent surgical treatment and were pathologically confirmed to have PTC. Patient BMI data were collected, and their relationship with lymph node metastasis in the lateral and central neck compartments was analyzed. Logistic regression models were employed to analyze the correlation between BMI and lymph node metastasis.

Results: The study found a significant correlation between BMI and the risk of lateral neck lymph node metastasis in patients (P=0.008), along with a corresponding increase in extrathyroidal extension risk (P=0.02). While elevated BMI did not directly increase the risk of central compartment metastasis, a significant increase was observed in the number of central compartment lymph node metastases (P=0.009) and their proportion among the total central compartment lymph nodes (P=0.01) in patients with higher BMI. Additionally, multifocality, age, and gender were identified as risk factors for lateral neck lymph node metastasis, whereas Hashimoto's thyroiditis did not exhibit a similar impact.

Conclusions: This study highlights that higher BMI is an important risk factor for lateral neck lymph node metastasis in patients with PTC and may exacerbate the severity of central compartment lymph node metastasis. These findings underscore the importance of considering BMI in the management of thyroid cancer and provide data support for future prevention and intervention strategies.

Keywords: Body mass index (BMI); papillary thyroid carcinoma (PTC); lymph node metastasis; extrathyroidal invasion; central lymph node

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Introduction

Background

Papillary thyroid carcinoma (PTC) constitutes the most prevalent type of thyroid cancer, accounting for approximately 80–85% of all cases. Epidemiological features of this disease indicate a significantly higher incidence among females compared to males, with a steady rise observed in recent decades, particularly in developed nations (1-4). While the prognosis for most PTC cases is favorable, aggressive forms such as lymph node metastasis and extrathyroidal extension substantially impact long-term survival rates and quality of life, underscoring the clinical importance of early detection and effective management (5-7).

Rationale and knowledge gap

As a critical indicator of public health, body mass index (BMI) has been widely utilized over the past decades to assess individuals' nutritional and health status. Elevated BMI is considered an independent risk factor for various chronic diseases, including cardiovascular diseases, diabetes, and several types of cancers (8-10). In the realm of thyroid cancer research, although data remain inconsistent, some epidemiological studies suggest a potential association between high BMI and increased incidence of thyroid cancer. Elevated BMI has been linked to the occurrence and progression of PTC (11-14). However, there are also reports suggesting no correlation between BMI and the progression of PTC (15-17). These studies often fail to adequately explore the relationship between BMI and specific patterns of lymph node metastasis in PTC patients, such as those involving the lateral and central neck compartments.

Objective

Against this backdrop, this study aims to explore the relationship between BMI and lymph node metastasis in the lateral and central neck compartments of patients with PTC. By delving into this specific clinical manifestation, this research not only seeks to address knowledge gaps but also intends to provide data support for the prevention and personalized treatment strategies of PTC, particularly within the context of considering patient weight management as a potential intervention. We present this article in accordance with the STROBE reporting checklist (available at https://gs.amegroups.com/article/view/10.21037/gs-24-164/rc).

Highlight box

Key findings

- Our study reveals that higher body mass index (BMI) is associated with increased risk of lateral cervical lymph node metastasis and extrathyroidal invasion in papillary thyroid carcinoma (PTC).

What is known and what is new?

- It is established that obesity affects cancer progression, but the specific impact on lymph node distribution in PTC has been less clear.
- Our study identifies high BMI as a distinct risk factor for increased lateral and central lymph node involvement in PTC, providing new insights into the anatomical specificity of obesity-related metastatic patterns.

What is the implication, and what should change now?

- These findings suggest the necessity for more nuanced preoperative evaluations and potentially more extensive surgical approaches for higher BMI patients to address the elevated metastatic risk.

Methods

Study design

This retrospective cohort study aims to investigate the relationship between BMI and lymph node metastasis in patients with PTC. We retrospectively collected clinical and pathological data from 1,067 consecutive inpatients who underwent thyroid surgery for PTC at Nanjing Drum Tower Hospital from June 2022 to December 2023. Seventy-four patients were excluded based on exclusion criteria, leaving 993 patients for retrospective analysis of clinical data. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the ethics committee of Nanjing Drum Tower Hospital (No. 2023-345-01) and individual consent for this retrospective analysis was waived. We collected basic patient information, including age, gender, BMI, preoperative thyroid function, preoperative parathyroid hormone levels, and presence of Hashimoto's thyroiditis. Our interest lay in exploring the biological behavior of BMI and PTC, as well as lymph node metastasis. Thus, we gathered pathological data from these patients. These data encompass multifocality, extrathyroidal extension, central compartment lymph node metastasis, and lateral compartment lymph node metastasis status. The 993

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patients were classified into four groups based on BMI: underweight (BMI <18.5 kg/m^2), normal (18.5 kg/m^2 ≤ BMI <24 kg/m^2), overweight (24 kg/m^2 ≤ BMI <28 kg/m^2), and obese (BMI ≥28 kg/m^2). There were 35 underweight patients, 450 normal-weight patients, 353 overweight patients, and 155 obese patients. Histological diagnosis confirmed PTC in all cases. Through systematic review of historical case data, the study analyzed patients' clinical and pathological characteristics along with their BMI-related metastatic risks.

Study subjects

Participants comprised patients diagnosed with and treated for PTC at the aforementioned hospital during the specified period.

Inclusion criteria

(I) Pathological diagnosis of PTC;
(II) Availability of complete clinical and pathological data, including BMI records.

Exclusion criteria

(I) Cases with other types of thyroid cancer or concurrent major malignancies;
(II) Patients with incomplete preoperative or postoperative treatment data;
(III) Patients who underwent thyroid surgery prior to or during the study period.

Data collection

Collected data included patients' basic information (age, gender, BMI, etc.) and clinical pathological features (such as tumor size, tumor grade, multifocality, and lymph node metastasis in the lateral and central neck compartments). Two researchers independently extracted and cross-checked all data to ensure accuracy and completeness.

Statistical analysis

Data analysis was conducted using SPSS statistical software (version 26.0). Initially, descriptive statistics were employed to summarize the basic characteristics of the sample (e.g., mean and standard deviation for continuous variables, frequency for categorical variables). Group comparisons were performed using the chi-squared test for categorical variables and *t*-test or analysis of variance (ANOVA) for continuous variables. Furthermore, logistic regression analysis was employed to evaluate the relationship between BMI and the risk of lymph node metastasis in the lateral and central neck compartments. The significance level for all statistical tests was set at a P value less than 0.05.

Results

Baseline characteristics

Table 1 summarized the key features of the study population. Our results indicated a significant gender disparity among obese patients (P=0.001), with a notable increase in the proportion of males. Moreover, the proportion of Hashimoto's thyroiditis decreased among obese patients (P=0.01). BMI changes were associated with alterations in thyroid stimulating hormone (TSH) levels (P=0.02), suggesting that both excessive and insufficient weight affect TSH. Interestingly, levels of thyroglobulin (TG) and TG antibody (Tg-Ab) correlated with BMI, while other factors such as thyroid function tests and age did not show significant differences (*Table 1*).

Associations between BMI and clinicopathological features of PTC

We examined the influence of BMI on pathological aspects of PTC, focusing on postoperative pathology including multifocality, extrathyroidal extension, central lymph node metastasis, and lateral lymph node metastasis. Our findings indicated that multifocality (P=0.31) and central lymph node metastasis (P=0.07) were not significantly associated with BMI. However, BMI was correlated with extrathyroidal extension (P=0.02) and lateral lymph node metastasis (P=0.008) in PTC. These results demonstrate that BMI impacts extrathyroidal extension and lateral lymph node metastasis in PTC (*Table 2*). PTC typically affects central lymph nodes more commonly, with lateral lymph node metastasis often following central lymph node involvement. However, there are cases where lateral lymph node metastasis occurs without prior central lymph node involvement. Therefore, we further explored the relationship between BMI and the number and proportion of central lymph node metastases (proportion of central lymph nodes involved relative to the total number of nodes

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Table 1 Baseline characteristics of participants

Characteristics	BMI (kg/m^2)				P
	<18.5 (n=35)	≥18.5 and <24 (n=450)	≥24 and <28 (n=353)	≥28 (n=155)	
Age (years)	35.2±12.58	41.96±11.92	44.58±11.41	41.65±11.01	0.14
Sex					0.001
Male	6 (17.14)	79 (17.56)	125 (35.41)	78 (50.32)	
Female	29 (82.86)	371 (82.44)	228 (64.59)	77 (49.68)	
Thyroid function					
FT3 (pmol/L)	4.75±0.51	4.81±0.71	4.94±0.60	5.06±0.61	0.30
TT3 (nmol/L)	1.70±0.18	1.67±0.28	1.75±0.27	1.77±0.25	0.19
FT4 (pmol/L)	17.26±2.28	16.97±2.86	16.53±2.41	16.87±2.38	0.72
TT4 (nmol/L)	96.55±13.54	93.84±18.01	93.71±16.04	95.47±16.74	0.22
TG (ng/mL)	38.37±51.88	25.45±35.64	28.09±41.73	40.90±49.43	0.001
TSH (mIU/L)	2.01±1.02	2.31±0.35	2.48±1.88	2.23±1.38	0.02
Tg-Ab (IU/mL)	145.70±271.90	128.94±267.29	105.32±282.31	47.65±145.62	0.001
TPO-Ab (IU/mL)	50.97±90.67	64.48±108.65	58.15±97.44	42.73±88.99	0.09
PTH (pmol/L)	4.35±1.41	4.98±2.19	5.41±2.67	5.67±2.16	0.36
Hashimoto's thyroiditis					0.01
Yes	9 (25.71)	117 (26.00)	91 (25.78)	21 (13.55)	
No	26 (74.29)	333 (74.00)	262 (74.22)	134 (86.45)	

Data are presented as n (%) or mean ± standard deviation. BMI, body mass index; FT3, free triiodothyronine; TT3, total triiodothyronine; FT4, free thyroxine; TT4, total thyroxine; TG, thyroglobulin; TSH, thyroid stimulating hormone; Tg-Ab, thyroglobulin antibody; TPO-Ab, thyroid peroxidase antibody; PTH, parathyroid hormone.

Table 2 Comparison of results of PTC patients with different BMI groups

Characteristics	BMI (kg/m^2)				P
	<18.5 (n=35)	≥18.5 and <24 (n=450)	≥24 and <28 (n=353)	≥28 (n=155)	
Multifocal carcinoma					0.31
Yes	6 (17.14)	92 (20.44)	81 (22.95)	42 (27.10)	
No	29 (82.86)	358 (79.56)	272 (77.05)	113 (72.90)	
Extrathyroidal extension					0.02
Yes	23 (65.71)	280 (62.22)	218 (61.76)	117 (75.48)	
No	12 (34.29)	170 (37.78)	135 (38.24)	38 (24.52)	
Centra lymph node metastasis					0.07
Yes	19 (54.29)	209 (46.44)	151 (42.78)	85 (54.84)	
No	16 (45.71)	241 (53.56)	202 (57.22)	70 (45.16)	
Lateral neck lymph node metastasis					0.008
Yes	7 (20.00)	77 (17.11)	66 (18.70)	46 (29.68)	
No	28 (80.00)	373 (82.89)	287 (81.30)	109 (70.32)	

Data are presented as n (%). PTC, papillary thyroid carcinoma; BMI, body mass index.

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Table 3 Comparison of the number of lymph node metastases of PTC patients with different BMI groups

Characteristics	BMI (kg/m^2)				P
	<18.5 (n=35)	≥18.5 and <24 (n=450)	≥24 and <28 (n=353)	≥28 (n=155)	
Centra lymph node metastasis					
Number of metastatic lymph nodes	1.63±2.32	1.29±2.14	1.35±2.55	2.02±2.77	0.009
Total number of lymph nodes cleaned	5.66±4.93	5.35±4.81	5.57±5.08	5.48±4.60	0.92
The proportion of metastatic lymph nodes to total cleared lymph nodes	0.29±0.34	0.24±0.34	0.24±0.35	0.34±0.39	0.01
Lateral neck lymph node metastasis					
Number of metastatic lymph nodes	0.86±2.14	0.57±1.55	0.83±2.34	1.41±3.06	0.001

Data are presented as mean ± standard deviation. PTC, papillary thyroid carcinoma; BMI, body mass index.

Table 4 Univariate and multivariate logistic regression to identify predictors of lateral neck lymph node metastasis

Characteristics	Univariate			Multivariate		
	OR	95% CI	P	OR	95% CI	P
Sex	1.607	1.156–2.233	0.005	1.505	1.053–2.151	0.03
Age	0.972	0.959–0.986	0.001	0.970	0.956–0.984	0.001
BMI	1.318	1.082–1.606	0.006	1.261	1.024–1.553	0.03
Hashimoto's thyroiditis	1.226	0.859–1.750	0.26	1.247	0.858–1.812	0.25
Multifocal carcinoma	2.169	1.538–3.058	0.001	2.273	1.596–3.238	0.001

OR, odds ratio; CI, confidence interval; BMI, body mass index.

removed). The data revealed a correlation between high BMI and both the number of central lymph node metastases (P=0.009) and the proportion of central lymph node metastases (P=0.01), independent of the total number of central lymph nodes removed. Additionally, we investigated the relationship between BMI and the number of lateral lymph node metastases, finding a significant correlation (P=0.001) (*Table 3*).

Risk factors for lateral lymph node metastasis

Lateral lymph node metastasis commonly indicates an advanced disease progression in PTC. Therefore, we examined the risk factors associated with lateral lymph node metastasis. In univariate logistic regression analysis, BMI emerged as a risk factor for lateral lymph node metastasis. Subsequently, multivariate logistic regression confirmed BMI as an independent risk factor for lateral lymph node metastasis (P=0.03). Additionally, our findings identified gender and multifocality as other significant risk factors for lateral lymph node metastasis in PTC, whereas age appeared to exert a protective effect. Notably, Hashimoto's thyroiditis did not show an association with lateral lymph node metastasis in PTC (*Table 4*).

Discussion

Our research findings indicate that with increasing BMI, the risk of cervical lymph node metastasis and extrathyroidal extension in PTC patients also increases. These findings may be associated with a chronic low-grade inflammatory state in individuals with higher BMI (18). Inflammation is considered a key factor in tumor progression, potentially influencing tumor invasion and metastasis by promoting the expression of cytokines and chemical factors in the tumor microenvironment (19-22). For instance, adipocytes in obese patients can secrete various pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), which can enhance the invasive and survival capabilities of tumor cells (23-25). Additionally,

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insulin resistance and elevated levels of insulin-like growth factor-1 (IGF-1) are more common in obese patients, which may promote the proliferation and metastasis of tumor cells through the activation of the PI3K/Akt and MAPK signaling pathways (26-30). The specific mechanisms underlying the association between increased BMI and lymph node metastasis and extrathyroidal extension in PTC patients require further investigation.

Our study results are consistent with the majority of existing research. Previous studies have also shown a positive correlation between BMI and lymph node metastasis in thyroid cancer patients (11-14,31). However, contrary to previous research findings, we found that while increasing BMI did not directly increase the risk of central compartment lymph node metastasis, in patients with higher BMI, both the number and proportion of central compartment metastatic lymph nodes were increased. This result suggests that the impact of obesity on lymph node metastasis may not be apparent in the initial stages; however, once lymph node metastasis occurs, obesity may exacerbate its progression, leading to disease advancement. Despite providing valuable insights, there are some limitations in this study. Firstly, being a retrospective study, it may be influenced by data incompleteness and retrospective bias. Secondly, despite efforts to adjust for various potential confounding factors, there may still be unobserved confounding variables. Additionally, since this study was conducted at a single center, the generalizability of the results may be limited. Future research should consider conducting prospective multicenter studies to validate the relationship between BMI and lymph node metastasis in PTC and explore additional biomarkers and molecular mechanisms. Furthermore, studies with larger sample sizes will help improve the statistical power and representativeness of the results, thereby more accurately estimating the impact of BMI on the clinical outcomes of thyroid cancer.

Considering the global prevalence of obesity, investigating its relationship with the prognosis of thyroid cancer is of significant public health importance (32). Given the global increase in obesity rates, our study results emphasize the importance of weight control in reducing the risk of cervical lymph node metastasis in PTC patients. Therefore, in clinical practice, targeted weight management and nutritional counseling should be provided to thyroid cancer patients, especially those with higher BMI, to help them control or reduce obesity-related cancer risks. Additionally, early identification and management of potential metabolic abnormalities associated with obesity, such as insulin resistance, may play a crucial role in preventing the progression of thyroid cancer (33). Based on the findings of this study, it is recommended to incorporate BMI as one of the assessment and monitoring criteria in the clinical management of thyroid cancer. Our study revealed that patients with higher BMI face elevated risks of lateral neck lymph node metastasis and extrathyroidal extension, indicating potentially more complex surgical challenges. Therefore, comprehensive preoperative assessments are crucial to thoroughly evaluate their condition. Researchers have conducted numerous studies on tumor diagnosis, vocal cord function assessment, and tumor recurrence risk to mitigate severe complications (34-36). Incorporating the latest research findings is paramount in developing preoperative assessment plans for high-BMI patients, enabling a comprehensive evaluation and effectively reducing surgical and treatment risks. Furthermore, health policymakers should consider implementing targeted public health interventions to alleviate the burden of obesity and enhance public awareness of the link between obesity and cancer risk through education and social support networks. These strategies can not only help reduce the incidence of thyroid cancer but also potentially have preventive effects on various other obesity-related cancer types.

Conclusions

In summary, this study underscores the correlation between BMI and cervical lymph node metastasis in PTC. Through meticulous analysis of cervical and central compartment lymph node metastasis, we identified BMI as a risk factor for cervical lymph node metastasis. Despite some limitations, the findings of this study provide new insights into how obesity affects the biological behavior of thyroid cancer and provide a basis for future clinical practice and public health strategies. Future research should further explore the relationship between BMI and other clinical features of thyroid cancer and evaluate the potential value of weight loss interventions in the treatment and prognosis of thyroid cancer.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://gs.amegroups.com/article/view/10.21037/gs-24-164/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the ethics committee of Nanjing Drum Tower Hospital (No. 2023-345-01) and individual consent for this retrospective analysis was waived.

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