ASSOCIATION OF OVERWEIGHT AND OBESITY WITH PAPILLARY THYROID CARCINOMA

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ABSTRACT

Background. Papillary Thyroid Carcinoma (PTC) is the most frequently diagnosed malignant neoplasm of the endocrine system, accounting for more than 80% of other histopathological types of thyroid cancer worldwide, including Ukraine. Both overweight (Body Mass Index (BMI) [25.0–29.9] kg/m^2) and obesity (BMI >30 kg/m^2) might be considered a risk factor for PTC development. Besides, it may be associated with negative clinical characteristics such as obesity and overweight or biological aggressiveness of PTC such as larger tumor size, invasion to thyroid structures or adjacent neck tissues, metastatic spread etc., which are not sufficiently studied in Ukraine.

Aim. To investigate and evaluate the features of the overweight and obesity in the patients with PTC and compare them with patients with PTC and normal weight.

Materials and Methods. Our study involved 91 patients with the diagnosis of PTC who underwent surgical treatment at Verum Expert Clinic (Kyiv, Ukraine). The study groups consisted of 65 patients with PTC and overweight/obesity (BMI ≥25 kg/m^2), and 26 patients with PTC and normal weight. Written informed consent to participate was obtained from all patients, and the study was approved by the local ethical committee. The non-parametric Mann-Whitney U test was applied to compare quantitative variables between groups. Categorical variables were compared using Fisher's exact test (two-tailed). Statistica 12 (TIBCO Software Inc., USA) and GraphPad Prism 10 (GraphPad Software, LLC, USA) statistical software were used for data analyses. Statistical significance was set at $p<0.05$.

Results. A statistically significant difference was found in the frequency of lateral neck dissection: it was performed in 12 (46%) patients with PTC and normal weight, compared to 22 (34%) patients with PTC and overweight/obesity ($p=0.031$).

Conclusions. Overweight and obesity are highly prevalent among patients with PTC in our cohort. However, the higher rate of lateral neck dissection in the normal-weight group suggests that factors other than BMI, possibly related to preoperative diagnosis, played a more critical role in surgical planning in this study.

Keywords: *cancer risk, lymph node excision, neoplasm invasiveness, body mass index, thyroid neoplasms, risk factors.*

Introduction

Papillary Thyroid Carcinoma (PTC) is the most common type of thyroid cancer, characterized by its generally indolent behavior and excellent prognosis [1]. Recent studies suggest a potential link between overweight, defined as a Body Mass Index (BMI) ≥25 kg/m², and an increased risk of PTC developing [2]. Obesity is associated with hormonal and metabolic changes such as elevated insulin levels, increased adipokines, and chronic inflammation, which may promote carcinogenesis in thyroid tissues [3]. Additionally, excessive body

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weight can influence thyroid hormone regulation and immune responses, potentially contributing to tumor development.

Epidemiological data indicate that individuals with higher BMI are more likely to develop PTC, underscoring the importance of weight management for cancer risk reduction. Although the exact mechanisms remain under investigation, the connection between overweight and PTC highlights the need for integrated approaches in prevention and early detection strategies [4; 5]. It is worth mentioning that obesity is a known risk factor for certain malignant neoplasms, not only type 2 diabetes mellitus. The body waist measuring might be also considered for the obesity diagnosis and management [6].

Obesity and overweight might have an impact on PTC carcinogenesis through the negative actions on cell proliferation, differentiation, apoptosis. Also, when assessing clinical and clinical-morphological parameters, cohorts evaluate various indicators, taking into account modern clinical practices in various medical specialties, which may have an impact on all organs and systems, including in the context of the war in Ukraine [7–9].

Research [10] suggests various drugs against inflammation and oxidative stress in relation to thyroid cancer. Previous publication by Song S. et al. showed that patients with PTC have elevated levels of the inflammatory molecules, suggesting a potential link between obesity-induced systemic inflammation and the development of PTC [11]. Gross signs, such as tumor proliferation into the adjacent tissues, are important prognostic indicators [12; 13]. It is worth mentioning that little is investigated in Ukraine concerning the relationship of overweight and obesity with PTC.

Aim of the study was to investigate and evaluate the features of PTC in obese and overweight patients and compare them with patients with PTC and normal weight.

Materials and Methods

A total of 91 patients diagnosed with PTC, who underwent surgical treatment at the Verum Expert Clinic (Kyiv, Ukraine), were included in the study. Body Mass Index (BMI) was calculated as weight in kilograms divided by the square of height in meters (kg/m²) [2]. To assess the association between elevated BMI and PTC characteristics, the patients were stratified into two groups: the overweight/obesity group (BMI ≥25 kg/m², n=65), which comprised patients with overweight (BMI [25.0–29.9] kg/m²) and obesity (BMI ≥30 kg/m²), and the normal weight group (BMI <25 kg/m², n=26). The clinical and histopathological data were compared between these groups.

Various pathohistological and clinical parameters such as weight, height (BMI constituents), gender, tumor size, neck dissection types were retrieved from the archived medical records. Preoperatively, all patients underwent physical examination, measuring thyroid hormones, assessment of electrolytes, serum glucose, liver enzymes, ionized calcium (Ca^{2+}), and coagulation testing. Ultrasound examination of the thyroid gland was performed in all patients using the Thyroid Imaging, Reporting and Data System (TIRADS) scale. Fine-needle aspiration biopsy was performed for all patients with thyroid nodules, followed by its cytological analyses by Bethesda classification [14]. Dissection of central compartment was not performed in the absence of suspicion of PTC at the preoperative stage TBSRTC (Thyroid, Bethesda, System for Reporting, Thyroid Cytology) category 2, in the absence of macroscopic extension to the locoregional lymph nodes at operation [15].

The diagnosis was verified pathohistologically according to the World Health Organization classification of endocrine tumors [16]. Fluorescence-guided surgery was performed for better verification of parathyroid glands in accordance with previously published protocols and equipment [17]. During thyroid surgery, the surgical team visually identified the parathyroid glands. Subsequently, the surgical field was analyzed using one of the available imaging systems. The confirmation of the visually identified parathyroid glands, along with their Near-Infrared Autofluorescence (NIRAF), was considered for guiding further surgical decisions. NIRAF was assessed using the Fluobeam-800 or Fluobeam LX imaging systems (Fluoptics, France). These systems are equipped with a Near-InfraRed (NIR) camera, a console for adjusting the NIR signal, and a touchscreen monitor. The NIRAF signal was evaluated after turning off the operating lights. Additionally, to enhance fluorescence imaging, an intravenous injection of the fluorophore Indocyanine Green (ICG) was administered. The parathyroid NIRAF signal was assessed by manually holding the NIR camera approximately 20 cm above the surgical field. No quantitative parameters were measured.

Ethical approval for the study was obtained from the local Ethical Committee of the Verum Expert Clinic. The study was conducted according to Helsinki Declaration and Ukrainian ethical standards. An informed consent to participate was received from all patients. This study was conduc-

ted in accordance with the ethical principles of the World Medical Association Declaration of Helsinki (1964–2024) and complied with the legislation of Ukraine, including the Laws "On Protection of Human Rights in Biomedical Research" (2006) and "On Personal Data Protection" (2010). Non-parametric statistical analyses were used for data evaluation processing by applying Mann-Whitney test, Fisher's exact test (two-tailed). The difference between the study groups was considered as significant with $p<0.05$.

Results and Discussion

Analyses of the parameters from the 91 patients revealed that group of the patients with PTC and overweight were 65 (71%) patients and the group of patients with PTC and normal weight were 26 (29%) patients ($p<0.05$). The analyses of clinical and morphological features of the studied groups of patients are shown in *Table*.

26 (29%) patients, in whom PTC was present against the background of normal body weight (BMI [18.0–24.9] kg/m^2). The results of data analysis based on this distribution of patients with PTC by groups are shown in *Table*.

The distribution indicated that overweight/obese patients outnumbered normal weight patients by 42%, indicating obesity as a significant factor associated with PTC. Further analysis of the data showed that the mean age at diagnosis was 46.2 years in PTC patients with BMI ≥25 kg/m^2, which was slightly higher than the similar figure of 41 years in PTC patients with a normal body weight ($U=610$; $p=0.039$). There were no significant changes found among the following morphological that indicators were evaluated: locoregional lymph nodes, multifocal growth of bilateral lesions of the thyroid lobes, the presence of psammoma bodies, invasion of thyroid structures, extrathyroid spread,

Table. Analyses of the clinical characteristics of the of the patients with papillary thyroid carcinoma in relation to the weight of the patients

Parameters	PTC overweight (n=65)	PTC normal weight (n=26)	p-values
Females, abs. (%)	46 (71)	22 (85)	n/s
Males, abs. (%)	19 (29)	4 (15)	n/s
Age, years, abs. (%)	46.2 (22.3–74.6)	41 (20.2–70.6)	0.039
Mean age at diagnosis in years (range)	46.2 (22.3–74.6)	41 (20.2–70.6)	0.039
Mean size of carcinoma, cm (range)	1.18 (0.15–4.0)	0.95 (0.2–2.7)	n/s
Central compartment neck dissection, abs. (%)	60 (92)	25 (96)	n/s
Lateral compartment neck dissection, abs. (%)	22 (34)	12 (46)	0.031

Notes: PTC – papillary thyroid carcinoma; n/s – non-significant at statistical analyses ($p>0.05$).

According to our results, both obesity and overweight are more frequently diagnosed in females as well as other clinical and histopathological parameters, which is in line with previously publicshed reports [6; 18; 19]. Among various pathological features, invasive characteristics of PTC are considered as one of the unfavorable features of PTC [20; 21]. The macroscopic spread of PTC is and remains a significant risk factor for patient prognosis and surgical treatment tactics [6; 18; 19; 22; 23]. Considering the possible associations not only of obesity, but also of the generally negative impact of BMI ≥25 kg/m^2, the hypothesis regarding the generally negative impact of excess weight was tested. The 91 patients with PTC were divided into two study groups – PTC with BMI ≥25 kg/m^2, which included 65 (71%) patients, and a group of

etc. Further analysis of the data was carried out regarding the volume of neck dissection: a significant difference in the frequency of lateral neck dissection was found. Upon further evaluation of this clinical material of 91 patients with PTC and overweight or obesity, a lower frequency of lateral neck dissection was found in 22 (34%) patients with PTC with BMI ≥25 kg/m^2 than in 12 (46%) patients with PTC with normal weight ($U=650$; $p=0.031$). The performance of central neck dissection was practically the same in both study groups – in 92% of patients with PTC with BMI ≥25 kg/m^2 and in 96% of patients with PTC with normal weight ($p>0.05$). Despite the comparable incidence of histologically confirmed metastases in the lateral lymph nodes (29% in the overweight/obesity group vs. 31% in the normal weight group,

p>0.05), lateral neck dissection was performed significantly less frequently in patients with BMI ≥25 kg/m². This discrepancy suggests that factors other than the confirmed nodal disease may have influenced the decision to perform lateral neck dissection. These results are consistent with data from other publications and trends in considering obesity as a negative factor in malignant tumors.

Conclusions

1. Overweight and obesity are highly prevalent among patients with papillary thyroid carcinoma in our study cohort.

2. Patients with normal weight underwent lateral neck dissection significantly more often than patients with overweight/obesity.

3. This difference does not appear to be directly linked to a higher incidence of confirmed lateral compartment metastases, suggesting that factors other than BMI, such as challenges in preoperative assessment of patients with higher BMI, may have influenced the surgical planning.

DECLARATIONS:

Disclosure Statement

The authors have no potential conflicts of interest to disclosure, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

Statement of Ethics

The authors have no ethical conflicts to disclosure.

Data Transparency

The data can be requested from the authors.

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Consent for publication

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