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THE RELATIONSHIP OF PAPILLARY THYROID CARCINOMA SIZE WITH OVERWEIGHT OR OBESITY

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Papillary Thyroid Carcinoma (PTC), a well-differentiated malignant neoplasm originating from thyroid follicular cells, has been increasingly studied for its association with obesity. In Ukraine, PTC accounts for approximately [1.7–1.8] % of all malignant tumors. Accumulated evidence suggests that obesity, characterized by a Body Mass Index (BMI) over 30 kg/m², promotes carcinogenesis through hormonal changes, chronic inflammation, oxidative stress, and insulin resistance. The aim of the study was to investigate the relationship of obesity or overweight with PTC size. This retrospective study examined 91 patients with histologically confirmed PTC, categorizing them based on BMI into normal weight, overweight, and obese groups. Patients were divided into groups in relation to their weight. The study group comprised patients with overweight and obesity based on their BMI. Informed consent was obtained from all participants. 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 $p < 0.05$. The study showed that in our cohort, 71 % of PTC patients were overweight or obese. Notably, larger tumors (≥ 1 cm) were more common in obese and overweight groups, whereas PTC microcarcinomas (< 1 cm) were more frequent in patients with normal weight, suggesting a potential correlation between obesity and larger tumor size ($p < 0.05$). This size differential suggests that metabolic factors associated with higher BMI may influence tumor growth in PTC. The results of the study indicate that PTC with a tumor diameter of ≥ 1 cm is more likely in obese and overweight patients. Thyroid microcarcinomas are more common in patients of normal weight. Obesity can be considered as a risk factor for faster growth of neoplasms in PTC.

Keywords: papillary thyroid microcarcinoma, cancer risk, body mass index, neoplasm staging, prognostic factors, morphometric parameters.



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Introduction

Papillary Thyroid Carcinoma (PTC) is a frequent malignant tumor originating from thyroid follicular cells and is considered as well-differentiated cancer. The frequency of PTC in Ukraine accounts for [1.7–1.8] % of all malignant neoplasms. As shown previously, PTC might be diagnosed in coexistence with other benign thyroid neoplasms as well as might be associated with such comorbidity as overweight or obesity [1]. The thyroid malignant transformation might be assessed in view of possible risk from overweight or obesity [2].

Obesity is an excess of white adipose tissue in the body, which is diagnosed by determining the Body Mass Index (BMI), where a BMI >30 kg/m² is classified as obese. Currently, various studies have shown the results indicating several mechanisms that explain why obesity may contribute to the development of various types of malignancies, including thyroid cancer. Among the mentioned factors are hormonal changes, chronic inflammation and oxidative stress, as well as hyperglycemia and insulin resistance [3]. In the case of such type of thyroid cancer as PTC, these mechanisms may play a significant role, but remain poorly studied in Ukraine.

It is well-established that obesity is linked to an increased risk of 13 types of cancer, including PTC [4]. Considering the relationship of such constitutional features as obesity or overweight, it is important to think about the risk stratification and to perform preventive measures among obese population for early diagnosis of PTC. Among the above-mentioned, it is believed that one of the main mechanisms for carcinogenesis of PTC is associated with the changes of certain hormones in obese population. It should be noted that adipose tissue

is not just a deposition of the body's energy resources, but also hormonally active tissue, synthesizing a biologically active substances, hormones, cytokines, to promote conditions for oxidative stress, which triggers and maintains a certain "circulus vitiosus". The mentioned "circulus vitiosus" contributes to the further accumulation of adipose tissue, or the maintenance of its mass in the event that the patient decides to lifestyle modification and plans to lose weight. The molecular pathogenetic changes in obesity described above have a proven effect on apoptosis, cell proliferation and differentiation, and on elements of the cell cycle, changes in which are key to malignant cell transformation [5].

Published studies have shown that patients with PTC often have elevated levels of inflammatory markers, suggesting a potential link between obesity-induced systemic inflammation and the development of this type of thyroid cancer [9]. Considerable evidence also indicates the role of insulin resistance in oncogenesis, which is usually associated with obesity, and is also a significant risk factor for the development of PTC. Insulin resistance leads to hyperinsulinemia, which can promote cell proliferation and suppress apoptosis [3]. These molecular and genetic changes in obese patients have been studied, but the actual changes in clinical and morphological parameters, such as carcinoma size, lymph node metastasis status, a number of parameters of carcinoma invasion, the number of mitoses in 10 fields at ×400 magnification, remain poorly studied, in particular in Ukrainian patients, and require additional scientific evaluation and further investigation.

The **aim** of the study was to investigate the relationship of obesity or overweight with papillary thyroid carcinoma size.

Materials and Methods

There were identified 91 patients who underwent surgical management for PTC at Verum Expert Clinic (Kyiv, Ukraine). Patients were divided into groups in relation to their weight. BMI was calculated for all patients in kg/m². The study group constitutes patients with overweight and obesity based on their BMI. The BMI below 25 kg/m² was considered as normal weight, and BMI [25.0–29.9] kg/m² – as overweight, ≥ 30 kg/m² – as obesity [2; 10].

For each patient, the size of the tumor (microcarcinomas < 1 cm in diameter and tumors ≥ 1 cm in diameter) was studied. Patients were divided into groups depending on their weight. Informed consent was obtained from all patients.

Non-parametric statistical analyses were used for data evaluation processing by applying Kruskal–Wallis, Fisher’s exact test (two-tailed). The difference between the study groups was considered as significant with p < 0.05.

Results and Discussion

Analysis of data from 91 patients with PTC showed that in the group of patients with obesity (BMI more than 30 kg/m²) were 20 (21 %) patients, in the group of patients with overweight there were 45 (50 %) patients, and in the group of patients with normal weight there were 26 (29 %) patients (p < 0.05). The summary of the analyses of clinical and morphological features of the studied groups of patients are presented in *Table*. Thus, a high prevalence of overweight/obesity (71 %) was observed in our PTC cohort. While this suggests a potential association, the role of obesity as a risk factor requires further validation in case-control studies.

Clinical-pathomorphological data from the patients were retrieved from the archived medical records. At preoperative stage, all patients were examined for thyroid hormones, liver function test (liver enzymes), total blood count test, coagulation testing, concentration of ionized calcium. Ultrasonography

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

Parameters	PTC and obesity (n = 20)	PTC and overweight (n = 45)	PTC and normal weight (n = 26)	P
Females, abs. (%)	11 (55)	35 (78)	22 (85)	ns
Males, abs. (%)	9 (45)	10 (22)	4 (15)	ns
Mean age at diagnosis, years (range)	49.6 (29.8–71.6)	44.8 (22.3–77.4)	41.0 (20.2–70.6)	ns
Mean size of carcinoma, cm (range)	1.60 (0.35–2.60)	1.00 (0.15–3.10)	0.95 (0.20–2.70)	0.043
Microcarcinoma, abs. (%)	6 (30)	28 (62)	16 (62)	0.041
PTC coexisting with benign thyroid pathology, abs. (%)	11 (55)	32 (71)	18 (69)	ns
Multifocality, abs. (%)	33 (66)	15 (33)	8 (31)	ns
Bilateral growth, abs. (%)	7 (35)	11 (24)	6 (23)	ns
Metastases to local lymph nodes, abs. (%)	8 (40)	14 (31)	13 (50)	ns
Psammoma bodies in lymph nodes, abs. (%)	2 (6)	0 (0)	2 (2)	ns
Relapse of PTC, abs. (%)	2 (4.4)	2 (4.4)	3 (11.5)	ns

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

examination of the thyroid gland was done with application of the Thyroid Imaging Reporting and Data System (TIRADS) scale according to suggested scoring [11].

Fine-needle aspiration biopsy was performed under the ultrasound guidance for thyroid nodules, followed by cytological examination with application of Bethesda classification (TBSRTC categories 1–6), as described by Juhlin C.C. et al. [12]. All thyroid operations were performed by applying the technique of capsular dissection. During surgery, identification and mobilization of all parathyroid glands was performed, and recurrent laryngeal nerves were identified and preserved. Intraoperative frozen section was done for patients with fine needle aspiration biopsy TBSRTC categories 3, 4, 5, and in case of the unilateral PTC without distinct confidence about the possible metastatic spread to the local lymphatic nodules. The volume of operative and postoperative treatment was carried out taking into account the valid recommendations of the American Thyroid Association at the time of operation [13]. The diagnosis was confirmed histopathologically according to the World Health Organization classification of endocrine tumors [14]. Fluorescence-guided surgery was applied for better discrimination of the parathyroid glands in accordance with previously published protocols and equipment [15].

Obesity and overweight were diagnosed more frequently in females. There were 55 % of women in PTC with obesity group, 78 % of women in the groups of PTC with overweight, as well as in the PTC with normal weight there were 85 % of women, which is consistent with the trends in overweight and obesity among the female population compared to men [3; 4; 10; 16]. It should also be noted that PTC is also more commonly diagnosed in females, with a female-to-male ratio of 3:1. No significant differences were found for the frequencies of locoregional lymph node metastases, multifocal growth of bilateral thyroid lobe involvement,

and the presence of psammoma bodies in the study groups [17–19]. Considering overweight and obesity as significant factors associated with the development of thyroid cancer and 12 other types of malignant tumors, it is also important to evaluate the relationship of overweight and obesity with clinical-morphological features of carcinoma, to determine possible negative effects.

Among various clinical-morphological features, PTC microcarcinoma is considered as one of the favorable features of PTC, which is associated with a lower frequency of biologically aggressive characteristics (locoregional metastasis, multifocal growth, invasive cancer characteristics, lower recurrence rate, etc.). Papillary thyroid microcarcinoma is usually associated with better prognosis [20; 21]. Analysis of clinical and morphological parameters of the studied groups revealed significantly different sizes of PTC: the average size of the carcinoma was 1.6 cm in the group of obese PTC patients, 1.0 cm in the group of overweight PTC patients, and 0.95 cm in PTC patients with normal weight ($p = 0.043$). The obtained results indicate a statistically significant higher frequency of microcarcinomas (i.e., PTC measuring less than 1 cm in the largest diameter) among patients with normal weight (i.e., BMI below 25 kg/m²).

The further evaluation of this clinical material of 91 overweight, obese and normal weight patients revealed a PTC microcarcinoma in 6 (30 %) patients in group of PTC with obesity, in 28 (62 %) patients in group of PTC with overweight, and in 16 (62 %) patients in group of PTC with normal weight ($p = 0.041$). Although analysis of the incidence of PTC recurrence among the study groups did not show a significant difference in the incidence of locoregional metastases or in the incidence of recurrence in the short-term postoperative follow-up (up to 1 year), the higher incidence of large cancers (> 1 cm) in obese PTC patients and overweight PTC patients indicates the importance

of considering the BMI of patients and taking this into account when planning the follow-up of patients in the postoperative period.

Conclusions

The results of the study indicate that PTC with a tumor diameter of > 1 cm is more likely

in obese and overweight patients. Thyroid microcarcinomas are more common in patients of normal weight. Obesity can be considered as a risk factor for faster growth of neoplasms in PTC.

Conflict of interest is absent.

References

1. Dinets A, Gorobeiko M, Hoperia V, Lovin A, Tarasenko S. Papillary thyroid carcinoma coexisting with benign thyroid and parathyroid pathology: clinical and pathomorphological features. *International Journal of Endocrinology (Ukraine)*. 2023;19(4):274-8. DOI: 10.22141/2224-0721.19.4.2023.1285.
2. Gorobeiko M, Zdorna V, Dinets A. Positive effect of vitamin D supplementation on weight loss in obese patients treated with glucagon-like peptide 1 and lifestyle interventions. *International Journal of Endocrinology (Ukraine)*. 2022;18(5):278-84. DOI: 10.22141/2224-0721.18.5.2022.1186.
3. Celescuekci LG, Pinto MP, Botelho IMB, Pavin EJ, Zantut-Wittmann DE. Insulin resistance factors associated with differentiated thyroid carcinoma and malignant cytology: serum thyroxine as an associated factor. *Ann Med*. 2025;57(1):2530697. DOI: 10.1080/07853890.2025.2530697. PMID: 40662255.
4. Sparavelli R, Giannini R, Signorini F, Materazzi G, Basolo A, Santini F, et al. Papillary Thyroid Carcinoma and Body Mass Index: The Role of Immune System in Tumor Microenvironment. *Int J Mol Sci*. 2025;26(17):8290. DOI: 10.3390/ijms26178290. PMID: 40943211.
5. Vitale E, Rizzo A, Santa K, Jirillo E. Associations between "Cancer Risk", "Inflammation" and "Metabolic Syndrome": A Scoping Review. *Biology (Basel)*. 2024;13(5):352. DOI: 10.3390/biology13050352. PMID: 38785834.
6. Kitana FI, Shobab L. The Interaction between Sex and Thyroid Cancer Development and Management. *Endocrinol Metab Clin North Am*. 2025;54(3):483-95. DOI: 10.1016/j.ecl.2025. 03.016. PMID: 40716901.
7. Shumakov OV, Parkhomenko OM, Lutay YaM, Khomiakov DV. Diagnostic value of clinical-instrumental and hematological indicators in predicting complications of the hospital period of STEMI in conditions of chronic stress caused by wartime. *Ukrainian Journal of Cardiology*. 2024;31(1):34-45. DOI: 10.31928/2664-4479-2024.1.3445. [In Ukrainian].
8. Haglund F, Rosin G, Nilsson IL, Juhlin CC, Pernow Y, Norenstedt S, et al. Tumour nuclear oestrogen receptor beta 1 correlates inversely with parathyroid tumour weight. *Endocr Connect*. 2015;4(1):76-85. DOI: 10.1530/EC-14-0109. PMID: 25648860.
9. Song S, Leng Z, Zhao X, Liu Z, Li Y, Zhang W, et al. ASAP1 Promotes Epithelial to Mesenchymal Transition by Activating the TGFbeta Pathway in Papillary Thyroid Cancer. *Cancer Med*. 2025;14(15):e71075. DOI: 10.1002/cam4.71075. PMID: 40742091.
10. World Health Organization. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. Geneva: WHO; 2000. 253 p. Available at: <https://apps.who.int/iris/handle/10665/42330>

11. Trimboli P, Bojunga J, Deandrea M, Frasca F, Imperiale A, Leoncini A, et al. Reappraising the role of thyroid scintigraphy in the era of TIRADS: A clinically-oriented viewpoint. *Endocrine*. 2024;85(3):1035-40. doi: 10.1007/s12020-024-03825-0. PMID: 38625504.
12. Juhlin CC, Baloch ZW. The 3rd Edition of Bethesda System for Reporting Thyroid Cytopathology: Highlights and Comments. *Endocr Pathol*. 2024;35(1):77-9. DOI: 10.1007/s12022-023-09795-9. PMID: 38032439.
13. Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, et al. 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. *Thyroid*. 2016;26(1):1-133. DOI: 10.1089/thy.2015.0020. PMID: 26462967.
14. Lloyd R, Osamura R, Kloppel G. Other encapsulated follicular-patterned thyroid tumours. *Classification of tumours of endocrine organs*. 4th ed. Lyon, France: World Health Organization; 2017. 355 p. Available at: <https://is.gd/4PaKWL>
15. Matson J, Bouvet M. Use of fluorescence image-guided surgery and autofluorescence in thyroid and parathyroid surgery. *Mini-invasive Surg*. 2023;7:10. DOI: 10.20517/2574-1225.2022.81.
16. Thomsen RW, Mailhac A, Lohde JB, Pottegård A. Real-world evidence on the utilization, clinical and comparative effectiveness, and adverse effects of newer GLP-1RA-based weight-loss therapies. *Diabetes Obes Metab*. 2025;27_Suppl 2(Suppl_2):66-88. DOI: 10.1111/dom.16364. PMID: 40196933.
17. Haglund F, Juhlin CC, Brown T, Ghaderi M, Liu T, Stenman A, et al. TERT promoter mutations are rare in parathyroid tumors. *Endocr Relat Cancer*. 2015;22(3):L9-11. DOI: 10.1530/ERC-15-0121. PMID: 25876648.
18. Suliman A, Mohamedosman R, Soud M, Suliman H. An atypical metastatic pathway: Bilateral inguinal lymphadenopathy as the initial presentation of papillary thyroid carcinoma. *Int J Surg Case Rep*. 2025;129:111189. DOI: 10.1016/j.ijscr.2025.111189. PMID: 40158358.
19. Rossi ED, Agarwal S, Erkilic S, Hang JF, Jalaly JB, Khanafshar E, et al. Psammoma bodies in thyroid: are they always indicative of malignancy? A multi-institutional study. *Virchows Arch*. 2024. DOI: 10.1007/s00428-024-03934-1. PMID: 39349665.
20. Song RY, Kim HS, Kang KH. Minimal extrathyroidal extension is associated with lymph node metastasis in single papillary thyroid microcarcinoma: a retrospective analysis of 814 patients. *World J Surg Oncol*. 2022;20(1):170. PMID: 35643530. DOI: 10.1186/s12957-022-02629-8.
21. Walgama E, Sacks WL, Ho AS. Papillary thyroid microcarcinoma: optimal management versus overtreatment. *Curr Opin Oncol*. 2020;32(1):1-6. PMID: 31633497. DOI: 10.1097/CCO.0000000000000595.

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ЗВ'ЯЗОК РОЗМІРУ ПАПІЛЯРНОЇ КАРЦИНОМИ ЩИТОПОДІБНОЇ ЗАЛОЗИ З ОЖИРІННЯМ АБО НАДМІРНОЮ ВАГОЮ

Папілярна карцинома щитоподібної залози (ПКЩЗ) в Україні зустрічається із частотою [1,7–1,8] % від усіх злоякісних пухлин. Ожиріння (при індексі маси тіла (ІМТ) понад 30 кг/м²) викликає канцерогенез через гормональні зміни, хронічне запалення, оксидативний стрес та інсулінорезистентність. Метою дослідження було вивчення впливу ожиріння або надмірної ваги на розмір ПКЩЗ. Ретроспективно було обстежено 91 пацієнта з гістологічно підтвердженим ПКЩЗ, яких розділили на групи з нормальною вагою, надмірною вагою та ожирінням відповідно до ІМТ. Для кожного пацієнта був вивчений розмір пухлини (мікрокарциноми < 1 см у діаметрі та пухлини ≥1 см в діаметрі). Пацієнтів було розділено на групи залежно від їхньої ваги, отримано інформовану згоду на участь у дослідженні. Для аналізу даних використовувалися програми Statistica 12 (TIBCO Software Inc., США) та GraphPad Prism 10 (GraphPad Software, LLC, США). Статистична значущість була встановлена при $p < 0,05$. Результати дослідження показали, що 71 % пацієнтів мали надмірну вагу або ожиріння, що вказує на значний зв'язок між підвищеним ІМТ та ризиком ПКЩЗ. Достовірно ($p < 0,05$) визначено, що більші пухлини (> 1 см) частіше зустрічалися в групах з ожирінням та надмірною вагою, тоді як мікрокарциноми частіше зустрічалися у пацієнтів з нормальною вагою. Результати дослідження свідчать, що ПКЩЗ з діаметром пухлини > 1 см більш вірогідний у пацієнтів з ожирінням та надмірною вагою. Мікрокарциноми щитоподібної залози більш притаманні пацієнтам з нормальною вагою. Ожиріння можна розглядати як фактор ризику швидшого росту новоутворень при ПКЩЗ.

Ключові слова: папілярна мікрокарцинома щитоподібної залози, онкологічний ризик, індекс маси тіла, стадіювання пухлини, прогностичні фактори, морфометричні параметри.

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