Original article

Histopathological characteristics and treatment options of papillary thyroid carcinoma less than 1 cm at Hue University of Medicine and Pharmacy Hospital

Dang Cong Thuan[1], Ngo Quy Tran[1], Tran Thi Nam Phuong[1], Tran Van Bao[1], Le Thanh Huy,[1] Le Vi[2]

[1]Hue University of Medicine and Pharmacy, Hue University

[2]Department of Pathology, Khanh Hoa Oncology Hospital

Abstract

Background: Thyroid cancer is the most common type of endocrine malignancy. More than 90% of cases are diagnosed as differentiated thyroid carcinoma, with the papillary type being the most prevalent. Papillary thyroid carcinoma (PTC) with a maximum diameter ≤1 cm is associated with a distinct prognosis and treatment approach compared to larger PTCs. **Objectives:** To investigate histopathological characteristics and treatment approaches for thyroid carcinomas ≤1 cm at the Hospital of Hue University of Medicine and Pharmacy. **Materials and Methods:** A cross-sectional and retrospective descriptive study on 122 patients definitively diagnosed with papillary thyroid carcinoma, with the size of the tumor ≤1 cm, at the University of Medicine and Pharmacy Hospital, Hue University, between February 2024 and December 2024. **Results:** 72.1% of patients were under 55 years of age, with a female-to-male ratio of 7:1. The classic variant accounted for 68.9%; 74.6% had solitary tumors; 15.6% with thyroid capsule invasion; 77.9% without lymph node involvement; 99.2% without vascular invasion; 95.1% were diagnosed at stage I. Total thyroidectomy was performed in 66.4% of cases, accompanied by 59% lymph node dissection, while 33.6% underwent lobectomy. 74.6% received I-131 therapy, and 67.2% received thyroid hormone suppression therapy. 12.3% had postoperative complications, and hypocalcemia was the most common complication (10.7%). **Conclusion:** The classic variant was the most common subtype of papillary thyroid carcinoma, accounting for 68.9%. Surgery is the primary treatment option (100%). The postoperative complication rate was relatively low (12.3%), with a statistically significant association between the type of surgical procedure and risk of postoperative hypocalcemia observed.

Keyword: *papillary thyroid carcinoma, histopathology, treatment*

1. INTRODUCTION

Thyroid cancer is the most common endocrine malignancy [1]. According to Globocan 2022, with over 821,000 cases worldwide, thyroid cancer ranks seventh in overall cancer incidence and fifth among women [2]. In Vietnam, thyroid cancer is the sixth most common cancer, accounting for approximately 3.4% of all new cancer cases in 2022. Although its mortality rate is low, the number of new cases is increasing, particularly among women [3]. More than 90% of patients are diagnosed with differentiated thyroid carcinoma (DTC), with the papillary type being the most prevalent (89.8%), followed by the follicular (4.5%) and oncocytic types (1.8%) [1].

The treatment of DTC typically involves surgery, radioactive iodine (I-131) therapy, and hormone therapy, with surgery playing the most critical role [4]. Papillary thyroid microcarcinoma (PTMC) is defined as papillary thyroid carcinoma (PTC) with a maximum tumor diameter of 1 cm or less. It has distinct prognostic and therapeutic implications compared to larger PTCs. In the latest (5th edition, 2022) WHO classification, PTMC is no longer categorized as a separate subtype of PTC. However, tumors ≤1 cm account for approximately 50% of all PTC cases and generally have an excellent prognosis, with a mortality rate of 1% for papillary variants [1, 5].

Some studies suggest that low-risk microcarcinomas may only require active surveillance, while others argue that a subset of PTMCs exhibit aggressive behavior and require active intervention [6]. Certain aggressive subtypes of PTC such as the diffuse sclerosing variant, solid variant, tall cell variant, columnar cell variant, and hobnail variant present distinct clinical, pathological, and molecular features, often associated with larger tumor sizes [5, 7]. Given these observations, we conducted this study to describe the histopathological

**Corresponding Author: Dang Cong Thuan. Email: dcthuan@huemed-univ.edu.vn*
DOI: 10.34071/jmp.2025.6.591
Received: 04/08/2025; Accepted: 26/12/2025; Published: 30/12/2025

characteristics and treatment options for papillary thyroid carcinomas measuring less than 1 cm at Hue University of Medicine and Pharmacy Hospital.

2. MATERIALS AND METHODS

2.1. Research Subjects

A total of 122 patients were diagnosed with papillary thyroid carcinoma at Hue University of Medicine and Pharmacy Hospital from February 2024 to December 2024.

2.1.1. Inclusion Criteria

- Patients diagnosed with PTC based on histopathological examination at Hue University of Medicine and Pharmacy Hospital.
- Tumor size measured by both ultrasound and gross examination was ≤ 1 cm.
- Patients had not undergone any previous treatment for the disease at the time of diagnosis.
- Complete medical records were available.

2.1.2. Exclusion Criteria

- Patients with histopathological results indicating metastatic carcinoma, sarcoma, or malignant lymphoma.
- Patients with ≥ 2 thyroid nodules, in which at least one lesion measured > 1 cm on ultrasound or gross examination.
- Patients who did not consent to participate in the study.

2.2. Research methods

2.2.1. Study design: A cross-sectional descriptive study combined with retrospective data collection.

2.2.2. Sampling method: All patients meeting the inclusion criteria were selected. Clinical data, treatment methods, and treatment outcomes were retrospectively collected from medical records.

2.3. Data Analysis

Data were analyzed using SPSS version 20.0.

2.4. Research ethics

This study was conducted in accordance with ethical guidelines. Informed consent was obtained from all participants, and confidentiality was strictly maintained.

3. RESULTS

3.1. General characteristics

Table 1. General characteristics

Characteristic		Frequency (n)	Percentage (%)
Age	< 55	88	72.1
	≥ 55	34	27.9
Sex	Male	15	12.3
	Female	107	87.7

The majority of patients were under 55 years of age (72.1%). Female patients were more common than male, with a female-to-male ratio of approximately 7:1.

3.2. Histopathological characteristics

Table 2. Histopathological characteristics

Characteristic			Frequency (n)	Percentage (%)
Histological type	Papillary thyroid carcinoma	Classic PTC	84	68.9
		Infiltrative follicular variant of PTC	30	24.6
		Warthin-like PTC	2	1.6
		Hobnail subtype	2	1.6
		Oncocytic PTC	1	0.8
		Encapsulated classic PTC	1	0.8
	Invasive encapsulated follicular variant of PTC		2	1.6
Tumor number	1		91	74.6
	≥ 2		31	25.4
Vascular invasion	Present		1	0.8
	Absent		121	99.2

Capsular invasion	Present	19	15.6
	Absent	103	84.4
Lymph node metastasis	Present	27	22.1
	Absent	95	77.9
Distant metastasis	Present	0	0.0
	Absent	122	100.0
Stage (AJCC 8th edition)	I	116	95.1
	II	6	4.9

Histopathological characteristics of thyroid carcinoma ≤1 cm in the study population:

- Histological type: The classic subtype was the most common (68.9%), followed by the infiltrative follicular variant (24.6%). Other variants were infrequently encountered. The invasive encapsulated follicular variant of papillary carcinoma were observed in only 1–2 cases.
- Solitary tumors were present in 74.6% of cases, while multiple tumors (≥2 lesions) were found in 25.4%.
- Most cases showed no vascular invasion (99.2%).
- Capsular rupture was identified in 15.6% of cases.
- Lymph node metastasis: Absent in 77.9% of patients; present in 22.1%.
- No cases of distant metastasis were recorded.
- The majority of tumors were stage I (95.1%), with 4.9% classified as stage II.

3.3 Treatment approaches

Table 3. Surgical methods used in thyroid cancer treatment

Surgical Method		Frequency (n)	Percentage (%)
Lobectomy	Without lymph node dissection	28	23.0
	With lymph node dissection	13	10.7
Total thyroidectomy	Without lymph node dissection	9	7.4
	With lymph node dissection	72	59.0

A total of 41 patients underwent lobectomy, while 81 patients underwent total thyroidectomy. Among those receiving total thyroidectomy, 59.0% had lymph node dissection, whereas only 7.4% did not. In contrast, for lobectomy, a higher proportion (23.0%) did not have lymph node dissection compared to those who did (10.7%).

Table 4. Additional treatment modalities

Surgical Method		Frequency (n)	Percentage (%)
Thyrosin therapy	Yes	82	67.2
	No	40	32.8
I-131	Yes	31	25.4
	No	91	74.6

The majority of patients (74.6%) did not receive radioactive iodine (I-131) treatment. However, 67.2% received thyroxin therapy.

3.4. Treatment outcomes

Table 5. Postoperative complications

Complication	Frequency (n)	Percentage (%)
Hoarseness	1	0.8
Hypocalcemia	13	10.7
Surgical infection	1	0.8

The overall complication rate was low (12.3%), with hypocalcemia being the most frequent (10.7%). Only one case of hoarseness and one case of surgical infection were reported.

Table 6. Association between surgical method and hypocalcemia

Surgical Method	Hypocalcemia (n, %)	No Hypocalcemia (n, %)	p-value
Total thyroidectomy	12 (92.3)	69 (62.3)	< 0.05
Lobectomy	1 (7.7)	40 (36.7)	

Hypocalcemia occurred predominantly in patients who underwent total thyroidectomy (92.3%), whereas lobectomy was associated with significantly fewer cases (7.7%), with a statistically significant difference ($p < 0.05$).

4. DISCUSSION

4.1. General characteristics of study subjects

In papillary and follicular thyroid carcinomas, patient age is incorporated into the staging system and serves as a binary risk stratification factor [8]. Advanced age is significantly associated with higher tumor stage, reflecting its correlation with disease progression, while younger age is more considerably involved in an increased incidence of lymph node metastases. However, this does not alter the overall stage classification, according to the 8th edition of the American Joint Committee on Cancer (AJCC), which categorizes patients under 55 years of age as stage I or II, regardless of lymph node or distant metastases [8], [9]. In the present study, the majority of patients (72.1%) were younger than 55 years, consistent with the report by Vu Thi Hai et al. [5]. The female-to-male ratio was approximately 7:1, consistent with previous studies conducted by Vu Thi Hai et al. [5] and Nguyen Thi Quynh Giang et al. [10], highlighting a marked female predominance in thyroid cancer incidence. This gender disparity may be attributed to hormonal influences, as the difference is more pronounced during the reproductive age range (15–50 years). It is also reflective of histopathological subtype distributions, wherein papillary and follicular carcinomas are more prevalent among women, while medullary and anaplastic types show comparable frequencies between the two genders. Although the gender-based disparity in thyroid cancer incidence has been documented and well explained, the underlying mechanisms responsible for the observed trend of more aggressive disease in male patients remain unclear [11].

4.2. Histopathological characteristics of study subjects

In our study, among papillary thyroid carcinoma (PTC), the classic subtype was the most common, accounting for 68.9%, followed by the infiltrative follicular subtype at 24.6%. These results are comparable to those of Nguyen Thi Quynh Giang et al. (2024) [10], who reported 86.7% and 7.6% for the classic and infiltrative follicular subtypes, respectively.

Of the 122 patients analyzed, solitary tumors were predominant, observed in 74.6% of cases, consistent with that of Nguyen Thi Quynh Giang et al. (2024) [10], who also reported a higher proportion of patients with solitary thyroid nodules compared to those with multinodular involvement.

Previous studies have reported variable associations between vascular invasion and clinical outcomes such as recurrence in PTC, suggesting that vascular invasion is not always a definitive negative prognostic factor unless accompanied by other adverse features [13]. In our study, only one patient (0.8%) with PTC exhibited vascular invasion, which differs notably from findings in international studies. For instance, Almukhtar et al. (2022) [14] reported a vascular invasion rate of 27.3% in PTC, which may be attributed to differences in sample size and selection criteria, as Almukhtar et al. focused specifically on the papillary thyroid carcinoma.

Thyroid capsule invasion was identified in 15.6% of cases in our study, which is slightly higher than the 14.19% reported by Vu Thi Hai et al. (2021) [5], but lower than the 16.7% observed by Almukhtar et al. (2022) [14]. A variation among these studies may be attributed to patient numbers, tumor location, and tumor aggressiveness. Additionally, certain studies have reported that thyroid capsule invasion does not negatively impact biological progression or long-term prognosis in PTC [13].

Cervical lymph node metastasis is considered a reliable prognostic factor, particularly affecting the risk of tumor recurrence, although it does not significantly impact overall survival in PTC patients [15]. In the present study, cervical lymph node involvement was observed in 22.1% of cases, also demonstrating that lymph node metastasis can occur even in tumors ≤1 cm in diameter. However, our result was lower than that reported by Vu Thi Hao et al. (2021) [5], who found a lymph node metastasis of 45.88%, which may be attributed to several factors, including the number of patients who underwent lymph node dissection, the surgeon's ability to identify and remove lymph nodes, as well as the experience of the pathologist in detecting lymph

node metastasis.

In patients with PTC, distant metastasis is the leading cause of mortality, with a reported clinical incidence ranging from approximately 9% to 14%, typically occurring later in the disease course [14]. In our study, no cases of distant metastasis were identified. This contrasts with the findings of Almukhtar et al. (2022) [14], who reported a distant metastasis rate of 7.5%, which may be attributed to differences in sample size, study subjects, and research design.

Regarding staging, all patients in our study were classified as stage I or II, which is due to in our study, the predominance of papillary and follicular thyroid carcinomas (accounting for 96.7% of cases) and the high proportion (72.1%) of patients under the age of 55, cut-off of age is important factor to classify stage according to the AJCC staging system for differentiated thyroid carcinoma [8].

4.3. Treatment Approach

Differentiated thyroid cancer (DTC) smaller than 1 cm can be managed with either active surveillance or thyroidectomy, according to several treatment guidelines [6],[16],[17]. The choice of treatment method depends on the risk stratification of the thyroid nodule at the time of diagnosis. In cases of PTC smaller than 1 cm with very low risk (no evidence of extrathyroidal extension, no lymph node metastasis, no distant metastasis, no family history of thyroid cancer, no history of radiation exposure to the head and neck), active surveillance every six months is a completely acceptable option. Other cases require minimal surgical intervention, including lobectomy or total thyroidectomy [18]. Postoperative adjuvant treatments may include radioactive iodine (I-131) and hormone therapy; however, surgery remains the most crucial step in the treatment process [4]. Although active surveillance has recently been strongly recommended for PTC <1 cm, the patient's treatment choice remains the primary factor. All patients in our study underwent surgical treatment after being informed about the available treatment options. Of these, 66.4% underwent total thyroidectomy and 33.6% underwent lobectomy. Intraoperative findings explain the relatively high rate of total thyroidectomy. According to surgical records, some tumors were found adjacent to the trachea or recurrent laryngeal nerve, or there was gross evidence of thyroid capsule invasion during surgery, leading to a change from planned lobectomy to total thyroidectomy. In addition, 25.4% of patients were reported to have multifocal tumors (≥2 tumors), which was another reason for indicating total thyroidectomy.

The majority of patients underwent cervical lymph node dissection, with a higher proportion of patients in the total thyroidectomy group performing lymph node dissection compared to those who underwent lobectomy, at rates of 59% and 10.7%, respectively. Lobectomy is generally associated with a higher risk of recurrence and worse survival outcomes compared to total thyroidectomy in patients with thyroid cancer who are not classified as very low risk. Routine cervical lymph node dissection does not improve recurrence or survival rates—except in cases of medullary thyroid carcinoma—and may increase the risk of postoperative complications. Therefore, selective lymph node dissection is recommended based on the presence of nodal involvement [4]. In our study, surgical reports documented multiple cases where firm cervical lymph nodes suspicious for metastasis were noted, as well as certain cases with gross evidence of capsular invasion or tumor infiltration into the trachea or recurrent laryngeal nerve.

Postoperative TSH suppression therapy plays an important role because of the established role of TSH in promoting the growth of thyroid carcinoma of papillary and follicular types. In patients who undergo total thyroidectomy, lifelong thyroid hormone replacement with Thyrosine is mandatory, as the entire thyroid gland has been removed. In our study, 82 patients were indicated for Thyrosine compared to 81 patients who underwent total thyroidectomy, which is explained by the fact that Thyrosine was also indicated for lobectomy patients who exhibited elevated postoperative TSH levels or had a higher risk of recurrence. In our cohort, one patient who underwent lobectomy with suspicion for capsular invasion was prescribed a low dose of Thyrosine.

In our study, 31 patients were treated with radioactive iodine (RAI), among whom 30 were PTC patients and 1 had oncocytic carcinoma. Radioactive iodine therapy is not routinely administered to all thyroid cancer patients, particularly those with tumors ≤1 cm. RAI is typically indicated for tumors >4 cm, tumors with extrathyroidal extension, distant metastasis, the majority of cases with oncocytic or follicular thyroid carcinoma, or tumors measuring 1–4 cm accompanied by high risk of recurrence—such as those with aggressive histologic types (tall cell or columnar cell), lymph node metastasis, or in patients over 45 years of age [4].

4.4. Treatment outcomes

In our study, 10.7% of patients experienced postoperative hypocalcemia, with a higher tendency observed in those who underwent total thyroidectomy compared to lobectomy; this difference was statistically significant ($p<0.05$). This finding was consistent with that of Nguyen Xuan Hau et al. (2021) [19], with a 10.8% rate of hypocalcemia 24 hours after surgery. One patient in our study experienced hoarseness and postoperative infection. Currently, thyroid surgery is considered relatively safe. However, recurrent laryngeal nerve injury remains a reported complication in various studies. For instance, Nguyen Xuan Hau et al. (2021) [19] documented an incidence of 8.8% one week postoperatively. Nonetheless, most cases involve temporary injury, with only 1–3% resulting in permanent damage, depending on the study [4].

5. CONCLUSION

5.1. General and histopathological characteristics of papillary thyroid carcinoma ≤ 1 cm

The majority of patients were under 55 years of age (72.1%), with a female-to-male ratio of 7:1. The classic variant was the predominant histological subtype of papillary thyroid carcinoma (PTC), accounting for 68.9%. Solitary tumors were observed in 74.6% of cases. Most tumors showed no vascular invasion (99.2%), and capsular invasion was present in 15.6% of cases. Lymph node metastasis was found in 22.1% of patients, while no cases of distant metastasis were recorded. The majority of patients (95.1%) were diagnosed at stage I.

5.2. Treatment approaches for papillary thyroid carcinoma ≤ 1 cm

Total thyroidectomy was performed in 66.4% of cases, while 33.6% underwent lobectomy. Among those who underwent total thyroidectomy, 59% also received lymph node dissection. The majority of patients received radioiodine therapy (I-131) (74.6%), and 67.2% were treated with thyroxine (T4) hormone therapy.

Postoperative complication rates were relatively low (12.3%), with hypocalcemia being the most common complication (10.7%). A statistically significant association was found between total thyroidectomy and the occurrence of hypocalcemia ($p < 0.05$).

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