

## Characterization and Follow-Up of Papillary Thyroid Microcarcinomas Documented in a Level IV Clinic in Cali-Valle Del Cauca

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### Keywords:

Thyroid neoplasia; Papillary thyroid microcarcinoma; Lymphatic metastasis; Total thyroidectomy; Lobectomy

## 1. Summary

**1.1. Introduction:** Papillary thyroid microcarcinomas are malignant tumors of papillary origin, with a diameter of  $\leq 1$  cm. They generally have a favorable prognosis, characterized by slow growth, an asymptomatic course, and an overall survival rate of approximately 99% at 10 years. The rates of locoregional progression are typically  $<5\%$ , while distant metastasis occurs in  $\leq 1\%$  of cases. Materials and methods: The descriptive observational study, performed in Cali in a level IV clinic between 2018-2023, analyzed 140 patients with Papillary Thyroid Microcarcinoma (PTMC). Results: Many patients were women aged 40 to 60 years, residing in Cali, and affiliated with the Contributive regime. Most were asymptomatic or presented with thyroid enlargement. Although 14% had a family history of cancer, only 4% had a history of thyroid cancer. Chronic comorbidities were present in 49.3% of cases, and 12% had a history of hypothyroidism. Pathological findings revealed multifocality in 27% of patients, extrathyroidal extension in 5%, and lymphatic metastasis in 19.3%. Treatment primarily consisted of total thyroidectomy (82.1%) and lobectomy (17.9%). A relapse was observed in 3.6% of patients requiring additional

surgery. Conclusions: Proper staging, assessment of relapse risk, and rigorous monitoring are crucial for achieving favorable outcomes in patients with MPT. In cases of multifocal disease or the presence of other risk factors, total thyroidectomy is recommended.

## 2. Introduction

Papillary Thyroid Microcarcinomas (PTMC) are malignant thyroid tumors, whose diameter is  $\leq 1$  cm, generally manage an adequate prognosis, characterized by slow growth, asymptomatic course, overall survival of approximately 99% at 10 years, and figures of locoregional progression  $<5\%$ , distant  $\leq 1\%$ . Occasionally, they may present aggressive features and develop lymph nodes or distant metastases. They may belong to histologic variants associated with worse prognoses such as tall cells or tack cells. The incidence of this type of tumor has increased in the last decades due to the greater access to ultrasound, detecting non-palpable nodules [1]. There are associations between factors that aggravate the prognosis such as capsular invasion, multifocality, lymph node metastasis, measurement greater than 5 mm, and the presence of signs of progression during follow-up.

According to the American Thyroid Association (ATA), the classification of PTMC is a high, intermediate, and low risk of recurrence; the relevant variables for stratification are age, tumor size, invasion, and presence of lymph nodes and distant metastases [2]. The European consensus classifies a very low-risk patient as one with unifocal microcarcinoma ( $\leq 1$  cm), without extrathyroidal extension, while a low-risk patient is one with T1N0M0 or multifocal T1 [3].

Among the therapeutic options in the management of papillary microcarcinoma of the thyroid (PTMC), thermal and chemical ablation is a technical, non-surgical procedure; its use in thyroid cancer is more focused on the management of thyroid nodules. Chemical techniques have been implemented for decades; which constitute dehydrated ethanol, their related consequences are ischemic and coagulative necrosis, while thermal techniques are more recent; raising their temperature  $>60^{\circ}\text{C}$  which sometimes causes tissue coagulative necrosis [2]. However, there are other surgical options such as total thyroidectomy when multifocal PTMC is identified, although the implementation of this surgery continues to be very controversial according to the characteristics of each nodule. Lobectomy is considered an adequate surgical option in differentiated thyroid cancer (unifocal, without thyroid extension) since it avoids comorbidities in the patient post-surgery [4].

The implementation of Radioiodine Ablation (RIA) is suggested when there is lymph node involvement or distant metastasis, recombinant human TSH (rhTSH) should be used as a preparation in patients without distant metastasis [5].

### 2.1. Objective

To characterize patients with papillary thyroid Microcarcinoma of the thyroid from an IV-level clinic in the city of Cali between the years 2018-2023.

### 3. Materials and Methods

Retrospective descriptive observational study with an analytical component. A review was conducted of the database of 1,473 patients diagnosed with thyroid carcinoma at a level IV clinic in the city of Cali from January 2018 to December 2023. Of this group, 140 patients with a diagnosis of Papillary Thyroid Microcarcinoma (PTMC) were identified through clinical history review. The variables considered included sociodemographic factors (age, location, marital status, affiliation, and gender) as well as clinical variables, such as risk characteristics, the type of management received, disease progression, and disease-free survival.

Univariate analysis was performed in which median and interquartile range were estimated for quantitative variables while proportions and frequencies were estimated for qualitative variables; associations between variables were analyzed using the Mann-Whitney U test for quantitative variables; Fisher's exact test was used for the remaining variables. Survival functions were estimated using the Kaplan-Meier method. Survival curves were compared by log-rank test.

### 4.1. Ethical aspects

The study was approved by the research and ethics committee of the clinical institution. Informed consent for the use and review of medical records was granted by the institution. In accordance with bioethical guidelines, the four fundamental principles—autonomy, non-maleficence, beneficence, and justice—were upheld. Ethical criteria were established within the regulatory framework, considering Resolution 8430 of 1993 and the CIOMS Guidelines for Epidemiological Studies, which emphasize values such as respect for individuals and international ethical standards for guiding epidemiological research. Furthermore, all participants adhered to the ethical commitment to protect the clinical records and patient information.

### 4. Results

In the present study, 140 patients with a diagnosis of papillary Microcarcinoma of Thyroid were identified. The median follow-up was 33.5 months, with an age range (of 40-60 years), more frequent in females gender 89%, most patients reside in the city of Cali 58% belong to the Contributive regime 88%, there was a higher frequency of asymptomatic clinical picture with 55%, the most frequent symptom was a diffuse increase of Thyroid, 25% had a family history of cancer, 4% of these were Thyroid Cancer; within the history of importance, 49.3% suffered from chronic comorbidities, such as DM, HTA, etc. 12.1% of the patients had thyroid disorders (hypothyroidism/hyperthyroidism) before a diagnosis of Microcarcinoma; the most frequent tumor characteristics were: unifocal, without extra-thyroid tumor extension, without lymphatic metastasis, without distant metastasis. 82.1% were surgically approached with total thyroidectomy; 7.9% underwent post-surgical iodine therapy. Surgical complications were present in 12.1%, the most frequent being post-surgical hypothyroidism persisting despite pharmacological management. Lobectomy was performed on 18% with a relapse rate of 3.6%, for which reason the patient must undergo surgery again (Table 1).

Relapse-free survival at one year in patients with papillary microcarcinoma of the thyroid who underwent surgery was 97.1% (95%CI 94.4%-99.9%), while relapse-free survival at 48 months in patients who underwent surgery was 96% (95%CI 0.935-1) (Graph 1).

Patients who underwent total thyroidectomy had better relapse-free survival compared to those who underwent lobectomy (P-value: 0.02), with relapse-free survival at one year in patients who did not undergo total thyroidectomy, is 92% (95%CI: 0.820-1), while relapse-free survival at 48 months in patients who did not undergo total thyroidectomy is 86.6% (95%CI 0.734- 1) (Graph 2).

Patients who did not present lymphatic metastasis presented better relapse-free survival compared to those who did present this type of metastasis. (P value: 0.02), survival at one year in patients who presented lymphatic metastasis was 93% (95%CI 0.832-1), while survival at 48 months in patients who did not present lymphatic metastasis was 98.2% (95%CI 0.958- 1) (Graph 3).

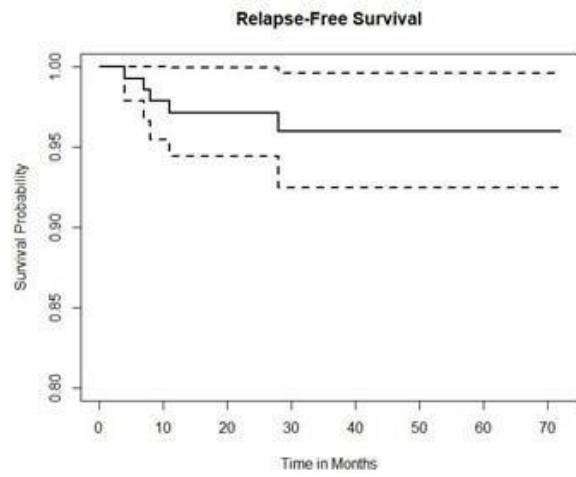
**Table 1:** Characterization of Sociodemographic and clinical variables of a patient with papillary thyroid microcarcinoma (2018- 2023) versus relapse variable

Characteristics	Description	Total n: 140	Relapse		Value-P
			St n: 5	No n: 135	
Years	Median/RIC	50,5 (40-60,5)	49 (40-51)	51 (40,5-61)	0,412
Sex	Feminine	124 (88,6%)	4 (80%)	120 (88,9%)	0,460
	Masculine	16 (11,4%)	1 (20%)	15 (11,1%)	
Civil State	Single	55 (39,3%)	2 (40%)	53 (39,3%)	0,309
	Married	48 (34,3%)	1 (20%)	47 (34,8%)	
	Free Union	32 (22,9%)	1 (20%)	31 (23,0%)	
	Widow	5 (3,6%)	1 (20%)	4 (3,0%)	
City of residence	Calí	81 (57,9%)	1 (20%)	80 (59,3%)	0,162
	Outside Calí	59 (42,1%)	4 (80%)	55 (40,7%)	
Regimen	Contributory	123 (87,9%)	4 (80%)	119 (88,1%)	0,482
	Subsidized	17 (12,1%)	1 (20%)	16 (11,9%)	
Symptomatic	No	77 (55,0%)	4 (80%)	73 (54,1%)	0,379
	yes	63 (45,0%)	1 (20%)	62 (45,9%)	
Diffuse thyroid enlargement	No	105 (75,0%)	5 (100%)	100 (74,1%)	0,331
	yes	35 (25,0%)	0 (0%)	35 (25,9%)	
Mild compressive symptoms	No	132 (94,3%)	5 (100%)	127 (94,1%)	1
	yes	8 (5,7%)	0 (0%)	8 (5,9%)	
Pain in neck region	No	131 (93,6%)	4 (80%)	127 (94,1%)	0,286
	yes	9 (6,4%)	1 (20%)	8 (5,9%)	
Dysphagia	No	134 (95,7%)	5 (100%)	129 (95,6%)	1
	yes	6 (4,3%)	0 (0%)	6 (4,4%)	
Dysphonia	No	134 (95,7%)	5 (100%)	129 (95,6%)	1
	yes	6 (4,3%)	0 (0%)	6 (4,4%)	
family history of cancer	No	121 (86,4%)	4 (80%)	117 (86,7%)	0,523
	yes	19 (13,6%)	1 (20%)	18 (13,3%)	
Degree of consanguinity	No	121 (86,4%)	4 (80%)	117 (86,7%)	0,523
	First Grade	8 (5,7%)	1 (20%)	7 (5,2%)	
	Second Grade	5 (3,6%)	0 (0%)	5 (3,7%)	
	Third Degree	6 (4,3%)	0 (0%)	6 (4,4%)	
thyroid cancer	No	135 (96,4%)	5 (100%)	130 (96,3%)	1
	yes	5 (3,6%)	0 (0%)	5 (3,7%)	
Others	No	124 (88,6%)	4 (80%)	120 (88,9%)	0,460
	yes	16 (11,4%)	1 (20%)	15 (11,1%)	
Comorbidity	No	71 (50,7%)	2 (40%)	69 (51,1%)	0,678
	yes	69 (49,3%)	3 (60%)	66 (48,9%)	
Other chronic comorbidity	No	90 (64,3%)	4 (80%)	86 (63,7%)	0,655
	yes	50 (35,7%)	1 (20%)	49 (36,3%)	
Thyroid Disease	No	122 (87,1%)	4 (80%)	118 (87,4%)	0,503
	Hypothyroidism	17 (12,1%)	1 (20%)	16 (11,9%)	
	Hyperthyroidism	1 (0,8%)	0 (0%)	1 (0,7%)	
Cancer	No	136 (97,1%)	5 (100%)	131 (97,0%)	1
	yes	4 (2,9%)	0 (0%)	4 (3,0%)	
Prior irradiation	No	138 (98,6%)	5 (100%)	133 (98,5%)	1
	yes	2 (1,4%)	0 (0%)	2 (1,5%)	
Histology type	BACAF	13 (9,3%)	0 (0%)	13 (9,6%)	1
	Pathology	127 (90,7%)	5 (100%)	122 (90,4%)	
Multifocality	No	102 (72,9%)	4 (80%)	98 (72,6%)	1
	yes	38 (27,1%)	1 (20%)	37 (27,4%)	
Extra thyroid tumor extension	No	133 (95%)	4 (80%)	129 (95,6%)	0,229
	yes	7 (5%)	1 (20%)	6 (4,4%)	
Lymphatic metastasis	No	113 (80,7%)	2 (40%)	111 (82,2%)	0,049*
	yes	27 (19,3%)	3 (60%)	24 (17,8%)	
Distant metastases	No	139 (99,3%)	4 (80%)	135 (100%)	0,035*
	yes	1 (0,7%)	1 (20%)	0 (0%)	
Total Thyroidectomy	No	25 (17,9%)	3 (60%)	22 (16,3%)	0,039*
	yes	115 (82,1%)	2 (40%)	113 (83,7%)	
Hemithyroidectomy	No	115 (82,1%)	2 (40%)	113 (83,7%)	0,039*
	yes	25 (17,9%)	3 (60%)	22 (16,3%)	
Type Hemithyroidectomy	No	115 (82,1%)	2 (40%)	113 (83,7%)	0,029*
	Both	13 (9,3%)	2 (40%)	11 (8,1%)	
	Right	5 (3,6%)	1 (20%)	4 (3,0%)	
Iodotherapy	Left	7 (5,0%)	0 (0%)	7 (5,2%)	0,340
	No	129 (92,1%)	4 (80%)	125 (92,6%)	
Surgical complications	yes	11 (7,9%)	1 (20%)	10 (7,4%)	0,482
	No	123 (87,9%)	4 (80%)	119 (88,1%)	
Post- surgical hypothyroidism	yes	17 (12,1%)	1 (20%)	16 (11,9%)	1
	No	132 (94,3%)	5 (100%)	127 (94,1%)	
Hypocalcemia	yes	8 (5,7%)	0 (0%)	8 (5,9%)	1
	No	137 (97,9%)	5 (100%)	132 (97,8%)	
Dysphonia	yes	3 (2,1%)	0 (0%)	3 (2,2%)	1
	No	137 (97,9%)	4 (80%)	133 (98,5%)	
Hashimoto's thyroiditis	yes	3 (2,1%)	1 (20%)	2 (1,5%)	1
	No	136 (97,1%)	5 (100%)	131 (97%)	
Size	> 5 MM	89 (63,6%)	2 (40%)	87 (64,4%)	0,354
	< 5 MM	51 (36,4%)	3 (60%)	48 (35,6%)	

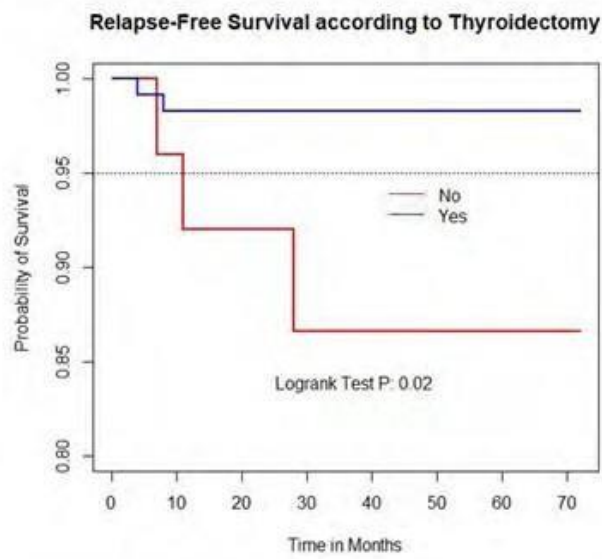
\*Significant at 0.05.

\*\*The Mann-Whitney U test (sometimes called the Wilcoxon rank sum test) was used.

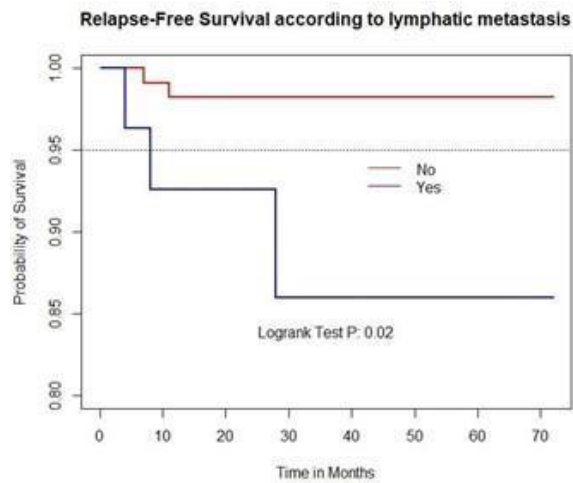
\*\*\*For the rest of the variables, Fisher's exact test was used.



**Graph 1:** Relapse-free survival in patients with papillary thyroid microcarcinoma (2018- 2023).



**Graph 2:** Relapse-free survival according to total thyroidectomy in patients with papillary thyroid microcarcinoma (2018- 2023).



**Graph 3:** Relapse-free survival according to lymphatic metastasis in patients with papillary thyroid microcarcinoma (2018- 2023).

## 5. Discussion

Papillary thyroid microcarcinoma is often discovered incidentally during ultrasound examinations, with the diagnosis being confirmed through surgical pathology. The effectiveness of the ATA risk stratification system in predicting recurrence of MPTC has raised concerns about over diagnosis, as it has a low Positive Predictive Value (PPV) for identifying recurrence. As a result, risk stratification may not be a reliable tool for accurately predicting the recurrence of MPTC [2].

The age range of patients with MPTC in our study was between 40 and 60 years, with 88% of them being female. Multiple studies have included larger cohorts of MPTC patients. For instance, in a study by Ki Wan Park in 2023, conducted in the United States, a cohort of 22,282 patients (from 2010 to 2015) was analyzed to determine Overall Survival (OS). In this cohort, 82.6% were women and 17.4% were men, with a mean age of 51 years [4]. According to this overview, most studies have been conducted in China, with a mean age of 45 to 50 years, and many patients are women [6].

Regarding the clinical presentation of the patients, more than 50% were asymptomatic. Among the symptomatic patients, the most common manifestations included diffuse thyroid enlargement, neck pain, mild compressive symptoms, dysphagia, and dysphonia. These findings align with those of other studies, which report that the characteristic presentation of MPTC is typically asymptomatic [7]. Occasionally, it may present at the time of diagnosis as a multifocal lesion, with extracapsular invasion, or with metastasis to cervical nodes, which gives it risk factors for recurrence, but the most usual pattern is the unifocal nodule, without extratemporal extension, encapsulated and without lymph node or distant metastasis. According to Tuttle et al. (2023) in their review of 5,074 cases, the majority of MPTC are unifocal. In this cohort, 27% of patients were presented with intrathyroidal nodules, and the average tumor size was 6 mm. The rate of lymph node metastasis was less than 1%, and no cases of distant metastasis were reported [6].

The approach to the patient with a diagnosis of MPTC is multidisciplinary, it is relevant to the stratification and proper diagnosis to provide the best treatment option; It was shown that observation can become a management option for papillary thyroid microcarcinoma without unfavorable characteristics, regardless of the patient's history and clinical features; thus understanding that the characteristics of the tumor, as well as the signs of progression such as increased tumor size and/or appearance of lymph node metastasis during follow-up, are decisive to define conduct with the patient; against negative characteristics:

- a: location adjacent to the trachea or dorsal surface of a thyroid lobe.
- b: invasion of recurrent laryngeal nerve, metastases in the neck.

- c: cytological findings suggesting a high degree of malignancy.
- d: presence of signs of progression during follow-up.
- e: tumor adjacent to the posterior capsule, surgery is recommended.

Among the surgical options, it is relevant to establish a total thyroidectomy or lobectomy [8].

According to a study by Park et al. (2023), a cohort analysis was conducted to assess Overall Survival (OS) and Disease-Specific Survival (DSS) in patients with MPTC who underwent total thyroidectomy or lobectomy. The study found that more than 70% of patients who underwent total thyroidectomy had multifocal tumor characteristics. The OS for patients who received surgical treatment was 98%, and the DSS was 99% at 2 years. The OS for patients who underwent total thyroidectomy and lobectomy was 69.54 and 68.95 months, respectively. In the present study, the OS for patients who underwent thyroidectomy was also higher, although with a significantly greater variation [4].

In a study published by Dimov (2023), 184 patients with MPTC who underwent surgery over a five-year period were included. The objective of the study was to identify factors associated with invasion. To achieve this, the sample was divided into two groups: 1) Patients who underwent total thyroidectomy and neck dissection, including those with capsular invasion, intra-organ metastasis, multifocal growth, and positive lymph nodes; and 2) Patients who underwent total thyroidectomy with central and lateral neck dissection, including those with lateral metastatic lesions, capsular invasion, and multifocality. The study demonstrated that capsular invasion and multifocality are closely associated with advanced disease and metastasis, typically to the neck lymph nodes. Based on these findings, total thyroidectomy, under these specific conditions, is considered the best therapeutic option for these patients [9].

The Endocrine and Metabolism Association conducted a retrospective study involving 11,570 patients with MPTC, identifying 177 subtypes of aggressive microcarcinomas, characterized by extra-thyroidal tumor extension and central and lateral metastatic lymph nodes in the neck. Among the aggressive subtypes identified were tall cells, diffuse sclerosing, wedge-shaped, and colloid cell variants. These aggressive subtypes were associated with greater capsular invasion compared to non-aggressive subtypes. Most of these cases exhibited multifocality, and a significant proportion of patients had lymph node metastasis in the central region of the neck. Surgical management of these aggressive subtypes typically involved total thyroidectomy and lateral lymph node dissection. Among high-risk patients, 3.5% experienced lymph node recurrence in either the central or lateral neck regions, with an average follow-up time of 58.6 months. These findings are consistent with the criteria considered in the present study when selecting between

total thyroidectomy and lobectomy [10].

Among the management options for patients with MPTC, active surveillance aims to destroy the small papillary thyroid cancer focus without having to undergo a surgical procedure. Ultrasound-guided percutaneous ablation technologies, developed as a non-surgical therapeutic option to destroy small intra-thyroid papillary thyroid cancer nodules, are used for this process. In Microcarcinoma without high-risk characteristics it is not suggested to use ablation, as the limitation of this technique involves the definitive histological analysis of a nodule, for this reason, there is a risk of under diagnosis.

We conducted a retrospective study reviewing published studies that evaluated the safety and efficacy of percutaneous thermal ablation in low-risk papillary thyroid cancer. Most of these studies were performed in Chinese institutions in adults; more than half of the ablations were performed by radiofrequency, approximately 25% were performed by microwave ablation, and 12.5% by laser. While 73% of the studies restricted ablation to a single thyroid cancer nodule, 27% of the series included patients who had multiple nodules ablated within the same lobe. While the median duration of follow-up was 3.3 years [6].

## 6. Conclusion

The conclusions of this study suggest that surgical management with the technique of total thyroidectomy is the most successful option for the management of papillary thyroid microcarcinoma with extrathyroid invasion, multifocality, or lymph node metastasis; for patients who do not meet the risk criteria mentioned previously, close observation with ultrasound controls is recommended and for those patients with difficulties in access to health services surgical management with hemithyroidectomy may be an option. For this reason, it is necessary to adequately stratify the risks of a patient with MPTC and establish surveillance protocols to obtain better results. Additionally, new studies are required, mainly prospective, for the application and validation of the results presented in this article.

## 7. Acknowledgments

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## 8. Conflict of Interest

The authors declare no conflict of interest.

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