

# Papillary thyroid microcarcinoma: A study of 44 cases

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## ABSTRACT

**Objective:** Papillary thyroid microcarcinoma (PTMC) frequency is increased recently. Treatment of these tumors is controversial: many aspects remain poorly elucidated. The aim of the study was to evaluate clinicopathological features of PTMC and to expose the therapeutic and evolutive characteristics of this entity.

**Methods:** This was a retrospective study including 44 patients with an incidental PTMC ( $\leq 1$ cm) treated and operated between 2006 and 2015.

**Results:** PTMC was diagnosed in patients operated for nodular goiter in 60%, thyroid adenoma in 25% and Graves' disease in 3%. Twenty-eight of our patients underwent total thyroidectomy. Frozen sections examination concluded to a benign lesion in 22 cases and doubtful one in six cases. Bilateral central lymph node dissection (CLND) was conducted in the latter cases. The remaining patients underwent a lobectomy which frozen section examinations concluded to a benign tumor in 12 cases and doubtful one in 4 cases. These patients underwent an ipsilateral CLND.

Out of the 44 PTMC, 25 cases were judged as invasive tumors. The invasive PTMC patients who had initially undergone a lobectomy were re-operated for total thyroidectomy and CLND. Full body Iodine screening was indicated in 29 cases. After a mean follow-up of 3 years, we have noted no cases of mortality, local recurrence or distant metastasis.

**Conclusion:** The treatment of patients with PTMC may vary from watchful waiting to total thyroidectomy with lymph node dissection and adjuvant radioactive iodine. treatment depends on the presence of aggressive characteristics.

**Key-words:** Thyroid cancer, papillary thyroid microcarcinoma, lymphatic metastasis, thyroidectomy, Watchful Waiting.

## INTRODUCTION

Recently, papillary thyroid microcarcinoma (PTMC) diagnosis rate had increased due to the extensive use of ultrasound examinations of the thyroid and the ultrasound-guided fine-needle aspiration cytology (FNABs) [1]. In fact, the latter allows the cytological evaluation of nodules smaller than 1 cm. Thus, it is possible to detect very small thyroid carcinomas [2]. Because PTMC is being diagnosed with increasing frequency, it is important to describe the clinical and histological characteristics that confer cancer aggressiveness. This knowledge will enhance the development of treatment guidelines for a cancer that may reach endemic proportions in the future [2].

The prognosis of PTMC is generally excellent with an overall 10-year survival rate superior than 90% [3]. Several conferences have established guidelines for diagnosis and treatment [2-4]. Nevertheless, many aspects remain poorly elucidated, especially concerning the indications for prophylactic central neck dissection or Iodine-131 remnant ablation, resulting in a wide spectrum of responses for this condition ranging from observation without treatment to total thyroidectomy with radioactive iodine treatment [1]. The aim of the study was to evaluate clinicopathological features of PTMC and to expose the therapeutic and evolutive characteristics of this entity. **Methods:**

This was a retrospective study including 44 patients with thyroid papillary microcarcinoma treated in the ENT department of Habib Thameur hospital between 2006 and 2015. The diagnosis of tumors was confirmed histologically. The follow-up of patients was conducted until December 2017. Thyroglobulin and anti-thyroglobulin autoantibodies values were routinely determined in the same serum samples, only in cases of total thyroidectomy. Also included.

Demographic characteristics, age and gender, ultrasonography aspects, the purpose and mode of surgery, tumour histopathological characteristics, adjuvant treatment with 131I and outcome were the main studied variables.

## RESULTS:

Among these 44 patients, 60% were operated for nodular goiter, 25% for thyroid adenoma and 3% for Graves' disease. The mean age of the patients was 46 years [range 13 -75 years]. Thirty-eight patients were women, and 6 were men. Patient medical history included auto-immune diseases in 2%. None of the patients had a history of external x-ray therapy. However, family histories of goiter and thyroid cancer were found respectively in 34% and 2% of cases. All of our patients were diagnosed with incidental PTMC found in



histopathology examination for patients who underwent total or hemithyroidectomy. Twenty eight of our patients underwent total thyroidectomy, for which the frozen sections examination has answered benign in 22 cases and doubtful in six cases. These 6 cases underwent then a bilateral central lymph node dissection (CLND). Sixteen patients underwent a lobectomy, for which the frozen sections examination has answered benign in 12 cases and doubtful in 4 cases. These 4 cases underwent then an ipsilateral CLND.

Histopathology confirmed that all our patients had papillary microcarcinoma in 64% and vesicular papillary microcarcinoma in 34%. The mean size of tumors was 4.62 mm.

Pejorative risk factors were also studied in the pathologic exam, such as: tumor size > 5mm, multiple tumor foci, capsule fraction, extra-glandular invasion (Table I).

**Table I: Pejorative histological risk factors**

Criteria	Prevalence
Tumor size > 5mm	43%
Single tumor focus	86%
Multiple tumor foci in one lobe	9%
Bilateral multifocal PTMC	5%
Capsule fraction	23%
Extra glandular invasion	0%
Vascular or lymphatic embolism	0%

Out of the 44 PTMC, 25 cases were judged as invasive and 19 as non-invasive and unifocal. Nine of the invasive PTMC patients had initially undergone an hemithyroidectomy. They were all re-operated with total thyroidectomy and CLND. Two cases of CLND had lymph node metastasis.

Seven of the non-invasive unifocal cases had initially underwent hemithyroidectomy with no indication for total thyroidectomy surgery, and therefore were subject to clinical and radiological surveillance.

Full body Iodine screening was indicated in 29 cases: all 25 cases of invasive PTMC and 4 cases of non-invasive PTMC who underwent total thyroidectomy (3 cases of lymph nodes present in Ultra-Sound (US) and one case of detectable Thyroglobulin). Out of the 25 cases of invasive PTMC, 18 presented with intense fixation of the thyroid bed and therefore continued with the radioactive Iodine 131 treatment, requiring one dose (100mCi) in 10 cases and 2 doses in 8 cases to obtain remission. Concerning the other 7 cases of invasive PTMC and the 4 cases of non-invasive PTMC, they presented with low fixation and therefore were subject to clinical and radiological surveillance.

Our different therapeutic patterns were summarized in figure 1 and 2.

All patients who underwent total thyroidectomy were prescribed a suppressive L-thyroxine opotherapy. Follow-up was clinical, radiological (neck US in 6 to 12

months) and biological (serum thyroglobulin levels in 6 to 12 months after surgery).

After a mean follow-up period of 3 years, we have noted no cases of mortality, local recurrence or distant metastasis.

## DISCUSSION:

The incidence of PTMC is increasing worldwide due to earlier diagnosis of thyroid cancers and possibly also to the increase in the real incidence of this disease [5-6-7]. In fact, since the introduction of US-guided FNAB, a progressive increase in the prevalence of PTMC has been observed to pass from 12% before 1980 to 25% after 1990 [8]. Furthermore, cancers less than or equal to 5 mm were more frequent from 1996 to 2001 than those between 5–10 mm [9]. These observations could be explained by a higher exposition to ionized radiations or other unidentified factors [7]. Papillary thyroid carcinoma represents, for many authors, the most common histological type of thyroid cancers [10-12].

PTMC prognosis is excellent and the survival rate of patients is comparable to that of a control group of same age and gender [13,14]. In a series of 900 PTMC, Hay et al. have shown that more than 99% of their patients have not developed metastasis nor died of their disease [10]. The death risk related to PTMC is very low around 0.3% [6-7]. In our study, no case of death was noticed. Therefore, the analysis of prognostic factors is mainly related to the risk of recurrence. Through different meta-analysis, Roti et al. have evaluated 9379 cases and calculated the risk of local and/or lymphatic recurrence to 2.4% and metastatic rate to 0.27% [6]. Whereas, Hay et al. found that the recurrence risk at 20 and 40 years of age were 6% and 8% respectively [10]. Certain histological variants of PTMC may be more aggressive, such as the tall cell variant found in 1% of cases in the Pelizzo et al. study [9] or the diffuse sclerosing variant found in 5% to 11.7% of PTMC according to studies [6]. Nevertheless, the prognostic impact of these histological variants has not been proven yet.

Many studies [1-15] found that age was not a significant factor in predicting disease recurrence or survival for PTMC. Other studies corroborated that an age superior to 45 years was classically associated to a higher risk of metastasis [10, 16-18].

Multifocality is a frequent event, found between 20 to 40% of cases in other series and in 5% in our study, but its prognostic significance is still controversial. Studies failed to demonstrate any statistically significant correlation between tumor multifocality and the following factors: age, gender, tumor size, extension beyond the thyroid, central neck lymph node involvement at diagnosis and risk of recurrence. In contrast, age < 45 years, male gender and tumor size > 5 mm were associated with a higher risk of central neck lymph node involvement at diagnosis [6,10,11,19-21]. Among the various parameters studied, tumor size (>5 mm; P = 0.008) was the only factor associated with a significantly



higher risk of tumor recurrence [1,4,6,11]. Initial central lymph node metastasis (CLNM) are relatively common in PTMC patients [6,16], varying between 30% and 64% in some studies [10,11,22]. Many authors suggested that CLNM was usually correlated to a higher risk of recurrence [6-23]. Hay et al. found that the risk of recurrence at 20 years moved from 0.8% in patients without CLNM to 16% in patients with CLNM [10]. According to some studies, male sex, tumor size > 0.5 cm, extrathyroidal extension, and multifocality were associated with a significantly increased risk of CLNM [3-24-25]. Moreover, lymph node involvement was detected on central neck dissection in 16% of patients when tumor size (T) was  $\leq 5$  mm versus 37% when T was  $> 5$  mm.

The diagnostic and therapeutic management of differentiated thyroid cancer has been regularly the subject of French, European and American consensus conferences and is therefore increasingly well-defined. One of these incompletely resolved issues concerns the indications for central neck dissection in the absence of identified lymph node metastasis (prophylactic dissection) and Iodine-131 therapy [16-23]. It is debatable whether total/near total thyroidectomy or lobectomy is the appropriate treatment for patients with microcarcinoma of the thyroid. There is a general agreement to indicate a total thyroidectomy everytime there was multifocality, extrathyroidal extension, CLNM, distant metastasis or a history of cervical radiation. In these cases, total thyroidectomy would decrease the recurrence risk, allow a radioactive Iodine therapy and facilitate postoperative follow up [16-18]. On the other hand, in case of unifocal, intrathyroidal PTMC, with no CLNM and without a history of cervical radiation, the latest American and European recommendations did not indicate a total thyroidectomy [6,7,16,17,18,26].

Many arguments about PTMC treatments have focused on routine central lymph node dissection (CLND). Different consensus conferences were not able to conclude whether CLND was beneficial or not. Arguments in favor of CLND were that CLNM was relatively frequent in PTMC. In the other hand, CLND allowed a better staging of the disease and may indicate thus an adjuvant treatment by radioactive Iodine [1-18]. On the contrary, arguments against CLND were the absence of clearly demonstrated profit of CLND over the recurrence rate, and the potentially morbid outcome of prophylactic CLND especially for the parathyroid glands [27,28]. There is, however, a consensus on the necessity of a CLND and/or lateral cervical dissection in case of lymph node metastasis detected before or during surgery [16-18].

It is unclear whether I-131 treatment after thyroidectomy is effective in reducing the recurrence rate of PTMC. According to the American Thyroid Association (ATA), Radioactive Iodine remnant ablation is not routinely recommended after thyroidectomy for patients with multifocal papillary microcarcinoma in absence of other adverse features (Strong recommendation, Moderate-

quality evidence) [26]. According to French guidelines for the management of patients with differentiated follicular thyroid cancer, radioactive Iodine treatment is indicated in case of extra thyroidal extension, CLNM or distant metastasis (doses of 100mCi). Whereas, there is no consensus concerning the need for adjuvant Iodine-131 therapy after surgery in patients with N0 or Nx unifocal, intrathyroidal PTMC. In the presence of multifocality or an aggressive histological variant, the indication of adjuvant Iodine-131 therapy is disputed. Some suggested a lower dose of radioactive Iodine (30 mCi) [17].

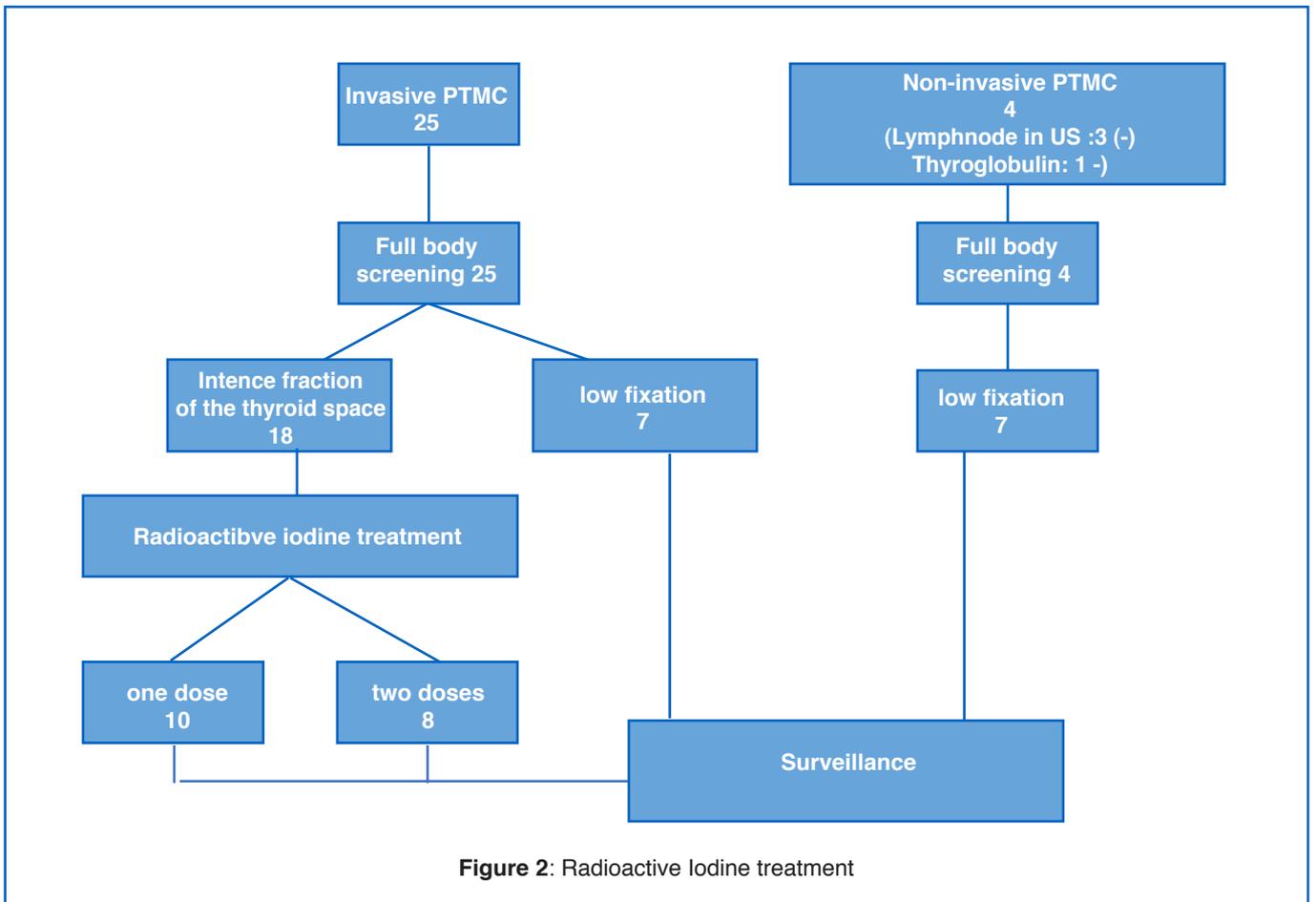
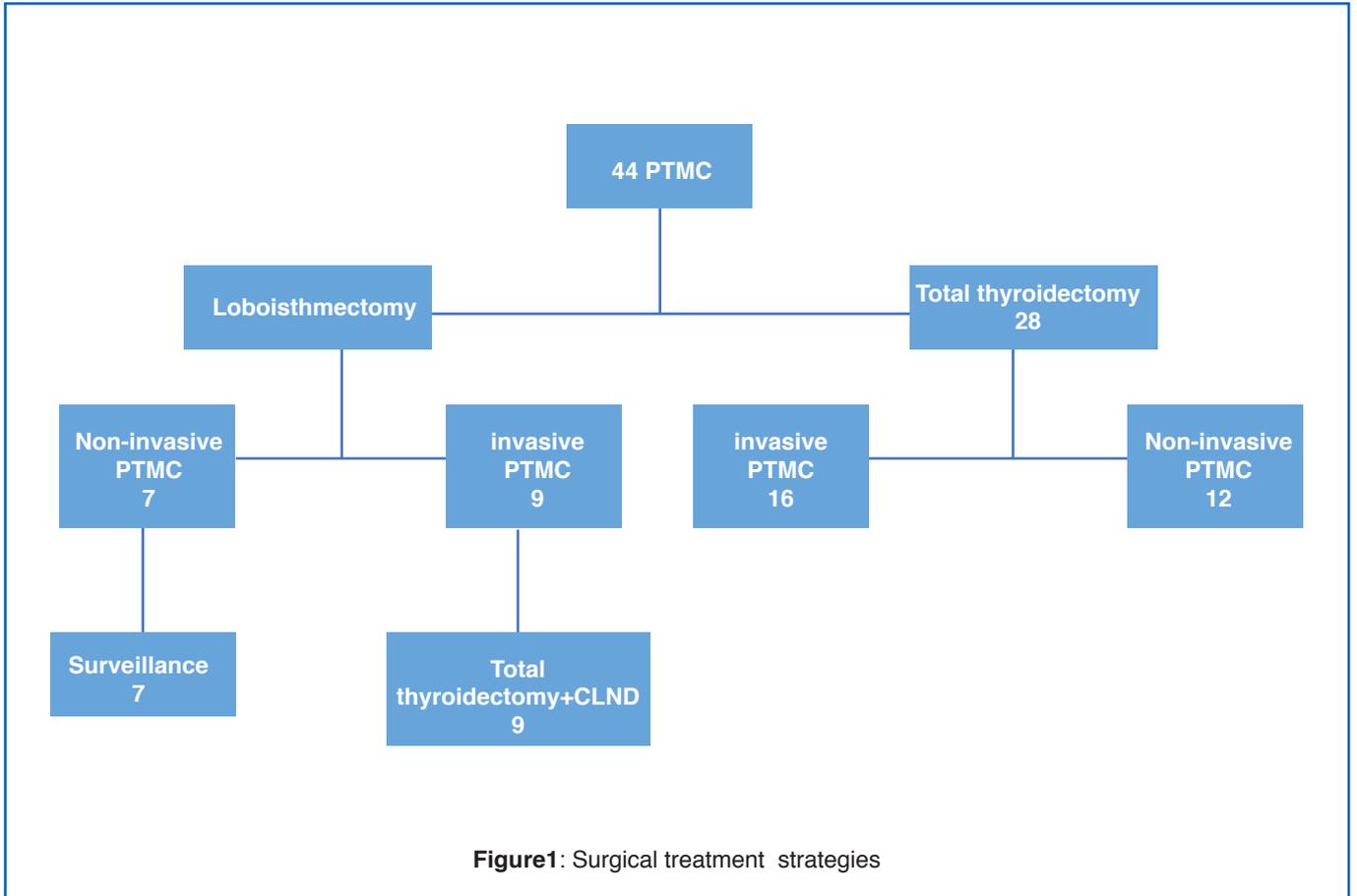
## CONCLUSION:

The treatment of patients with PTMC is controversial. It may vary from active surveillance to total thyroidectomy with lymph node dissection followed by radioactive Iodine treatment depending on the presence of aggressive characteristics. We practiced total thyroidectomy with CLND in all cases of invasive PTMC. Radioactive Iodine treatment was indicated every time a risk factor was found (invasive PTMC, CLNM, lymph node enlargement in US and detectable thyroglobulin after surgery).

## Compliance with ethical standards

**Conflict of interest:** The authors stated that there is no conflict of interest.

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