



Locoregional and Distant Recurrences of Papillary Thyroid Carcinoma: A Case Series of 12 Patients

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DOI: [10.36347/gamj.2023.v04i01.001](https://doi.org/10.36347/gamj.2023.v04i01.001)

| Received: 22.11.2022 | Accepted: 27.12.2022 | Published: 04.01.2023

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Abstract

Original Research Article

Papillary thyroid carcinoma (PTC) is the most common type of thyroid malignancy, constituting more than 80% of thyroid cancers. Patients with PTC usually have excellent outcomes with appropriate therapy, while up to 30% of patients present with aggressive disease, including patients with locoregional recurrence and distant metastasis. **Aim:** The aim of this study is to analyze the characteristics of patients with papillary carcinoma of the thyroid with locoregional and distant recurrences. **Materials and methods:** Our study was retrospective and included 12 patients with locoregional and distant recurrences of papillary thyroid carcinoma, followed in the Day-Hospital unit of the endocrinology, diabetology, metabolic diseases and nutrition department of the Mohammed VI University Hospital of Marrakech. **Results:** We included 12 cases of locoregional and distant recurrence of papillary thyroid carcinoma. 10 of our patients are female and 2 are male with a sex ratio of 1/5. The mean age of our patients was 47 years [22 - 69], 8 patients were younger than 55 years, and 4 were older than 55 years, the majority of our female patients are younger than 55 years. The initial surgical treatment consisted of lobo-isthmectomy in one patient, total thyroidectomy in 9 of our patients and thyroidectomy with lymph node dissection in 2 cases. Five of our patients had a tumor size greater than 4cm, in 3 cases the tumor size was between 2.1cm and 4cm, and in 4 patients it was less than 2cm. In our series we noted multifocality in only one patient. Capsular invasion was observed in 6 patients, representing half of the cases. As for the aggressive histological type, we noted only one case of a patient with the oncocyctic variant of papillary carcinoma on anatomical-pathological study. Two of our patients had lymph node metastasis in the cervical region at the time of diagnosis. None of our patients had distant metastasis at the time of diagnosis. In one case the ATA risk stratification of recurrence was in favor of a low recurrence risk. In 3 patients the risk of recurrence was intermediate and in 8 cases the risk of recurrence was high. All our patients received radioiodine therapy, 6 patients had received a single cure of radioiodine therapy, 4 patients had received two cures, only one patient had received 3 cures and one patient had received 4 cures of radioiodine therapy. Only one patient had received 2 lines of targeted therapy: sorafenib and sunitinib. The average follow-up time of our patients was 51 months [12 - 96]. The mean thyroglobulin level at the time of diagnosis of recurrence was 1250.16 ug/l [0.3 - 14245]. Eight patients had locoregional lymph node recurrence alone, one patient had lymph node and lung metastasis, one case had lymph node and bone recurrence in the right sacroiliac joint. One case had a bone metastasis in the tibia. One case had pulmonary and bone metastases in the femur. During the follow-up period, none of our patients died. **Conclusions:** Papillary thyroid carcinoma is an indolent disease, but cases having certain characteristics are likely to show recurrence and even become life-threatening, fortunately, various tools and treatment recommendations are available to help detect a recurrence.

Keywords: Papillary thyroid carcinoma (PTC), thyroid malignancy, thyroid cancers, metabolic diseases, radioiodine therapy.

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INTRODUCTION

The incidence of thyroid cancer has rapidly risen over the last four decades worldwide [1, 2]. There were 586,202 new cases of thyroid cancer worldwide in 2020, accounting for 3.0% of all cancer patients. Papillary thyroid carcinoma (PTC) is the most common type of thyroid malignancy, constituting more than 80% of thyroid cancers. Patients with PTC usually have

excellent outcomes with appropriate therapy, while up to 30% of patients present with aggressive disease, including patients with locoregional recurrence and distant metastasis [3, 4].

The aim of this study is to analyze the characteristics of patients with papillary carcinoma of the thyroid with locoregional and distant recurrences.

MATERIALS AND METHODS

Our study was retrospective and included 12 patients with locoregional and distant recurrences of papillary thyroid carcinoma, followed in the Day-Hospital unit of the endocrinology, diabetology, metabolic diseases and nutrition department of the Mohammed VI University Hospital of Marrakech.

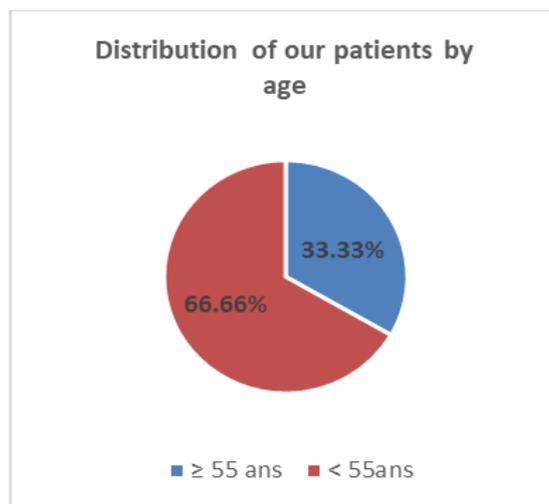
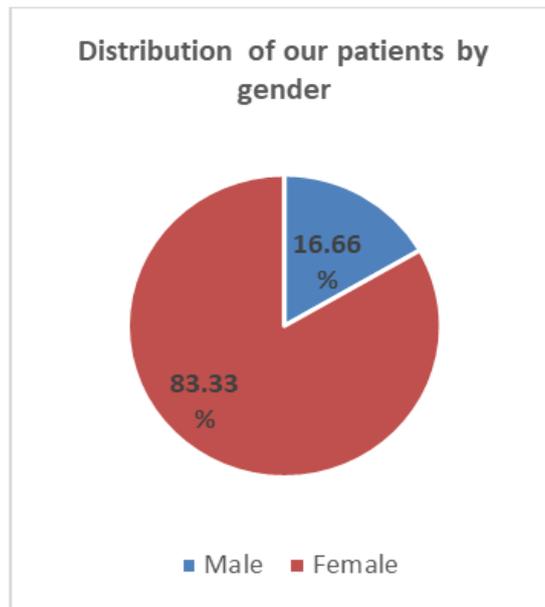
All patients were followed by blood tests (thyroid stimulating hormone, thyroglobulin and anti-thyroglobulin antibodies) and imaging tests such as neck ultrasound once or twice a year. We considered cases to have recurrent papillary carcinoma when recurrent lesions were detected by imaging exams and/or increasing thyroglobulin measurements.

Clinical and para-clinical data were collected from the patients' medical records. For each case we recorded the clinical and para-clinical elements as well as the anatomopathological parameters.

RESULTS

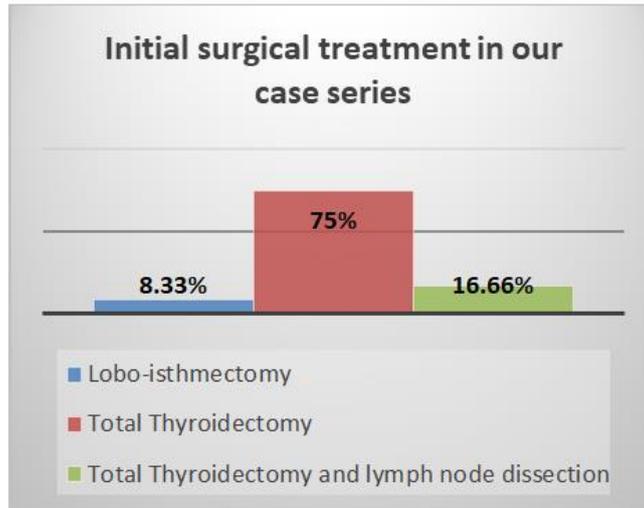
We included 12 cases of locoregional and distant recurrence of papillary thyroid carcinoma. 10 of our patients (83.33%) are female and 2 (16.66%) are male with a sex ratio of 1/5.

The mean age of our patients was 47 years [22 - 69], 8 patients (66.66%) were younger than 55 years, and 4 (33.33%) were older than 55 years, the majority of our female patients are younger than 55 years.



The initial surgical treatment consisted of lobo-isthmectomy in one patient (8.33%), total thyroidectomy in 9 of our patients (75%) and

thyroidectomy with lymph node dissection in 2 cases (16.66%).

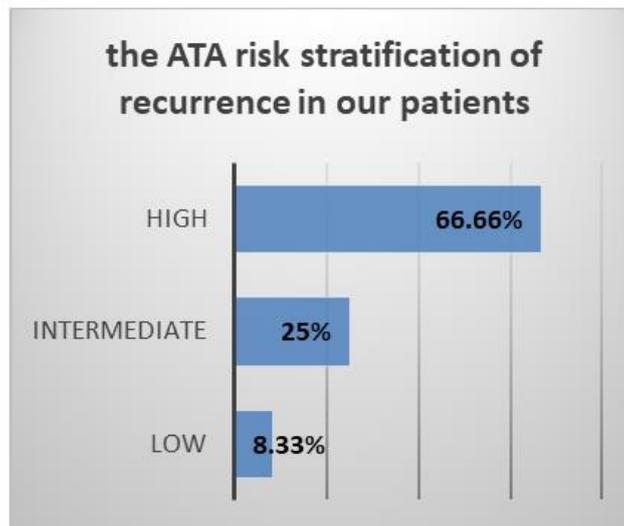


Five of our patients (41.66%) had a tumor size greater than 4cm, in 3 cases (25%) the tumor size was between 2.1cm and 4cm, and in 4 patients (33.33%) it was less than 2cm.

In our series we noted multifocality in only one patient (8.33%). Capsular invasion was observed in 6 patients, representing half of the cases (50%). As for the aggressive histological type, we noted only one case (8.33%) of a patient with the oncocytic variant of papillary carcinoma on anatomical-pathological study.

Two of our patients (16.66%) had lymph node metastasis in the cervical region at the time of diagnosis. None of our patients had distant metastasis at the time of diagnosis.

In one case (8.33%) the ATA risk stratification of recurrence was in favor of a low recurrence risk. In 3 patients (25%) the risk of recurrence was intermediate and in 8 cases (66.66%) the risk of recurrence was high.

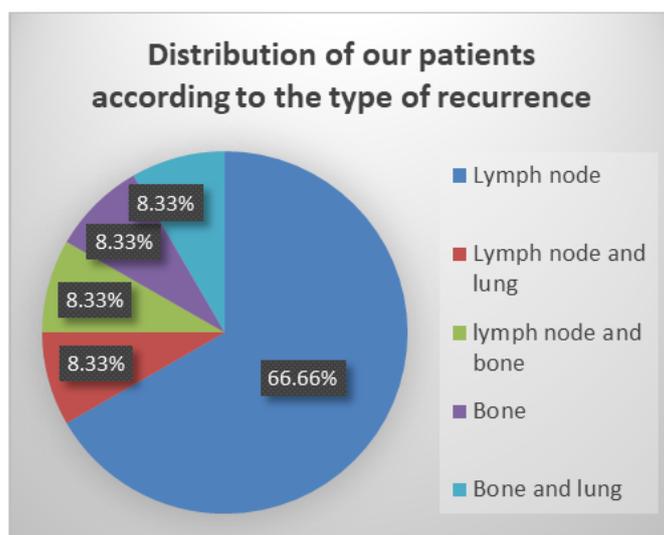


All our patients received radioiodine therapy, 6 patients (50%) had received a single cure of radioiodine therapy, 4 patients (33.33%) had received two cures, only one patient (8.33%) had received 3 cures and one patient (8.33%) had received 4 cures of radioiodine therapy. Only one patient (8.33%) had received 2 lines of targeted therapy: sorafenib and sunitinib.

The average follow-up time of our patients was 51 months [12 - 96]. The mean thyroglobulin level

at the time of diagnosis of recurrence was 1250.16 ug/l [0.3 - 14245].

Eight patients (66.66%) had locoregional lymph node recurrence alone, one patient (8.33%) had lymph node and lung metastasis, one case (8.33%) had lymph node and bone recurrence in the right sacroiliac joint. One case (8.33%) had a bone metastasis in the tibia. One case (8.33%) had pulmonary and bone metastases in the femur.



During the follow-up period, none of our patients died.

DISCUSSION

The rate of papillary thyroid cancer among woman is nearly three times higher than men. In females [7], the age-specific incidence rate rises sharply at the beginning of the reproductive years, with increasing age peaking at 40–49 years, while in men the peak is at 60–69 years. The incidence rates equalize by 85 years of age [5, 6].

To date, several studies employing large numbers of patients have investigated the prognostic significance of patient age. In recent studies, 55 years has generally been adopted as the cutoff age [9].

Jonklaas *et al.*, reported that women <55 years old had improved disease-specific compared survival with men, while both men and women >55 years had similar outcomes [8]. In our study, we observe the same results within the literature [7-9]. During initial thyroid surgery for primary tumors, it is essential to identify patients at high risk for cancer recurrence.

The size of papillary thyroid carcinoma nodules is the first and most important piece of information used by clinicians in planning for treatment of these cancers [11]. Most high-risk papillary and follicular thyroid carcinoma patients receive 131I ablation therapy [10]. Micrometastases are detectable during the first postsurgical year through whole body therapeutic or diagnostic scanning.

Although the relationship between LN metastasis and prognosis remains controversial, most studies agree that LN metastasis is an important risk factor for locoregional recurrence and distant metastasis, and complete removal of the metastatic LN is generally performed to reduce the risk for local

recurrence [12, 13] the majority of our patients underwent aggressive surgery.

For the therapeutic component, there are some conventional strategies for distant metastasis/recurrence, such as reoperation, RAI therapy and extrabeam radiotherapy, but controlling distant metastasis/recurrence by these modalities is often difficult and new therapeutic strategies are expected. Recently, tyrosine kinase inhibitors such as sorafenib and lenvatinib became available for differentiated thyroid carcinoma with RAIrefractory metastases, due to the prolonged progressionfree survival of patients treated with these agents [14, 15].

One phase III study demonstrated that lenvatinib significantly improved the OS of the subset of patients older than 65 years (median age 71 years) [16], suggesting that this is one of the promising therapeutic strategies for PTC recurrence in older patients.

In our study, only one patient (8.33%) had received 2 lines of targeted therapy: sorafenib and sunitinib. Recurrence of PTC may be loco-regional or distant, with the central compartment typically being the first region to develop metastatic disease, followed by ipsilateral lateral neck nodes [17].

Recurrence to distant organs such as the lung and bone is less frequent than recurrence to nodes. More than 80% of recurrences took place during the first decade.

Though most recurrences occur within the first 10 post-operative years, there have been reports of locoregional recurrences a decade or more after this initial window. Cirotchi reports that local relapses can occur as late as 20 years after the initial diagnosis and treatment [17]. 66.66% of our patients had locoregional

lymph node recurrence alone, which is consistent with the results of the literature.

As a whole, thyroid cancer generally has a good prognosis with a 5-year survival rate of 98% [18, 19]. Compared with a recent investigation, our study showed lower rates of the mortality related to recurrence in our series.

CONCLUSIONS

Papillary thyroid carcinoma is an indolent disease, but cases having certain characteristics are likely to show recurrence and even become life-threatening, fortunately, various tools and treatment recommendations are available to help detect a recurrence.

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