

CLINICAL OUTCOMES OF PAPILLARY THYROID MICROCARCINOMA IN FILIPINO PATIENTS: A 12-YEAR EXPERIENCE AT MAKATI MEDICAL CENTER

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ABSTRACT

Background: Various studies have shown that papillary thyroid microcarcinoma (PTMC) has a favorable prognosis but has the capacity to be aggressive; thereby, requiring effective treatment.

Objectives: To determine the clinical characteristics and outcomes of PTMC in Filipino patients diagnosed and treated at Makati Medical Center

Study Design: This is a retrospective, descriptive study.

Subjects and Methods: Medical and clinic records of twenty two patients diagnosed and treated for papillary thyroid microcarcinoma from 1993-2004 were reviewed. Statistical means and percentages were used.

Results: The patients' age ranged from 19-73 years old with a mean of 46 years. There was a female predominance at 95.45%. One patient (4.5%) had papillary microcarcinoma by fine needle aspiration biopsy (FNAB). Another patient had lymph node and distant metastases (bone) at presentation after near total thyroidectomy without ablation in another medical center and later received 200mCi of radioactive iodine therapy but was lost to follow up. Multifocality was seen in two patients (9%). Five patients (22.7%) had lobectomy while one (4.5%) underwent subtotal thyroidectomy. Near total thyroidectomy was done in five patients (22.7%) while 11 (50%) had total thyroidectomy. Only 12 patients (54.5%) received radiation remnant ablation therapy. One patient who had lobectomy was noted to have nodule recurrence in the remaining lobe while another patient who underwent total thyroidectomy with no radioactive iodine treatment had elevated thyroglobulin (Tg) on follow up. Follow up period ranged from one to 11 years (mean of six years). All patients have survived and were asymptomatic but in some of the patients the cancer activity could not

be accurately assessed due to absence of thyroglobulin and thyroid ultrasound determinations.

Conclusions/ Recommendations: Our study compared to foreign studies had a smaller population. Multifocality considered as a predictor of poor prognosis was seen in only two patients. PTMC may have latent/ indolent course and favorable outcomes but may be persistent/ metastatic in some. Combination therapy of near total/ total thyroidectomy with radiation remnant ablation offered greater benefit. Thyroglobulin served as a powerful prognostic factor of persistent/ recurrent disease. Repeat thyroid ultrasound/ biopsy were necessary to document thyroid cancer activity in patients not amenable to thyroglobulin determinations.

Keywords: papillary thyroid microcarcinoma (PTMC), fine needle aspiration biopsy (FNAB), radiation remnant ablation (RRA), thyroidectomy, Thyroglobulin (Tg)

INTRODUCTION

Microcarcinoma of the thyroid gland is defined by the International Histological Classification of Tumors of the World Health Organization (WHO) as thyroid cancer measuring less than or equal to 10 mm (1 cm) in its greatest diameter.¹ It is almost exclusively papillary (80-90%), followed by follicular variant (<10%) and by the rare, more problematic type tall cell variant.^{1,2,3} Before the 1988 WHO definition, papillary thyroid microcarcinoma (PTMC) was called as small papillary or micropapillary carcinoma (tumor measuring 1.5 cm), occult papillary carcinoma and incidentaloma. The latter terms are connotative of PTMC's clinically silent behavior and thus, become diagnosed as an incidental finding during surgery for goiter or other benign thyroid disorders and at autopsy with no clinical suspicion of malignancy.^{1,3,4}

Thyroid nodules (22% solitary, 45% multiple) were seen in 67 percent of the population. A significant number of individuals who died of other reasons have thyroid cancers incidentally identified at autopsy that apparently did not adversely affect the patients' health. Some experts claimed that PTMC has a good prognosis both in terms of overall and relapse-free survival.^{5,6} The question therefore is, should we treat it or not? The different outcomes of major scientific works divided the investigators who were searching

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for the most favorable and optimum treatment of PTMC, into conservative and non-conservative groups. The proponents of observation, sole medical (levothyroxine suppression therapy) or less surgical interventions (subtotal thyroidectomy, lobectomy/hemithyroidectomy) constituted the conservative group while those who employed near total or total thyroidectomy with or without radiation remnant ablation (RRA) followed by suppression therapy comprised the non-conservative group.

OBJECTIVES

General

To determine the clinical outcomes of papillary thyroid microcarcinoma (PTMC) in Filipino patients treated and followed up at Makati Medical Center

Specific

To know the clinical profile of Filipino patients diagnosed to have papillary thyroid microcarcinoma (PTMC)

Significance of the Study

Undertaking this study, may help redefine our aggressiveness in diagnosing and treating PTMC and thereby increase our awareness of the clinical impact of a disease with a generally accepted favorable course and outcome but has the tendency to have dreadful consequences in terms of morbidity and mortality. With the rising prevalence of PTMC brought forth by sophisticated sonographically guided biopsy and non conservative surgical approach as boasted by our foreign counterparts, this study will help intensify the histological accuracy and acumen of our practicing endocrinologists doing fine needle aspiration biopsy (FNAB) as well as our pathologists to increase the positive yield of thyroid cancer less than 10 mm in diameter. Guided by the principles of *Primum non nocere* and *Non malifescens* (first do no harm) on patient treatment, it is very timely to embark on a study that would provide supporting evidences/ideas that would initially lay down the ground work of a diagnostic and treatment protocol apt for local setting and not just being submissive to foreign guidelines. The result of this study may not furnish the outright optimum treatment regimen but it may give the guiding factors needed to come up with a modality that is cost effective, safe and efficient. Presently, no local study exists discussing the clinical characteristics and outcomes of PTMC. The result of this study may not address all the questions imposed by foreign investigators and even by local

practitioners but certainly, this may help alleviate the confusion and controversy revolving around PTMC.

MATERIALS AND METHODS

This a retrospective, descriptive study which reviewed the medical records and clinic charts of 22 Filipino patients diagnosed to have PTMC from 1993 – 2004 at Makati Medical Center. The list of these patients was obtained after manually examining 300 volumes of the Surgical Pathology records of the Department of Pathology and Laboratories, which contained the official histopathologic diagnosis. In the 12 year period, there were 2,181 surgical operations which resulted to diagnosis of 1,697 (77.8%) benign thyroid tumors and 484 (22.19%) thyroid carcinomas. There were 49 patients (10% of malignant tumors or 2.2% of sample population) diagnosed to have PTMC. Unfortunately, most of the patients' medical and clinic records were already non-existing. Some of the patients did not come back after the initial post-operative follow up and if ever they followed up, they were not properly worked up. These led to the diminution of the sample size of this study. A questionnaire was filled up, which included patient's clinical profile, treatment modalities, post-treatment surveillance work up and outcomes (Appendix 1). Statistical means and percentages were used.

RESULTS

A total of 22 patients aged 19-73 years old with a mean of 46 years were used as subjects. Twenty one (95.4%) were females with only one male (4.5%). Based on clinical, thyroid function and ultrasonographic examinations 11 (50%) had nodular nontoxic goiter (single nodule), seven (31.8%) had multinodular nontoxic goiter (>1 nodule) and four (18%) had multinodular toxic goiter undergoing treatment with thionamides. All presented with complex masses (cystic to solid nodules) on initial ultrasound of the thyroid gland, with diameters ranging from 0.5 to 4.2 cm. Abnormal sonographic features seen were calcifications in five patients (22.7%), hypoechoic nodules in two patients (9%) and increased vascularity in the same patient who has hypoechoic nodule (4.5%). Among the four with multinodular toxic goiter, two (9%) had hypoechoic nodules. Thyroid scan was done in only two (9%) patients which revealed cold nodule in one. FNAB results were adenomatous colloid goiter in 14 (63.6%) cystic with one presenting as hemorrhagic in four (18%), and papillary microcarcinoma in one patient (4.5%). Two patients (9%) underwent direct surgery

without an FNAB. Aspiration biopsy was also not done in one patient who was previously diagnosed outside Makati Medical Center to have PTMC and later on developed lymph node and bone metastases. This patient (4.5%) had lymphadenopathy documented by ultrasound at initial presentation.

Using the sonographic and aspiration biopsy results, there were nine (40.9%) patients with nonincidental tumors (tumors proven by biopsy or with abnormal sonographic features). There was one patient (4.5%) with bone metastases at presentation noted in our study (the same one with positive cervical lymph nodes). Five subjects (22.7%) underwent lobectomy, one (4.5%) had subtotal thyroidectomy, five (22.75) had near total thyroidectomy and 11 (50%) underwent total thyroidectomy. Of the 11 who had total thyroidectomy, two patients (9%) originally had lobectomy but later decided to have completion thyroidectomy three weeks after official histopathology diagnosis was released and the other, one year after developing cervical lymphadenopathy post-surgery. Only two patients (9%) had precise frozen section result of PTMC. Twenty patients (91%) had adenomatous goiter as secondary histopathological diagnosis while two (9%) had Hashimoto's thyroiditis. PTMC diameter ranged from 1.1 to 10 mm with mean of 5.5 mm. Multifocality was seen in only two patients (9%), each lobe having one focus of thyroid tumor. There was a predilection of the tumor in the right lobe as seen in 18 (90%) out of the 20 patients who had unifocal malignancy. Using the 6th edition of the American Joint Committee on Cancer Staging, all 22 patients (100%) had Stage 1 (T1NOMO), if we are to consider the first time they were diagnosed to have PTMC. Radiation remnant ablation (RRA) was not done in those six patients (27.2%) who had lobectomy and subtotal thyroidectomy. Among the 16 patients who had near total/ total thyroidectomy, four (18.1%) did not receive radioactive iodine. The rest had ablation therapy of 50-200 mCi of radioactive iodine (I-131).

Follow up period ranged from one to 11 years (mean of six years). Latest thyroid stimulating hormone (TSH) at hand was within therapeutic level of <0.1 uIU/ml in 18 patients (81.8%) while four (18%) were above this value. All patients were prescribed levothyroxine therapy ranging 50-200 mcg/day. Repeat ultrasound showed negative results in 18 patients (81.8%). One patient (4.5%) who underwent lobectomy had positive cervical lymph nodes while three patients had no thyroid ultrasound on follow-up. Eleven patients who underwent near total/total thyroidectomy (50%) had <1 ng/ml thyroglobulin (Tg)

levels. One (4.5%) who refused ablation therapy after total thyroidectomy had elevated Tg level of >10 ng/ml. Those who underwent subtotal thyroidectomy and lobectomy had no Tg determination. Three patients (13.6%) who had near total/ total thyroidectomy but did not undergo RRA had no Tg levels as well. At the time of this study, 21 patients (95%) are still following up and asymptomatic except for one patient who had bone metastases but was lost to follow up after ablation therapy.

DISCUSSION

As compared to foreign studies, our local study had a smaller population (see Table II); nonetheless female predominance (95.4%) was evident.^{1,2,3,7,8} The prevalence of PTMC varied. In the review of literature by Pisello *et al* in 2007, papillary carcinoma increased from 12 percent in 1980 to 25 percent in 1990 in Italy, with a mean diameter of five millimeters.⁹ This can be attributed to greater expertise in ultrasound guided fine needle aspiration biopsy or to the aggressive total thyroidectomy giving a greater yield of thyroid specimens. In Guatemala, there was a two percent prevalence rate during autopsy of 150, making PTMC a much more common pathology than clinically evident thyroid cancer.¹⁰ Twenty four percent of 425 patients in Canada had PTMC based on the study by Fink *et al*.⁵ The Hong Kong Cancer Registry revealed 20 percent prevalence in the past decade.³ The study by Harach, *et al*, which involved thyroid specimens from 101 autopsies, gave a prevalence rate of 35.6 percent, the highest reported rate in the world. The authors of this Finnish study found out that the great majority of the tumors remained small and circumscribed. Even from those few tumors that grew larger and became invasive, only a minimal proportion became clinical carcinomas. Consequently, they concluded that PTMC which they called previously as occult papillary carcinoma can be regarded as a normal finding. This should not be treated when incidentally found. In order to avoid unnecessary operations they suggested that incidentally found tumor of less than five millimeters in diameter should be called occult papillary tumor instead of carcinoma.¹¹ There are no existing data among Filipinos.

In our study only one patient had outright PTMC by FNAB alone. In foreign medical centers, the increasing use of high resolution ultrasonography in FNAB increased the proportion of newly diagnosed thyroid cancers of less than one centimeter dimension. Less than 10 mm nodules may possibly harbor thyroid cancer.^{1,2} Many authorities believed

that it is important to diagnose thyroid cancer at an early stage because this may reduce the risk of recurrence and possibly mortality.^{5,6,14} The question now lies on whether less than 10 mm nodules be aspirated or not. The American Thyroid Association (ATA) and the Society of Radiology recommended that nodules smaller than one centimeter may require evaluation if there are suspicious ultrasound findings (microcalcifications, hypoechogenicity, irregular margins, mainly solid components, enhanced intranodular vascularity, and the nodule being taller than wider), history of head and neck irradiation or a positive family history of thyroid cancer.^{15,16} The guidelines of the American Association of Clinical Endocrinologists (AACE) emphasized sonographic characteristics rather than nodule size in determining which nodule(s) to aspirate and suggested that at least two of the sonographic criteria will make the sensitivity for malignancy between 87 and 93%.¹⁷ In the 2006 Burman editorial, it was suggested that the largest nodule be aspirated and that particular nodules with worrisome sonographic features should also be considered for aspiration. He emphasized that the critical aspect was to monitor the patient with periodic clinical and sonographic examinations.¹² The study by Roti et al showed that nonincidental microscopic papillary thyroid cancer (tumors with proven aspiration biopsy results or with abnormal, suspicious clinical/ ultrasonographic features) was more aggressive.²

The conservative group believed that PTMC has low mortality, low recurrence rate and rare metastatic capacity. Back up studies of conservative treatment are as follows. The study of 535 PTMC patients by Hay et al revealed a low mortality rate of less than one percent (0.4%) and a 20 year recurrence rate of only six percent over a 48 year span.¹⁸ Mazzaferri and Jhiang showed a linear relationship between tumor size and recurrence and cancer mortality. Tumors less than one and a half centimeter (1.5 cm) had 30 year mortality of 0.4 percent. Tumors less than four and a half centimeters (4.5 cm) had seven percent mortality while tumors larger than four and a half centimeters had 18 percent mortality.¹⁹ Observation protocol as promulgated by the studies of Sugitani et al and Ito et al^{7,20} was adopted in one of our patients. He had only lobectomy and levothyroxine suppression but later on had positive thyroid nodules of the remaining lobe. The predicament in this case was whether the thyroid nodules were part of the multifocality left undetected and unevaluated because the involved lobe was not removed or whether the nodules were part of a recurring tumor. Ito et al in 2003 observed by clinical and sonographic evaluations that 72 percent of tumors of 162 patients whose cancers were proven

by aspiration biopsy alone, either got smaller or did not change size over about eight years and node metastases occurred in only less than two percent (1.2%). Ito et al in another study; however, discovered that out of 626 patients, who had thyroidectomy, 50.5 percent had local node metastases, 42.8 percent had multifocality and five percent had recurrence, eight years after surgery.²⁰ The new protocol of conservative treatment was adopted by Sugitani et al and proved in their retrospective study the absence of disease progression of twenty one patients with PTMC for at least three years.⁷

In contrast, the non-conservative group found out that despite the benign behavior of PTMC, its outcome is of no significant difference from thyroid cancers of more than one centimeter. Two patients in our local study who presented with multinodular toxic goiter rather than Graves' disease had hypoechoic nodules on ultrasound signifying the claim of Pellegriti et al that autoimmune disease heightened tumor characteristic and aggressiveness. Graves' disease was positively associated with relapse and persisting lymph nodes possibly due to the immunologic effect of the TSH-R antibodies.

Multifocality considered as a poor prognostic predictor was seen in two of our patients who underwent more aggressive surgical approach just like in the works of Roti et al and Fink et al.^{2,5} According to Pellegriti et al, PTMC may become aggressive owing to its capacity to have multifocality (30%), lymph node metastases (30%), vascular invasion (4.7%) and distant metastases (2.7%) as seen in 25.7 percent of 292 patients.¹ All of these along with non-incidental thyroid cancer and bilateral tumor constituted the prognostic factors of persistent/recurrent PTMC. Sakorafas et al revealed that more than seven percent (7.1%) of 280 patients had incidental PTMC associated with benign thyroid diseases.⁴ In our study, lymph node and distant metastases at initial presentation considered as predictors of persistent/recurrent disease¹⁻⁵ were seen in one subject diagnosed to have PTMC and underwent near total thyroidectomy without radiation treatment in another institution. This patient underwent ablation therapy at Makati Medical Center but was later lost to follow up. In 2006, Roti et al concluded that higher cancer aggressiveness was seen in tumors less than ten millimeters and was defined by neck lymph node metastases, distant metastases at presentation and recurrence on follow up.² Even the results of the conservative studies made by Hay et al and Baudin et al less than 10 years ago revealed that the most effective predictor of local relapse was the presence of multiple foci correlated with metastatic lymph

nodes at presentation.^{18,21} In 2003, Chow *et al* showed that PTMC was associated with one percent cancer-related deaths, five percent lymph node recurrence rate and less than three percent (2.5%) distant metastases rate (lungs, bones).³

In our study, there were six patients who only underwent lobectomies/ subtotal thyroidectomy. These six patients who were treated conservatively had survived and were apparently symptom free. However, thyroid cancer activity could not be accurately assessed due to the absence of thyroglobulin (Tg) test which was considered as the best marker of persistent/ recurrent disease,^{1,3,5} (Tables I and II). The drawback of having only lobectomy or subtotal thyroidectomy was that ablation therapy and Tg determination post treatment could not be instituted because of very large thyroid remnant tissues. These would deter the radioactive effects and give falsely high Tg levels. As part of the conservative group, Dewil *et al* in 2005 adhered to their routine management of completion thyroidectomy once the histopathological report concluded the presence of carcinoma, except in cases of papillary carcinoma measuring less than one centimeter.²²

Table I. Clinical and Demographic Profile of Filipino Patients with PTMC at Makati Medical Center

Age	19-73 y/o, mean of 46 y/o
Gender	
Male patient	1 (4.5%)
Female patients	21 (95.4%)
Thyroid disorder at presentation	
Nodular nontoxic goiter	11 (50%)
multinodular nontoxic goiter	7 (31.8%)
multinodular toxic goiter	4 (18%) with 2 having hypoechoic nodules
Initial thyroid ultrasound	
complex masses: cystic to solid nodules	22 (100%)
calcifications	5 (22.7%)
hypoechoic nodules	2 (9%)
hypervascularity	1 (4.5%)
Thyroid scan	Done in 2 patients only (9%)
Cold nodule	1 (4.5%)
Warm nodule	1 (4.5%)
Fine Needle Aspiration Biopsy	
not done	2 (9%)
cystic/ hemorrhagic	4 (18%)
papillary microcarcinoma	1 (4.5%)
adenomatous, colloid	15 (68%)
Lymph node metastases at presentation	
Negative	21 (94.5%)
Positive	1 (4.5%)
Incidental tumor	13 (59%)

(Table I continue next column)

(Table I continuation. . . .)

Age	19-73 y/o, mean of 46 y/o
Non-incident tumor	9 (40.9%)
Distant metastases at presentation (bone)	1 (4.5%)
Types of Surgery	
Lobectomy	5 (22.7%)
Subtotal thyroidectomy	1 (4.5%)
Near total thyroidectomy	5 (22.7%)
Total thyroidectomy	11 (50%)
Frozen section positive for PTMC	2 (9%)
Radiation remnant ablation	
Near total/ total thyroidectomy with ablation	12 (54.5%)
Near total/ total thyroidectomy without ablation	4 (18.18%)
Lobectomy and subtotal thyroidectomy without ablation	6 (27.2%)
Multifocality	2 (9%)
Tumor staging	
Stage 1	22 (100%)
Follow up period	1-11 years, mean of 6 years
Thyroid stimulating hormone while on levothyroxine	
<0.1 uIU/mL	18 (81.8%)
>1.01 uIU/mL	4 (18%)
Repeat thyroid ultrasound	
Not done	3 (13.6%)
Recurrent nodule	1 (4.5%)
Negative results	18 (82%)
Thyroglobulin on follow up	
<1 ng/mL	11 (50%)
>10 ng/mL	1 (4.5%)
Not done despite near total/ total thyroidectomy	3 (13.6%)
Not done due to lobectomy/ subtotal thyroidectomy	6 (27.2%)
Lost to follow-up	1 (4.5%)
Persistent/ recurrent disease	
With elevated Thyroglobulin	1 (4.5%)
With nodule recurrence	1 (4.5%)
Metastases (lymph node and bone)	1 (4.5%)
Mortality	0% (one lost to follow up)

Our study showed that some physicians believed that near total/ total thyroidectomy combined with RRA offered more advantageous therapeutic effects. No one among those who had combination therapy had recurrent disease. Two patients in our study despite having multifocality responded well with surgery combined with radiation therapy. However, one patient who had no RRA developed lymph node and bone metastases even after near total thyroidectomy. Another patient who received more invasive surgery but refused ablation therapy had persistent disease. With regards to these, the members of the conservative group had the following views. In 2007, Solares CA impelled no doubt that if PTMC was treated with total thyroidectomy and radioactive iodine, the recurrence rate will be low. His question was

whether patients with PTMC or occult papillary thyroid carcinoma (OPTC) really needed treatment at all. In his opinion, only patients with other risk factors for aggressive disease such as male gender, history of total body radiation and women over age 45 may require a total thyroidectomy. He argued that recurrent laryngeal nerve injury, postoperative hypoparathyroidism, bleeding and infection were surgical risks that should be weighed against the potential added benefit of a total thyroidectomy.²³ Sugitani *et al* showed in another scientific work that 30 symptomatic PTMC patients with lymph node metastases and hoarseness did not benefit from total thyroidectomy with radiation remnant ablation.²¹ Mazzaferri *et al* concluded similarly, after their 10 year follow up of 576 patients showed that the recurrence and mortality rates of tumors (<1.5 cm) receiving less than total thyroidectomy and post-operative levothyroxine therapy were not statistically different from those with more aggressive treatments.⁸ Baudin *et al* found out that recurrence rates did not differ in PTMC, with or without radioactive iodine therapy.²¹ Lastly, no significant salutary effects of radioactive ablation in low risk (<1 cm) papillary thyroid carcinoma were seen by Sawka *et al* in their 2004 study.²⁴

The non-conservative group, however, believed that near total thyroidectomy/ total thyroidectomy combined with radiation remnant ablation was the best therapeutic regimen. These reduced the incidence of recurrence and metastases particularly in those with poor prognostic factors. These resulted to less than four percent (2-3.7%) recurrence rate as opposed to nearly ten percent (9.8%) in those with less aggressive approach.^{3,11,25} Constanzo *et al* claimed that all 600 patients who received this combined modality from 1999 up to 2003 were alive and free of disease.²⁶ Near-total/ total thyroidectomy identified multifocal or bilateral cancer foci with high accuracy and maximized the sensitivity of whole body scan (WBS) and serum thyroglobulin (Tg) to detect persistent/recurrent disease. Twenty percent (20%) of cases of less than one and a half centimeters (1.5 cm) papillary thyroid carcinoma had extrathyroidal invasion/ bilateral foci and were overlooked in previous studies due to lobectomy or nonuniform surgical approaches.¹⁻³ PTMC was found in more than eight percent (8.9%) of patients who underwent lobectomies, 10.8 percent who had hemithyroidectomies and 24.1 percent of those who had total thyroidectomies.¹³

Table II.

Parameters	Pellegriti <i>et al</i> 2004	Roti <i>et al</i> 2006	Chow <i>et al</i> 2003	Silva and Aragon 2008
No. of patients and duration	299 pts; 26 years	243 pts; 9 years	203 pts; 10 years	22 of 49 pts; 12 years
Age range; mean	13-79 y/o; mean 41.9 y/o	16-85 y/o; mean 50.5 y/o	17-77.2 y/o; mean 42 y/o	19-73 y/o; mean 46 y/o
Gender	86% female, 14 % male	81% female, 19% male	86.% female, 14% male	95% female, 5% male
Toxic goiter	36 (12%)- Graves'	14 (5.8%)- Graves'	-	4 (18%)- multinodular toxic
LN mets at presentation	90 (30.1%)	32 (13%)	50 (24.6%)	1 (4.5%)
Distant mets at presentation	8 (2.7%)	4 (1.6%)	2 (1.0%)	1 (4.5%)
Incidental tumor	151 (50.5%)	52 (23%)	-	11 (50%)
Non incidental tumor	148 (49.4%)	191 (78.6%)	-	9 (40.9%)
Surgery	NTT/TT 292 (97.7%) Lobectomies 7 (2.3%)	NTT/TT 243 (100%)	NTT/TT 187 (92.1%) Lobectomies 16 (7.9%)	NTT 5 (22.7%), TT 11 (50%) Lobectomies 5 (22.7%) Subtotal thyroidectomy 1 (4.5%)
Multifocality	95 (31.7%)	78 (32%)	63 (31%)	2 (9%)
Radiation Ablation Tx	292 (97.6%)	243 (100%)	137 (67.5%)	12 (54.5%)
Years of follow up	1-21 years; mean 4 years	2.4-10.6years;mean 5.1 years	1-10 years; mean 5years	1-11 years; mean 6 years
Lymph Node mets on follow up	17 (5.7%)	32 (13.1%)	12 (10.3%)	1 (4.5%)-had mets from start lost to follow up
Distant mets on follow up-bone	4 (1.3%)	4 (1.6%)	5 (2.5%)	1 (4.5%)-had mets from start lost to follow up
Mortality	0%	0%	2 (0.98%)	0%

Serum thyroglobulin (Tg) below one ng/ml was the best predictor of no relapse (<1.0 ng/ml: 1.1% relapse, 1-10 ng/ml: 16% relapse, >10 ng/ml: 68.7% relapse) at the first post surgical evaluation during levothyroxine withdrawal. It was the only sign of disease seen in twelve percent of 37 patients on follow up in the study by Pellegriti *et al.* Thyroid residue ablation increased the accuracy of serum thyroglobulin as a predictor of relapsing/ persisting disease. The role of thyroglobulin antibodies was not well elaborated, however, possibly due to the high percentage of negative results on follow up (92% of patients).¹ Nonetheless, its value as a predictor of disease persistence or recurrence was still highly regarded as stated in the guidelines of the American Thyroid Association.⁸

CONCLUSIONS/ RECOMMENDATIONS

Based on our study, PTMC among Filipino patients in our institution has female predominance and mostly presented as nodular nontoxic goiter with adenomatous complex masses. Abnormal ultrasound findings were calcifications, hypoechogenicity and increased vascularity. Multifocality considered as a predictor of poor prognosis was seen in only two patients. All patients had Stage I disease and there was a predilection of the tumor in the right thyroid lobe. PTMC may have latent /indolent course and favorable outcomes but may also be persistent/ metastatic (lymph node and bone metastases). Our local study was not designed to recommend the optimal treatment of PTMC but only to give supporting factors, evidences and ideas on how Filipino patients were treated in our institution. Our study indicated that combination therapy of near total/ total thyroidectomy and radioactive iodine was still the first choice in dealing with PTMC. This modality stressed the important role of thyroglobulin as a powerful index of cancer persistence/ recurrence. Most patients on follow up were within the therapeutic level of levothyroxine suppression based on their TSH. Repeat thyroid ultrasound/ biopsy were necessary to document thyroid cancer activity in patients not amenable to thyroglobulin determinations.

Local institutions should devise more complete and concise thyroid cancer registry and database in order to generate beneficial research output. A bigger sample size in a prospective, multicenter study dealing with the clinical outcomes of PTMC patients in the near future and employing basic results of our descriptive study, may give greater significance. Posttreatment follow-up and surveillance plans of our patients should always be at hand and properly done. Indeed, papillary thyroid microcarcinoma may have a generally favorable outcome but it has the capacity to be aggressive. Because of this, the physician should be well-informed of its nature and the recent therapeutic modality for PTMC in order not to compromise the welfare of the patient.

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APPENDIX 1: QUESTIONNAIRE

Clinical and Demographic Profile:

Age, gender

Thyroid disorder at presentation

Initial thyroid ultrasound

Thyroid scan

Fine Needle Aspiration Biopsy

Lymph node metastases at presentation

Incidental vs non incidental tumor

Distant metastases at presentation

Types of surgery: lobectomy, subtotal thyroidectomy, near total/ total thyroidectomy

Frozen section

Radiation Remnant Ablation: Near total/ total thyroidectomy with or without ablation therapy

Multifocality

Tumor staging

Outcomes

Follow up period

Work up on follow up: thyroid stimulating hormone (TSH), repeat thyroid ultrasound, thyroglobulin (Tg)

Persistent/ recurrent disease

Metastases: lymph node, distant

Mortality: