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. It is almost exclusively papillary (80-90%), followed by follicular variant (<10%) and by the rare, more problematic type tall cell variant. 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.

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. The question therefore is, should we treat it or not? The different outcomes of major scientific works divided the investigators who were searching...
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 noncercé 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
thyroidectomy (50%) had <1 ng/ml thyroglobulin (Tg)
up. Eleven patients who underwent near total/total
lobectomy had positive cervical lymph nodes while
patients (81.8%). One patient (4.5%) who underwent
Repeat ultrasound showed negative results in 18
were above this value. All patients were prescribed
of <0.1 uIU/ml in 18 patients (81.8%) while four (18%)
hormone (TSH) at hand was within therapeutic level
(mean of six years). Latest thyroid stimulating
Follow up period ranged from one to 11 years
131).
therapy of 50-200 mCi of radioactive iodine (I-
not receive radioactive iodine. The rest had ablation
patients who had near total/ total thyroidectomy, four (18.1%) did
subtotal thyroidectomy. Among the 16 patients who
Radiation remnant ablation (RRA) was not done in
(100%) had Stage 1 (T1NOMO), if we are to consider
Joint Committee on Cancer Staging, all 22 patients
malignancy. Using the 6th edition of the American
in 18 (90%) out of the 20 patients who had unifocal
prevalence in the past decade.3 The study by Harach,
Canada had PTMC based on the study by Fink et al.
(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.
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.\textsuperscript{\text{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, hypoechoogenicity, 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.\textsuperscript{\text{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\%.\textsuperscript{\text{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.\textsuperscript{\text{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.\textsuperscript{\text{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.\textsuperscript{\text{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.\textsuperscript{\text{19}} Observation protocol as promulgated by the studies of Sugitani \textit{et al} and Ito \textit{et al}\textsuperscript{\text{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.\textsuperscript{\text{20}} The new protocol of conservative treatment was adopted by Sugitani \textit{et al} and proved in their retrospective study the absence of disease progression of twenty one patients with PTMC for at least three years.\textsuperscript{\text{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 \textit{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 \textit{et al} and Fink \textit{et al}.\textsuperscript{\text{2,5}} According to Pellegriti \textit{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.\textsuperscript{1} All of these along with non-incidental thyroid cancer and bilateral tumor constituted the prognostic factors of persistent/recurrent PTMC. Sakorafas \textit{et al} revealed that more than seven percent (7.1\%) of 280 patients had incidental PTMC associated with benign thyroid diseases.\textsuperscript{4} In our study, lymph node and distant metastases at initial presentation considered as predictors of persistent/recurrent disease\textsuperscript{1-5} 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 \textit{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.\textsuperscript{2} Even the results of the conservative studies made by Hay \textit{et al} and Baudin \textit{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.\textsuperscript{18,21} In 2003, Chow \textit{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).\textsuperscript{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.\textsuperscript{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 \textit{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.\textsuperscript{22}

\begin{table}[h]
\centering
\begin{tabular}{l|l}
\hline
\textbf{Age} & 19-73 y/o, mean of 46 y/o \\
\hline
\textbf{Gender} & \\
Male patient & 1 (4.5\%) \\
Female patients & 21 (95.4\%) \\
\hline
\textbf{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 \\
\hline
\textbf{Initial thyroid ultrasound} & \\
complex masses: cystic to solid nodules & 22 (100\%) \\
calcifications & 5 (22.7\%) \\
hypoechoic nodules & 2 (9\%) \\
hypervascularity & 1 (4.5\%) \\
\hline
\textbf{Thyroid scan} & \\
Cold nodule & 1 (4.5\%) \\
Warm nodule & 1 (4.5\%) \\
\hline
\textbf{Fine Needle Aspiration Biopsy} & \\
not done & 2 (9\%) \\
cystic/ hemorrhagic & 4 (18\%) \\
papillary microcarcinoma & 1 (4.5\%) \\
adenomatous, colloid & 15 (68\%) \\
\hline
\textbf{Lymph node metastases at presentation} & \\
Negative & 21 (94.5\%) \\
Positive & 1 (4.5\%) \\
Incidental tumor & 13 (59\%) \\
\hline
\end{tabular}
\caption{Clinical and Demographic Profile of Filipino Patients with PTMC at Makati Medical Center}
\end{table}

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. 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. 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 postoperative levothyroxine therapy were not statistically different from those with more aggressive treatments. Mazzaferri et al found out that recurrence rates did not differ in PTMC, with or without radioactive iodine therapy. 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.

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%) recurrence rate as opposed to nearly ten percent (9.8%) in those with less aggressive approach. Constanzo et al claimed that all 600 patients who received this combined modality from 1999 up to 2003 were alive and free of disease. 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. 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.

Table II.

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

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.

**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, hypochochogenicity 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: