**Thyroid Papillary Microcarcinoma: Etiology, Clinical Manifestations, Diagnosis, Follow-up, Histopathology and Prognosis**

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**KEY WORDS**

Thyroid cancer
Papillary thyroid carcinoma
Thyroid microcarcinoma

**ABSTRACT**

**Background:** Thyroid carcinoma is the most common malignancy of the endocrine system. Papillary thyroid carcinoma (PTC) is the most common type of thyroid cancer, accounting for 70–90% of well-differentiated thyroid malignancies. Thyroid papillary microcarcinoma is a subtype of papillary carcinoma that included tumors with less than 10mm diameter. As a result of diagnostic methods improvement, prevalence of this tumor is increasing. In this study we reviewed different characteristics of tumor.

**Methods:** We searched various factors about this tumor in different databases (PubMed, Ovid, Google scholar, Iran medex and SID databases, from July 2012 until August 2013), after that, the articles were classified. Data of each article were extracted and sorted in tables. Data of each factor in different articles were summarized.

**Results:** Etiology, clinical presentation, prognosis, histopathology, follow-up, diagnosis and also age, gender, tumor size and treatment were factors about this tumor described in details here.

**Conclusion:** Awareness and better understanding of the characteristics of this tumor and manage it as an individual and valuable tumor can take an effective step in promoting public health practice.

**Introduction**

Thyroid carcinoma is the most common malignancy of the endocrine system with incidence of approximately 9/100,000 per year. These cancers have a spectrum of behavior that ranges from incidentally detected and clinically inconsequential microcarcinomas to aggressive and virtually untreated anaplastic malignant neoplasms (1, 2).

Most thyroid cancers present as thyroid nodules that are either asymptomatic or associated with local cervical symptoms or adenopathy. Less often, thyroid cancers first present with manifestations of metastatic disease, such as a pulmonary mass or bone pain (1).

Papillary and follicular thyroid cancers arise from follicular epithelium and often retain responsiveness to TSH, produce thyroglobulin, and concentrate iodide. They are distinguished...
by their histopathologic appearances and characteristic patterns of progression (1).

Papillary thyroid carcinoma is the most common form of thyroid cancer, accounting for 70–90% of well-differentiated thyroid malignancies. Whereas the mean age at diagnosis is 45 yr, papillary thyroid carcinoma does occur in children and increases in incidence with age (1, 2).

Papillary thyroid microcarcinoma (PTMC) is a specific subgroup of papillary thyroid carcinoma (PTC) and defined by WHO on the largest dimension of 1.0 cm or less. Most of PTMC are not detectable at clinical examination and are diagnosed incidentally during pathologic examination of thyroid specimens after surgery for benign thyroid diseases, or in autopsies. Characteristic cytologic features of PTC help make the diagnosis by FNA or after surgical resection; these include psammoma bodies, cleaved nuclei with an “orphan-Annie” appearance caused by large nucleoli, and the formation of papillary structures (2, 3).

Moreover, the increased accuracy of the pathologic thyroid examination, in particular with the thinness and the number of the anatomical slices obtained for thyroid specimens, led to a more frequent pathologic; diagnosis of incidental PTMC. On the other hand, the widespread use and the technical improvement of thyroid ultrasonography and fine-needle aspiration biopsy (FNAB) contributed to an increase in the rate of preoperative diagnosis of PTMC over the last few decades (3).

The advent of sensitive imaging devices has led to an increase in the detection rate of small thyroid cancers (4). Consequent greater access to diagnostic procedures resulted in increased detection of PTMC (5). With the widespread use of ultrasound, the detection rate for small thyroid nodules continues to increase (6). The improvement of fine-needle aspiration biopsy is useful for cancers larger than 10mm, and microcarcinomas may be detected by this method (7). Expanded thyroid ultrasound screening and fine needle aspiration biopsies (FNA), and greater specimen sampling by pathologists, account for some of the rise in PTMC incidence (8).

Thyroid cancer incidence rates have been steadily increasing all over the world including Iran (8-10). This trend has also included higher detection of papillary thyroid microcarcinoma due to the improvement of diagnostic methods. PTMC has a benign behavior with excellent prognosis in most cases (11, 12).

In this article, we reviewed the previous studies about PTMC to promote physicians awareness of this tumor characteristics and methods of treatment in order to diagnose and treat the tumor earlier, which may help to improve the prognosis of PTMC patients and decrease cancer mortality.

Materials and Methods

Search Strategy

In this systematic review, at first step we used the relevant key words to our title, Thyroid Papillary Microcarcinoma (TPM); TPM AND etiology OR cause; TPM AND histopathology; TPM AND diagnosis; TPM AND clinical presentation OR clinical symptoms; TPM AND follow-up; TPM AND prognosis OR outcome for searching. Articles were searched in PubMed, Ovid, Google scholar, Iran medex and SID databases, July 2012 till August 2013 with no language limitations.

The search strategy is showed completely in Figures 1-5.

Exclusion Criteria

We excluded the articles with following criteria: a) Review articles about thyroid papillary microcarcinoma; b) Articles used as reference in review articles of TPM; c) Results which were books not articles; d) The same articles resulted from different databases; e) Articles about other
thyroid tumors except TPM; f) and Articles about other TPM characteristics rather than those in this article title. Initially, we found 1012 articles but after implementation of exclusion criteria finally 110 articles were accepted for analysis.

At the next step, we divided articles in accordance with title and the main subject of each article into 6 groups: Etiology with 5 articles, clinical presentation with 25 articles, diagnosis with 19 articles, follow-up with 20 articles, histopathology with 14 articles and prognosis with 27 articles.

Data Extraction

In this step we inserted each article data about main factors in the title as a table in Excell 2010 software. Each row was about one article and variables were in columns. Variables were the following factors as follows: Article title, year, number of TPM patients, age, sex, etiology, size, clinical presentation, prognosis, treatment, diagnosis, follow-up and histopathology. Data of case-report articles were not appropriate, so finally 87 out of 110 articles were sorted in the table.

Results:

We assessed 87 articles in our search. Our findings in articles are described below:

1- Sex: Among 25953 patients of papillary thyroid microcarcinoma (PTMC) in 75 articles (13-17,19,21-30,32,33,36,38,40-43,45-61,63-66,68,70-80,82-88,90-99) which evaluated the gender of patients, 4485 (18 percent) of them were male and 21468 (82 percent) were female. In 4 articles, females were less than males; in only one article male and female number were the same and 70 articles showed the preference of females.

2- Age: As result of 66 articles (13,15-17,19,21-30,32,33,36,38,40,42-43,45-46,48-49,51,53-61,65-68,71-80,82-85,87-92,94-98) which explained the age of their patients, mean age of PTMC patients concluded 47.2 years. The range of their age was between 8 to 88 years. In 29 articles (13-14,17,22,24-25,38,47-48,50,52,54,56,58,60,63-64,66,77-79,82,84,86,88,91,93-97,99) the patient’s age was divided into 2 groups, one group included patients of 45 years-old or older, other group was patients younger than 45 years. Finally, we found that 7854 (59%) of patients were patients of the first group and 5395 (41%) of them were patients of the other group.

3- Tumor size: For this factor, one group contained patients with tumors of 5mm or smaller and the other group patients had tumors larger than 5mm, but as the patients had PTMC so all tumors were less than 10 mm in diameter. Overall, 4263 (34%) of patients formed the first group and 8224 (66%) were of the second group. Tumor size ranged between 0.1-10 mm with mean of 5.9 mm as described in 52 articles (13-15,17,19-21,23-26,28,32,35-38,42-43,46-49,51,54-56,58-59,61,64-65,67,71-77,79-80,82,84-85,87,90-92,95-97).

4- Etiology: For evaluation of this part 2 factors were assessed, “family history of thyroid cancer” and “patient’s history of radiation”. In 6 articles (13,17,24,63,68,99) mean of 19.3% of patients were positive for family history. On the other hand, only one article (32) with mean of 3% represented the history of radiation in patients.

5- Clinical presentation: Factors for evaluation of this part are described below; a) Presentation of autoimmune thyroid diseases: 3 articles (24,25,88) had this presentation in mean of 35.6% of their patients. b) Presentation of tumor in low stages of 1&2: The average of 77.5% of PTMC patients were in these stages as 17 articles (17,24,25,31,47-48,52,58,63,66,72-73,75,79-80,90,92) explained. c) Presentation of tumor in high stages of 3&4: Mean of 23.33% of patients in 15 articles (17,24-25,47-48,52,58,63,73,75,79-80,90,92) were in stage 3&4. d) Presentation of lymphocytic thyroiditis: 22 articles (22,37,39,42-43,48,55,59,62,64-65,67,70-71,73-
Fig. 1
Algorithm of search in Google scholar database

Thyroid Papillary Microcarcinoma...
Fig. 2
Algorithm of search in Ovid database
Fig. 3
Algorithm of search in PubMed database
Fig. 4
Algorithm of search in Iran medex and SID databases
Fig. 3
Algorithm of classification of articles of search
74.79-80,82,88,96-97) presented this disease in average 19.85% of PTMC patients. e) Vascular emboli were the other factor that presented in 4% of patients only in one article (16). f) Multinodular goiter was presented in mean of 44% of patients in 22 articles (16,27,31,33,37,39-40,43-44,49-50,54-55,62,65,70,82,86,89,91,97,99). And finally 13 articles (16,24,37,44,50,54-55,68,74,82,88,91,99) described presentation of Graves’ disease in average of 12% of patients.

6- Prognosis: The first factor was lymph node metastasis, evaluated in 60 articles (13,15-17,19,21-22,24-26,28,31-33,36,40,44,47,50-54,56-61,63-69,71-73,75-79,82-84,86,88-92,94-99) by mean of 26 percent. Distant metastasis with mean of 3% was the other factor that 15 articles (17,25-26,28,32,42,46-47,54,61,63,82,86,91,93) expressed. Finally, 3 articles (15,47,58) described patients with low risk for tumor recurrence as a factor of prognosis in average of 29%.

7- Treatment: These factors in this part are explained, total or near-total thyroidectomy in 57 articles (14-20,22,24-26,28,31,33,36,40,44-47,49-51,53-57,59-61,65,67,70,74-77,79-80,82-84,86,96,98-99) with mean of 77%, lobectomy in 36 articles (15,25-26,28,36,40,44-45,47,50-51,53-57,60-61,67,70,74,76,79,82,84,86-87,89-92,94-96,99) by mean of 22% and radioactive iodine therapy with mean of 59% in 33 articles (16-17,20,24,28,32-33,40,47,49-51,53-59,61,67,73-75,79,82-83,86,88-89,91,93-94). Lymph node dissection with 2 types of central and lateral was also described. Central form was seen in 28 articles (14-15,18-20,22,25,38,40,44-45,47-48,54-55,59-60,74-77,84,86,88,91,95,99) with mean of 53% but lateral form in 15 articles (19-20,22,25,38,44-45,47,60,77,79,86,90,95,99) with mean of 17%.

8- Diagnosis: Tumor diagnosis was incidental or non-incidental. Twenty five articles (15,19,24,32,38,44-47,49-50,53-54,57,61,67,74-75,82-83,86-88,91,94) with mean of 57% diagnosed tumor incidentally versus 28 articles (15-16,19,24,28,32-33,38,45-47,49-50,53-54,57,61,63,67-68,73-74,82-83,86,88,91,94) in mean of 45% of patients diagnosed it non-incidentally.

9- Follow-up: Factors in this part were as follows: Temporary postoperative hypoparathyroidism in 8 articles (14,19,47,59,75,86,88,94) with mean of 24% of patients, permanent postoperative hypoparathyroidism in 10 articles (14,19,24,47,59-60,75,86,88,94) with mean of 3%, temporary postoperative recurrent laryngeal nerve paralysis in 6 articles (14,19,55,59,75,88) with mean of 3%, permanent postoperative recurrent laryngeal nerve paralysis in 5 articles (24,47,59-60,94) with mean of 1%, duration of patient’s follow-up in 37 articles (16-17,20,25,28,32,34,38,40,45-47,49-52,54-61,73-75,79,82,86-89,91,99) with mean of 63 months, number of disease-related deaths in 11 articles (17,28,45-46,50-52,54,61,86-87) with mean of 1.7%, number of tumor recurrence or distant metastasis during follow-up in 28 articles (17,20,32,34,38,45-47,50-52,54-61,72-73,79,82,87-88,91,93-94,99) with mean of 6% and number of disease-free patients at the end of follow-up in 9 articles (16-17,40,52,54,57,82,86,93) with average of 91%.

10- Histopathology: In this part, different clinical and paraclinical factors were assessed. Details of each factor were number of dissected central lymph nodes in 5 articles (14,19,75,80,94) with mean of 7.86 lymph node, number of dissected lateral lymph nodes in 1 article (19) with average of 15.75 lymph node, MACIS score was reported in 2 articles (14,92) that in both of them more than 90% of patients (93% & 97%) had score of less than 6 and less than 10% (3% & 7%) had score of more than 6. Location of thyroid tumor in 5 articles (14,20,72,77,96) with mean of 48.22% was in upper lobe and with mean of 33.76% was in lower lobe. 3 articles (19,27,67) with mean of 56.42% reported it in the right lobe and with mean of 34% in the left lobe. Solitary tumor was seen in 14 articles (14-15,17,20,25,27,41,55,57,73,86-88,91) with mean...
of 61.6%, as multiple tumors were reported in 7 articles (14,19,25-27,41,79) with mean of 24%. Intrathyroidal invasion was reported in 2 articles (17,24) with mean of 22% but extrathyoidal invasion was seen in 33 articles (13-14,17,21-22,24-25,31-32,45-46,48,50,54,58-61,63-65,72-73,76-80,82,84,86,91,97) and the mean expression of it was in 24.2% of patients. The other presentation of invasiveness was lymphovascular invasion with mean expression of 19.4% in 11 articles (14,21,24,32,47,51,56,64,75,80,88). Capsular invasion was another presentation of aggressiveness with average of 31.1% in 19 articles (14,16,20-21,24,51,54-55,67-68,75,88,90,92,94-98). Ipsilateral central pathologic lymph node positivity was reported in 31.3% of patients in only one article(14).

PTMC has different pathologic variants, classic variant which is most common was reported in 36 articles (15,17,20-21,24,26,30-31,33,35-37,40-44,47,50-51,54,59-60,63,65,69-71,76,84,88,91-92,97-98) with mean of 71% although 30 articles (15,17,20,26,30,33,36-37,40-44,47,50-51,54,65,67,70,76,78,83-84,88,91-92,97-98) with mean of 19% reported follicular variant. Other variants of PTMC in 19 articles (17,26,30,36-37,40-44,47,51,54,69-70,76,88,91-92,98) had average of 11%. Multifocality in 57 articles (15-17,20-22,24-26,28,31-33,37-38,43,45-48,50-59,61,63-65,67,69-73,75,77-82,86-88,90-92,94-97) had mean expression of 28%, in 8 articles (16,48,50,73-74,86-87,97) with mean of 25% the tumor was unilateral while bilateral was reported in 26 articles (16-17,22,24,48,50,54-55,64,73-76,79-81,86-88,91-92,94-98) with mean of 23%.

Various paraclinical factors are detected in PTMC patients, Antimicrosomal antibody in only one article(22) with mean positivity of 5%, thyroglobulin antibody in 6 articles (17,22,24,40,49,99) with mean of 16%. One article (23) reported TSH level with mean level of 1.4 mIU/L in range of 1.07-1.72 mIU/L.

Expression of molecular characteristics in PTMC patients were reported in some articles. Fas ligand positivity in one article(24) in 62.7% of patients, BRAFV600E mutation in 7 articles (25,31,44,72,78,90,98) with mean of 51.28% of patients, P53 gene expression in 2 articles(66,67) with mean of 29.2% and cyclin D1 positivity in 2 articles(78,92) with mean of 60.3%. Some factors were only reported in one article, these factors are listed below: CK-19, HBME-1, galectin-3(34) expression in 98.7%, TSHR mRNA(40) in 59.4%, RET gene rearrangement(42) in 52.3%, Bcl-2 expression(66) in 94.8%, Bax expression(66) in 74.3%, S100A4(78) in 68.6%, P27 gene(78) expression in 36.8%, MUC1 gene expression(78) in 48.4%, FDG positivity(84) in 55% and finally surviving positivity(92) in 66.6% of patients were positive (Table 1).

| Main Factor | Subsidiary Factor | Number of Articles | Mean Value (%) |
|-------------|------------------|-------------------|----------------|
| Gender      | Male             | 75                | 4485(18)       |
|             | Female           | 21468(82)         |                |
| Age         | Mean             | 66                | 47.2           |
|             | Range            |                   | 8-88           |
|             | >= 45 yr         | 29                | 7854(59)       |
|             | <45 yr           |                   | 5395(41)       |

Table 1
Summary of articles’ results

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| Main Factor       | Subsidiary Factor                      | Number of Articles | Mean Value (%) |
|-------------------|----------------------------------------|--------------------|----------------|
| Tumor Size        | Mean                                   |                    | 5.9            |
|                   | Range                                  | 52                 | 0.1-10         |
|                   | >5 mm                                   |                    | 8224(66)       |
|                   | <=5 mm                                  |                    | 4263(34)       |
| Etiology          | Family history                         | 6                  | (19.3)         |
|                   | Radiation history                       | 1                  | (3)            |
| Clinical presentation | Autoimmune thyroid disease           | 3                  | (35.6)         |
|                   | Tumor stage 1&2                         | 17                 | (77.5)         |
|                   | Tumor stage 3&4                         | 15                 | (23.33)        |
|                   | Lymphocytic thyroiditis                 | 22                 | (19.85)        |
|                   | Vascular emboli                         | 1                  | (4)            |
|                   | Multinodular Goiter                     | 22                 | (44)           |
|                   | Graves’ disease                         | 13                 | (12)           |
| Prognosis         | Lymph node metastasis                  | 60                 | (26)           |
|                   | Distant metastasis                     | 15                 | (3)            |
|                   | Low risk for recurrence                 | 3                  | (29)           |
| Treatment         | Total or near-total thyroidectomy      | 57                 | (77)           |
|                   | Lobectomy                               | 36                 | (22)           |
|                   | Radioactive iodine therapy              | 33                 | (59)           |
|                   | Central lymph node dissection           | 28                 | (53)           |
|                   | Lateral lymph node dissection           | 15                 | (17)           |
| Diagnosis         | Incidental                              | 25                 | (57)           |
|                   | Non-incidental                          | 28                 | (45)           |
|                   | Temporary postop. hypoparathyroidism    | 8                  | (24)           |
|                   | Permanent postop. hypoparathyroidism    | 10                 | (3)            |
| Follow-up         | Temporary postop. recurrent laryngeal nerve paralysis | 6 | (3) |
|                   | Permanent postop. recurrent laryngeal nerve paralysis | 5 | (1) |
|                   | Duration of follow-up                   | 37                 | 63 months      |
|                   | Disease-related death                   | 11                 | (1.7)          |
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Summary of articles’ results

| Main Factor | Subsidiary Factor                          | Number of Articles | Mean Value (%) |
|-------------|---------------------------------------------|--------------------|----------------|
| Follow-up   | recurrence or distant metastasis during follow-up | 28                 | (6)            |
|             | Disease-free patients at end of follow-up   | 9                  | (91)           |
|             | No. of dissected central lymph nodes        | 5                  | 7.86           |
|             | No. of dissected lateral lymph nodes        | 1                  | 15.75          |
|             | MACIS score <=6                            | 2                  | (95)           |
|             | MACIS score >6                             | 2                  | (5)            |
|             | Upper-lobe tumor location                  | 5                  | (48.22)        |
|             | Lower-lobe tumor location                  | 5                  | (33.76)        |
|             | Right-lobe tumor location                  | 3                  | (56.42)        |
|             | Left-lobe tumor location                   | 3                  | (34)           |
|             | Solitary tumor                             | 14                 | (61.6)         |
|             | Multiple tumors                            | 7                  | (24)           |
|             | Intrathyroidal invasion                    | 2                  | (22)           |
|             | Extrathyroidal invasion                    | 33                 | (24.2)         |
|             | Lymphovascular invasion                    | 11                 | (19.4)         |
|             | Capsular invasion                          | 19                 | (31.1)         |
|             | Ipsilateral central pathologic lymph node positivity | 1 | (31.3)         |
|             | Classic variant                            | 36                 | (71)           |
|             | Follicular variant                         | 30                 | (19)           |
|             | Other variants                             | 19                 | (11)           |
|             | Multifocality                              | 57                 | (28)           |
|             | Unilaterality                              | 8                  | (25)           |
|             | Bilaterality                               | 26                 | (23)           |
|             | Antimicrosomal antibody                     | 1                  | (5)            |
|             | Thyroglobulin antibody                      | 6                  | (16)           |
|             | Mean TSH level                             | 1                  | 1.4 mIU/L      |
|             | Range of TSH level                         | 1                  | 1.07-1.72 mIU/L|
|             | Fas ligand positivity                      | 1                  | (62.7)         |
|             | BRAFV600E mutation                         | 7                  | (51.28)        |
|             | P53 expression                             | 2                  | (29.2)         |
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Summary of articles’ results

| Main Factor | Subsidiary Factor | Number of Articles | Mean Value (%) |
|-------------|-------------------|--------------------|----------------|
| Histopathology | Cyclin D1 positivity | 2 | (60.3) |
| | CK-19, HBME-1, galectin-3 expression | 1 | (98.7) |
| | TSHR mRNA | 1 | (59.4) |
| | RET gene rearrangement | 1 | (52.3) |
| | Bcl-2 expression | 1 | (94.8) |
| | Bax expression | 1 | (74.3) |
| | S100A4 positivity | 1 | (68.6) |
| | P27 expression | 1 | (36.8) |
| | MUC1 gene expression | 1 | (48.4) |
| | FDG positivity | 1 | (55) |
| | Survivin positivity | 1 | (66.6) |

Discussions

Differentiated thyroid cancer is the most common endocrine malignancy, with rapidly increasing incidence worldwide. Up to 43% of all thyroid cancers are papillary thyroid microcarcinomas (PTMCs) and nearly 50% of new cases of papillary thyroid carcinoma (PTC) are PTMCs (13,72). PTMC is a type of PTC with a maximum diameter of 1.0 cm or less (72,78). PTMCs have been largely perceived as tumors that are characterized by benign behavior, of little clinical significance, and do not affect patients’ survival. However, PTMCs show very diverse disease extent with widely varying reported frequencies of the aggressive features (13, 15, 26).

These tumors are usually encountered during the histopathologic examination of the thyroid glands removed during necropsy or surgery for nonthyroid or nonmalignant thyroid disease (26). A papillary microcarcinoma may occasionally be the primary lesion of a lymph node metastasis presenting clinically as a neck mass (78).

High-resolution ultrasound-guided fine needle aspiration biopsy has led to a rapid rise in the incidence of papillary thyroid microcarcinoma. The wide availability of ultrasound (US) and fine needle aspiration biopsy (FNAB) and the improved accuracy of histopathologic examination of surgical specimens have been suggested to be reasons for the increased rate of detection (14,15,17,21,54,72,78,89).

PTMC is a specific subgroup of PTC that requires attention because of its increasing frequency among patients with PTC in clinical practice and the implications for patient management (77). According to these points, it is important to know more about this tumor and its characteristics. As systematic reviews evaluate a large number of patients therefore, reliable study of this subject can be obtained.

The clinical significance of PTMC is still unclear. Most PTMCs have an indolent course and excellent prognosis, although some are thought to be associated with recurrence, distant metastasis, or mortality (25,76). Papillary microcarcinomas have an excellent prognosis and may even behave like benign lesions (with even possible partial spontaneous regression) which can justify
a minimalist therapeutic approach. However, microcarcinomas are “true” cancers, which may require aggressive treatment in some cases (16). The clinical importance of papillary thyroid microcarcinoma is debatable. Some authors (12-15,22-33,55) have reported a benign behavior with no progression, whereas others (9,66,73) have found a surprisingly aggressive cancer. Only rarely is lymph node or distant metastasis the first presentation of thyroid microcarcinoma (17). In this study, the value of lymph node metastasis was 26% whereas distant metastasis had been reported in 3% of PTMC patients (17).

Although the long-term outcome of PTMC is excellent, with a less than 1% cause-specific mortality rate at 20 years, it frequently spreads to the cervical lymph nodes and may occasionally metastasize to distant sites (54). Patients with PTMC have very low mortality. However, 4-16% of patients with PTMC develop recurrent disease with many of these patients developing distant metastasis (51). In our study mean rate of tumor related mortality was 1.7% and rate of recurrence or distant metastasis after follow-up was 6%.

Furthermore, PTMC is often multifocal (15.5-40% in surgical series and over 80% in systematic autopsy studies) and extrathyroidal tumor extension, a factor correlated with a higher risk of locoregional recurrence, is also observed (10-20% in surgical and pathologic studies) (54). The mean rate of tumor multifocality in our study was 28% and it was 24.2% for extrathyroidal extension.

Despite the absence of palpable neck nodes, PTMC has a considerable rate of lymph node metastasis to the central compartment (80). Extracapsular spread is thought to have predictive value for central compartment LN metastasis. Central compartment LN metastasis in PTMC is associated with a risk of disease recurrence and is a reliable prognostic factor (77). As in previous studies, central LNM was significantly related to bilaterality in our study (97). In this study, extracapsular invasion and bilaterality rates were 31.1% and 23%.

Although PTMC is relatively common, standard treatment for these tumors remains controversial. Some consider PTMC to be a less aggressive subset of papillary thyroid cancers that require only minimal treatment. However, other groups have reported a high incidence of metastasis from microcarcinomas and thus favor an aggressive surgical approach followed by ablation therapy (21, 77, 76). In general, total or near-total thyroidectomy is performed when tumor foci is preoperatively detected in a bilateral lobe. However, in PTMC confined to the unilateral lobe, two options regarding resection extent seem to be applicable: total thyroidectomy vs. unilateral lobectomy (21). It is debatable whether total thyroidectomy or lobectomy is the appropriate treatment for patients with PTMC (54). In the American Thyroid Association guidelines, the recommended treatment in patients with isolated PTMC at low risk consists of thyroid lobectomy, whereas near-total or total thyroidectomy is considered the treatment of choice in patients with a history of radiation therapy to the head and neck or a first-degree member with differentiated thyroid cancer or age greater than 45 years (82). In our study total or near-total thyroidectomy was performed in 77% of patients versus 22% lobectomy.

The identification of patients with aggressive PTMC is of great importance because they need a radical therapeutic approach, as classical PTC, based on total thyroidectomy, lymphadenectomy, central compartment, and radioiodine therapy (82). Although there is a body of literature that advocates the use of I-131 therapy for patients with PTMC (particularly those patients with poor histological features), few studies have been able to demonstrate a clinical benefit of I-131 therapy for patients with PTMC (51). In our study, I-131 therapy was used in approximately half of patients in 59% of them.

Aggressive PTMC treatments can cause adverse outcomes, such as surgical damage to the
recurrent laryngeal nerve, hypoparathyroidism, and the development of new primary cancers after radioiodine treatments (72). In the present study complications of thyroid surgery were divided into groups of temporary and permanent. Temporary hypoparathyroidism in 24%, permanent hypoparathyroidism in 3%, temporary recurrent laryngeal nerve paralysis in 3% and finally permanent form of paralysis was seen in 1% of patients.

Conclusion

The numbers of detected PTMCs are increasing due to the development of diagnostic methods. This tumor can manifest as a marker of advanced papillary carcinomas. Although the tumor naturally is benign and develops slowly, sometimes it can present unfavorable with recurrence and distant metastasis. Overall, identifying this tumor and paying attention to its markers has double benefits, one of them is prevention of advanced tumors that need heavier and longer treatments and also the other benefit is managing the tumor as an distinct disease.

Since in systematic reviews a larger number of patients are analyzed, so there is confidence that recognition of each subject by this type of study is more reliable. At last we hope that by introducing characteristics of this tumor as a review article could have a little but useful role in cancer managements.

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