# Papillary Thyroid Carcinomas in Patients under 21 Years of Age: Clinical and Histologic Characteristics of Tumors ≤10 mm

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**Objective** To compare clinical and histologic characteristics of papillary thyroid carcinomas (PTCs) ≤10 mm in patients ≤21 years old with larger ones and with microcarcinomas in adults.

**Study design** Retrospective study of patients with PTC diagnosed between 1983 and 2012. Medical records were reviewed and information about age, sex, tumor size, intra/extrathyroid extension, lymph node, and distant metastases were collected.

**Results** Patients ≤21 years old (n = 93) and adults (n = 1235) with PTC were identified. Among the former, 34 had PTC ≤10 mm (37.4%) and among the latter, 584 had papillary thyroid microcarcinoma (PTM) (47.3%), $P = .082$. Patients with tumors ≤10 mm less frequently had extrathyroidal extension and lymph node metastases compared with larger tumors (8.8% vs 33.3%, $P = .017$, and 60.0% vs 95.2%, $P = .001$, respectively). The percentage of PTC ≤10 mm increased with age (7.1%, 32.0%, and 48.1% in age groups ≤15, 15-18, and >18 to ≤21 years old, respectively; $P = .016$). Mean tumor size was larger (6.8 ± 2.7 vs 5.8 ± 2.8 mm, $P = .030$), and lymph nodes metastases were more frequent (41.2% vs 18.6%, $P = .003$) in patients ≤21 years of age compared with adults with PTM. The frequency of multifocal cancers decreased between 1983-1992, 1993-2002, and 2003-2012 (66.7%, 53.6%, and 27.1%, respectively, $P = .019$).

**Conclusions** The frequency of PTC ≤10 mm is low in children, increases in adolescents, and reaches that of adults at 18-21 years of age. Mean tumor size is larger and metastases to regional lymph nodes more frequent in comparison with PTM in adults. Whether their treatment and follow-up could be based on guidelines used for PTM in adults is questionable. *(J Pediatr 2015;166:451-6)*.

Thyroid carcinoma is a rare disease in the first 10 years of life.[1] The most common histologic type in adults and children is papillary carcinoma.[2] Usually, children present with large tumors and lymph node metastases in up to 90% of the cases, but the prognosis is generally good.[3,4] Interest in pediatric thyroid cancer has increased, mainly after the Chernobyl nuclear power plant accident in 1986, which resulted in an increased incidence of thyroid cancer in children in the early 1990s.

The prevalence of papillary thyroid carcinoma (PTC) in adults has increased during the last decades,[5-8] largely because of earlier detection of small size (≤10 mm) PTCs called microcarcinomas (papillary thyroid microcarcinoma [PTM]), incidentally found by ultrasonography and fine needle aspiration cytology or after thyroidectomy for benign thyroid disease.[9-11] In different published studies, PTM represent 1%-35% of all cancers.[12,13] Information regarding frequency and characteristics of PTC ≤10 mm in childhood is scanty, with frequency ranging from 1.5%-37% as reported by the few published series.[14-19]

The aims of the present retrospective study were to evaluate clinical and histologic characteristics of PTC in patients ≤21 years old, focusing on the frequency and characteristics of PTC ≤10 mm, and to compare PTC ≤10 mm in this age group with larger tumors and with PTM in adults. As the term "microcarcinoma" in children is not universally accepted in the literature, we preferred to avoid its use in this work.

## Methods

We studied the medical records of 1328 patients with PTC followed in Theagenio Cancer Hospital between January 1983 and December 2012. For each patient, the following characteristics were recorded (by K.P. and P.I.): year of diagnosis of thyroid cancer, age at diagnosis, sex, symptoms and signs leading to diagnosis, history of familial thyroid cancer, history of external radiation therapy, type of surgery, ablation therapy, histologic type (papillary, papillary-follicular variant, papillary-other variants),

| | |
|---|---|
| PTC | Papillary thyroid carcinoma |
| PTM | Papillary thyroid microcarcinoma |
| RAI | Radioactive iodine |
| Tg | Thyroglobulin |

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tumor size, number of tumor foci (unifocal/multifocal), presence of lymph node metastases, tumor or thyroid capsule invasion, vascular invasion, infiltration of thyroid parenchyma or surrounding soft tissues, and presence of distant metastases. In cases with multifocal disease, the size of the largest focus was recorded. Postoperative staging was as per the tumor, nodes, metastasis system as proposed by the American Joint Committee on Cancer.[20] For patients ≤21 years old, data about follow-up duration, radioactive iodine (RAI) administration, detection of residual disease, or local recurrences and new metastases were also recorded. Serum thyroglobulin (Tg) concentration (under thyrotropin stimulating hormone suppression and/or after TSH stimulation), neck ultrasonography, and whole body scan when necessary were used during follow-up to evaluate the course of the disease.

For patients aged ≤21 years, clinical and tumor characteristics were analyzed according to: (1) decade of diagnosis (1983-1992, 1993-2002, 2003-2012); (2) sex and age at diagnosis (≤18 years old and >18 years old); and (3) tumor size (≤10 and >10 mm). Moreover, the frequency and histologic characteristics of PTC ≤10 mm in children and adolescents were compared with those of PTM in adults.

Data analysis was performed using the statistical package SPSS (v 17.0; SPSS Inc, Chicago, Illinois). Data are reported as means ± SD. Differences in thyroid cancer characteristics between groups were assessed with the $\chi^2$ test and with one way ANOVA (with the Holm-Sidak method for post-hoc comparisons). In all cases, a $P$ value of <.05 was considered significant. All data were analyzed anonymously. The study was approved by our Institutional Review Board.

## Results

### Clinical and Histologic Characteristics of PTC in All Patients ≤21 Years Old

Ninety-three patients ≤21 years old with PTC and its variants were identified. Female to male ratio was 7:2 and mean age (±SD) at diagnosis was 18.2 ± 3.0 years. All patients presented with palpable neck mass that corresponded to a single nodule or multinodular goiter or enlarged cervical lymph nodes. No patient had previously received external radiation therapy in the neck or head for the treatment of other primary malignancy nor had been exposed to higher than usual levels of ionizing radiation. Eight patients (8.6%) had a history of familial PTC.

Near total or total thyroidectomy was performed in all patients and central and/or lateral lymph node dissection in 64 of 93. Tumor size was 19.5 ± 15.0 mm. There were no differences between males and females regarding age at diagnosis, tumor size, and histologic characteristics (Table I). Furthermore, we found no differences in clinical and tumor characteristics, including multifocality, between patients with familial and sporadic cancer. The frequency of bilateral cancers decreased during the study period (80.0%, 32.1%, and 16.9% between 1983-1992, 1993-2002, and 2003-2012, respectively; $P$ = .004) and that of multifocal cancers also decreased during the same period (66.7%, 53.6%, and 27.1%, respectively; $P$ = .019).

**Table I. Clinical and histologic characteristics of patients aged ≤21 years diagnosed with PTC**

| Characteristics | Study population, n = 93 | M, n = 22 | F, n = 71 | P value |
|---|---|---|---|---|
| Age at diagnosis (y) | 18.2 ± 3.0 | 17.3 ± 4.0 | 18.5 ± 2.6 | .410 |
| Familial PTC | 8 (8.6) | 1 (4.5) | 7 (9.9) | .675 |
| Histologic type | | | | |
| Classic papillary | 63 (67.7) | 13 (59.1) | 50 (70.4) | .607 |
| P-fv | 23 (24.7) | 7 (31.8) | 16 (22.5) | |
| Papillary-other variants* | 7 (7.5) | 2 (9.1) | 5 (7.0) | |
| Tumor size (mm) | 19.5 ± 15.0 | 23.7 ± 18.1 | 18.2 ± 13.8 | .263 |
| Bilateral location | 23 (25.0) | 6 (27.3) | 17 (24.3) | 1.000 |
| Multifocal disease | 35 (37.6) | 9 (40.9) | 26 (36.6) | .912 |
| Tumor capsule invasion† | 9 (50.0) | 2 (40.0) | 7 (53.8) | 1.000 |
| Infiltration of thyroid parenchyma | 52 (55.9) | 10 (45.5) | 42 (59.2) | .376 |
| Thyroid capsule invasion | 32 (34.4) | 8 (36.4) | 24 (33.8) | 1.000 |
| Infiltration of surrounding soft tissues | 23 (24.7) | 4 (18.2) | 19 (26.8) | .595 |
| LNM‡ | 54 (84.4) | 11 (78.6) | 43 (86) | .677 |
| Vascular invasion | 14 (15.4) | 2 (9.1) | 12 (17.4) | .504 |
| Lymph vessel invasion | 10 (10.9) | 3 (13.6) | 7 (10.0) | .698 |
| Vascular embolus | 4 (4.3) | 0 (0.0) | 4 (5.6) | .570 |

*F*, female; *LNM*, lymph node metastases; *M*, male; *n*, number of patients; *P-fv*, papillary-follicular variant.
Data are presented as mean ± SD or absolute numbers and percentages (in parentheses).
*Variants: trabecular (n = 3), sclerosing (n = 3), and solid (n = 1).
†Among the 18 patients with encapsulated PTC.
‡Among the 64 patients who underwent lymph node dissection.

Tumor size was larger in patients ≤18 years old compared with those aged 18-21 years. It is interesting to note that when patients were divided according to age (≤15, 15-18, and >18 years), it was found that the younger the patient's age the larger their tumor size (29.9 ± 17.3 vs 22.5 ± 15.8 vs 15.3 ± 12.4 mm, respectively; $P$ = .002) (Table II). The negative correlation (Pearson $r$ = −0.346, $P$ = .001) between age and tumor size in patients ≤21 years of age is shown in the Figure. Moreover, infiltration of the surrounding soft tissues and distant metastases were more frequent in patients ≤18 years old compared with those 18-21 years old (40.0% vs 13.2 %, $P$ = .006 and 17.5% vs 0.0%, $P$ = .002, respectively).

### Comparison of PTC ≤10 mm to PTC >10 mm in Patients ≤21 Years Old

Patients were divided according to tumor size in 2 groups: ≤10 mm and >10 mm. Thirty-four patients (37.4%) had papillary cancers ≤10 mm (10 of them ≤5 mm) in their maximal diameter. Patients with tumor ≤10 mm were older than those with larger tumors ($P$ = .004). Thyroid parenchyma infiltration, thyroid capsule invasion, infiltration of surrounding soft tissues, and lymph node metastases were less frequent in patients with tumor size ≤10 mm compared with patients with larger tumors ($P$ < .001, $P$ = .005, $P$ = .017, $P$ = .001, respectively; Table III).

The percentage of tumors ≤10 mm did not change during the study period (40.0%, 25.0%, and 43.1% between 1983-1992, 1993-2002, and 2003-2012, respectively; $P$ = .264), but increased with age (7.1%, 32.0%, and 48.1% between