

## Incidental Papillary Thyroid Microcarcinoma: is Completion Surgery Required?

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### Rezumat

**Microcarcinomul papilar tiroidian descoperit incidental: este necesară reintervenția pentru completarea tiroidectomiei?**

**Introducere:** Indicațiile chirurgiei de completare la pacienții cu microcarcinom papilar tiroidian (PMC) descoperit incidental pe piesa de tiroidectomie, după rezecții pentru afecțiuni benigne, rămâne un subiect controversat.

**Metoda:** Într-un studiu retrospectiv, transversal, de cohortă a 187 PMC, descoperite incidental în cursul examenului histopatologic al glandei tiroide, la 2168 pacienți operați pentru afecțiuni tiroidiene benigne, am analizat influența tratamentului chirurgical inițial și al celui de completare asupra caracteristicilor anatomo-patologice asociate cu recidiva locală și mortalitatea prin cancer tiroidian.

**Rezultate:** La pacienții cu tiroidectomie totală sau aproape totală la prima operație, limfadenectomia ganglionilor suspecți de malignitate la ultrasonografia postoperatorie a fost urmată de o creștere statistic semnificativă ( $p < 0.01$ ) a cazurilor cu metastaze ganglionare la examenul anatomopatologic. Chirurgia de completare efectuată la 38 din cei 42 pacienți cu lobectomie sau tiroidectomie subtotală la prima intervenție chirurgicală nu a fost urmată de o creștere semnificativă a numărului sau mărimii tumorilor, multifocalității, bilaterali-

tății, invaziei extratiroidiene sau metastazelor ganglionare. În privința complicațiilor postoperatorii, nu au fost diferențe statistic semnificative între cele două grupuri de pacienți.

**Concluzii:** La pacienții cu lobectomie sau tiroidectomie subtotală și PMC descoperite incidental pe piesa de rezecție, având dimensiuni 1-5 mm și fără invazie extratiroidiană, chirurgia de completare nu a fost urmată de o creștere semnificativă a caracteristicilor patologice asociate cu morbiditatea și mortalitatea prin cancer tiroidian.

**Cuvinte cheie:** microcarcinom papilar tiroidian, tiroidectomie de completare, limfadenectomie

### Abstract

**Background:** The indications for completion surgery in patients with thyroid papillary microcarcinoma (PMC), incidentally found in thyroids removed for benign conditions, remains a subject of debate.

**Methods:** In a retrospective, transversal, cohort study of 187 incidental PMCs, found during histological examination of the thyroid gland in 2168 patients operated for benign thyroid conditions, we evaluated the influence of initial and completion surgery on pathological features associated to local recurrence and cancer-related mortality.

**Results:** In the patients with almost total or total thyroidectomy at the first operation, lymphadenectomy of lymph nodes with features suggestive of malignancy on postoperative ultrasound resulted in a statistically significant ( $p < 0.01$ ) increase of node positive patients in pathological examination. Completion surgery in 38 out of 42 patients who underwent less than a total

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thyroidectomy doesn't result in a significant increase of tumor size, number, multifocality, bilaterality, invasion or nodal metastases. There were no significant differences in postoperative complications between the two groups.

**Conclusions:** In patients with less than total thyroidectomy and incidentally found PMC in resection specimens, 1-5 mm in greatest dimension and without extrathyroidal extension, completion surgery was not followed by a significant increase of pathological features associated to cancer related morbidity and mortality.

**Key words:** papillary thyroid microcarcinoma, completion thyroidectomy, lymphadenectomy

## Introduction

The incidental finding of papillary thyroid microcarcinoma (PMC - papillary tumors with the greatest dimension  $\leq 10$  mm) during pathological examination of the resection specimens in patients operated for multinodular goiter, Hashimoto's thyroiditis or Graves-Basedow disease remains a common scenario, in spite of advances in preoperative investigation, mainly ultrasound and fine needle aspiration cytology (FNAC)(1-3). The reported incidence of carcinoma following thyroidectomy for a presumably benign thyroid disease varies in large limits: 3.4% (4); 7.1% (5); 10.4% (6); 11% (7); 13.4% (8); 13.7% (9); 14.07 (10); 21.6% (11).

The ideal therapeutic approach in PMC patients remains a subject of debate among endocrinologists and surgeons. What should be done in patients with incidentally found PMC when less than total or almost total thyroidectomy has been done (12) is even more controversial. A few authors recommend that the treatment of patients with PMC should be no different from the treatment of patients with papillary thyroid carcinoma (PTC), and recommend systematic completion thyroidectomy (CTT) (5,11,13). Other authors consider that further surgery, such as completion total thyroidectomy or lymph node dissection is not necessary unless gross nodal metastases are present (14,15), extracapsular invasion (16,17) or multicentricity (18,19) are present. There is also a lot of controversy regarding radioiodine and suppressive therapy.

The purpose of this study was to evaluate the surgical approach in patients with unsuspected PMC on thyroidectomy specimens, operated in a community hospital. We compared the PMC's pathological features associated to local recurrence and cancer-related mortality in the group of patients with almost total thyroidectomy or total thyroidectomy (ATT / TT) at the first operation, with the patients in whom a subtotal thyroidectomy or lobectomy (STT / LT) have been initially performed. We also examined the change of the pathological parameters in patients in whom a completion surgery has been performed.

## Methods

A total of 2168 patients underwent partial or total thyroidectomy for presumed benign thyroid conditions in a community hospital, during a 10-year period, from the 1<sup>st</sup> of January 2002, to the 31<sup>st</sup> of December, 2011. After the approval from the Hospital Ethical Review Board, a cross-sectional population analysis of the prospectively maintained database, including surgical and pathological reports and follow-up recordings, was performed. All patients provided written informed consent for the collection of clinical and laboratory data and for the use of their data in scientific reports.

All the patients included in the study were scheduled for surgical treatment of benign thyroid pathology, i.e. multinodular goitre, Hashimoto's thyroiditis or Graves-Basedow disease. The pre-therapeutic freeT3 (FT3), free T4 (FT4), thyroid-stimulating hormone (TSH) and anti-thyroid peroxidase antibodies (AbTPO) were measured in all patients and thyroid hormone receptor antibody (TRab) and calcitonin only when indicated by the endocrinologist. All the patients with hyperfunction (suppressed TSH) were treated with anti-thyroid drugs. Thyroid ultrasound was performed in all patients and thyroid scan in 390 (18%). The FNAC of thyroid nodules with features for malignancy on ultrasonography (US) (hypoechoogenicity, microcalcifications, absence of peripheral halo, irregular borders, intranodular hypervascularity and regional lymphadenopathy) and/or scintigraphy ("cold nodules") was performed in 615 patients (28.37%). In patients with multiple nodules, one dominant/suspicious for malignancy or two nodules larger than 10mm in maximal diameter were biopsied. We included in the study only the patients with benign or non(-)diagnostic cytology on FNAC. Vocal cord examination was performed by indirect laryngoscopy in all patients.

Thyroidectomies were performed by 9 general surgeons, and more than 80% by a single surgeon of our team. The extension of the thyroidectomy, subtotal (STT), total lobectomy (TL), almost total thyroidectomy (ATT) or total thyroidectomy (TT) was decided by the operating surgeon, depending on the extension of lesions, patient's wish and intraoperative findings. Frozen sections were performed when requested by the operating surgeon. The patients with cancer on frozen sections had ATT or TT and prophylactic or therapeutic central compartment lymphadenectomy and lateral neck dissection of the involved lymph nodes. They were excluded from the study.

Pathological examination was performed by two pathologists, according to the hospital examination protocol, standardized according to Rosai et al. (20) and Sneed (21). The mean number of paraffin blocks per resected thyroid specimen was 6.8 (4-10 blocks / patient). All patients with PMC, i.e. papillary tumors with the greatest dimension  $\leq 10$  mm, incidentally found in goitre removed for presumed benign conditions were included in the study.

After the release of the pathology report (mean 5 days after surgery; limits: 4-8 days) all the patients with thyroid cancer on permanent sections were evaluated by a team, consisting of the endocrinologist, the operating surgeon and the nuclear medicine specialist. According to the clinical,

laboratory and imaging data, intraoperative findings/surgical protocol and pathology report, the patient was included in a risk category (22,23) After a thorough discussion with the patient and his family about therapeutic alternatives, the patient was assigned to completion surgery, radioiodine administration or suppressive therapy.

The status of the parathyroid glands and the RLN was assessed clinically, and when changes were noticed, by total and ionized serum calcium respectively by indirect laryngoscopy, at the discharge (the day after surgery/completion surgery), in the 5-th postoperative day and 3 months after surgery. Recurrent laryngeal nerve (RLN) injury and hypoparathyroidism were considered permanent if they persisted 6 months after surgery.

The radioiodine ablation (I-131) was indicated for patients from the intermediate or high risk group, with previously ATT or TT +/- lymphadenectomy, after appropriate TSH raising at levels above 40 mIU/L (N.V. 0.4-4.2 mIU/L). The mean radioiodine activity was 72.3 mCi (2.7 GBq) and ranged between 30 mCi (1.1 GBq) and 150 mCi (5.5 GBq). The recombinant human TSH (rhTSH) was never used in our cohort for ablation; it was reserved only as alternative for thyroid hormone withdrawal during the follow-up.

The patients' follow-up was performed according to European Thyroid Association – ETA (23) and American Thyroid Association – ATA (22) recommendations. In patients in complete remission, i.e. on US; undetectable serum Thyroglobulin (Tg) and no anti-Thyroglobulin anti-bodies (AbTg) at any time during follow-up, the Levothyroxine (LT4) therapy was shifted from suppressive to replacement.

We studied the following parameters: extent of the surgery at the first operation, extent of the completion surgery and postoperative complications (temporary and permanent RLN

lesions and hypoparathyroidism); tumor size, number (multi-centricity), bilaterality, capsular invasion/extrathyroidal extension and cervical lymph node metastases; radioiodine treatment. SPSS 16.0 (SPSS Onc., Chicago, IL) was used for statistical analysis.  $\chi^2$ , Mann-Whitney and Fisher's exact tests were used as appropriate, and two-tailed P value <0.05 was considered significant.

## Results

In a 10-year interval, between 2002-2011, we performed 2340 partial or total thyroidectomies, 2168 (92.64%) for presumed benign conditions and 172 (7.36%) for cancer. In 138 patients the cancer was diagnosed by FNAC and in 24 intra-operatively, by frozen sections. Of the 2168 patients, 12 were lost during the follow-up and were excluded from the study. In the 2156 patients operated for presumed benign conditions (multinodular goiter, Hashimoto's thyroiditis, Graves-Basedow disease or adenoma), PMC was found in permanent sections in 187 cases (8.67%). In 66 out of 187 cases PMC was multifocal (35.3%), and in 31(16.5%) bilateral (Table 1).

The initial surgical procedure was ATT or TT in 145(77.5%) patients, TL in 12(6.5%) and STT in 30(16%). Most STTs were performed during the initial part of this interval and none in the last two years.

Therapeutic neck dissection was proposed to 12 patients with ATT or TT and regional lymphadenopathy on neck post-operative US with features suggestive of malignancy (22,23) (FNAC confirmation in 4 patients). Three central bilateral (24) and 9 selective lateral (IIa, III,IV and Vb) (25) were performed. In the three patients with central node dissection two were positive for cancer (N1a) and one negative (N0), and in the 9 selective lateral neck dissections 4 were positive for

**Table 1.** Extent of surgery and pathological characteristics of 255 PMCs found on permanent sections in 187 patients operated for benign thyroid conditions (CTT-completion thyroidectomy)

| Surgical procedure |                 | No. of patients | No. of tumors | No. of multi-focal tumors | No. of bilateral tumor | Mean tumors size (mm) | No. of tumors ≤5mm | No. of tumors >5mm | Pathological staging (No. of patients) |    |     |      |      |      |           |
|--------------------|-----------------|-----------------|---------------|---------------------------|------------------------|-----------------------|--------------------|--------------------|--|----|-----|------|------|------|-----------|
|                    |                 |                 |               |                           |                        |                       |                    |                    | T1a                                    | T3 | NX  | N0   | N1a  | N1b  | N1 (a+ b) |
| TOTAL              | Final           | 187             | 255           | 66                        | 31                     | 3.67                  | 200                | 55                 | 176                                    | 11 | 125 | 47   | 11   | 4    | 15        |
| TT + ATT           | Initial         | 145             | 202           | 56                        | 26                     | 3.69                  | 156                | 46                 | 135                                    | 10 | 133 | 6    | 6    | 0    | 6         |
|                    | Lymphadenectomy | 12              | 0             | 0                         | 0                      | 0                     | 0                  | 0                  | 0                                      | 0  | 0   | 6    | 2    | 4    | 6         |
|                    | Final           | 145             | 202           | 56                        | 26                     | 3.69                  | 156                | 46                 | 135                                    | 10 | 121 | 12   | 8    | 4    | 12        |
|                    | p               | -               | -             | -                         | -                      | -                     | -                  | -                  | -                                      | -  | -   | 0.25 | 0.80 | 0.06 | <0.01     |
| LT                 | Initial         | 12              | 12            | 0                         | 0                      | 3.16                  | 12                 | 0                  | 12                                     | 0  | 12  | 0    | 0    | 0    | 0         |
|                    | CTT             | 12              | 1             | 1                         | 1                      | 2                     | 1                  | 0                  | 12                                     | 0  | 0   | 12   | 0    | 0    | 0         |
|                    | Final           | 12              | 13            | 1                         | 1                      | 3.07                  | 13                 | 0                  | 12                                     | 0  | 0   | 12   | 0    | 0    | 0         |
|                    | p               | -               | -             | -                         | -                      | -                     | -                  | -                  | -                                      | -  | -   | -    | -    | -    | -         |
| STT                | Initial         | 30              | 33            | 3                         | 1                      | 4.18                  | 24                 | 9                  | 29                                     | 1  | 30  | 0    | 0    | 0    | 0         |
|                    | CTT             | 26              | 8             | 6                         | 3                      | 2.14                  | 8                  | 0                  | 8                                      | 0  | 0   | 23   | 3    | 0    | 3         |
|                    | Final           | 30              | 41            | 9                         | 4                      | 3.82                  | 32                 | 9                  | 29                                     | 1  | 4   | 23   | 3    | 0    | 3         |
|                    | p               | -               | -             | -                         | -                      | -                     | -                  | -                  | -                                      | -  | -   | 0.01 | 0.13 | -    | 0.13      |
| LT + STT           | Initial         | 42              | 45            | 3                         | 1                      | 3.88                  | 36                 | 9                  | 41                                     | 1  | 42  | 0    | 0    | 0    | 0         |
|                    | Final           | 42              | 54            | 10                        | 5                      | 3.66                  | 45                 | 9                  | 41                                     | 1  | 4   | 35   | 3    | 0    | 3         |
|                    | p               | -               | 0.53          | 0.13                      | 0.12                   | -                     | 0.47               | -                  | -                                      | -  | -   | 0.01 | 0.13 | -    | 0.13      |

cancer (N1b) and 5 negative (N0) (Table 1). The therapeutic neck dissection of the 12 patients resulted in a pathological up-stage in 5 patients over 45 years old.

The CTT was proposed to all patients with limited resections. Four patients with STT, all with unifocal, intrathyroidal,  $\leq 5$  mm tumors, refused CTT and were followed at 6 months, by US, serum Tg and AbTg. On completion thyroidectomy, ATT or TT plus prophylactic bilateral central neck dissection was performed in 38 out of 42 patients with limited resections. In the 12 patients with TL (all with unifocal, intrathyroidal,  $\leq 5$  mm tumors), a single 2mm tumor was in the contralateral lobe in one patient and no tumor involved lymph nodes in the central compartment. In the 26 patients with STT at the first operation, CTT resulted in eight  $\leq 5$  mm tumors found in 6 patients. The 26 bilateral central compartment dissections detected lymph node metastases in 3 patients and were negative in 23 patients (Table 1). CTT and prophylactic central compartment dissection resulted in a pathological up-staging in one female patient, 53 years old.

Table 1 depicts the size of tumors in the TT+ATT and LT+STT groups. We found no difference in the proportion of thyroid nodules size between the two groups ( $p=0.51$ ). Of the 255 tumors found in 187 patients, 200(78.4%) were  $\leq 5$  mm and 55(21.6%) between 6 and 10mm diameter. The mean tumor size of the 255 PMCs was 3.67 mm, 3.69 mm in the TT+ ATT group and 3.66 mm in the LT + STT group. There were no significant differences between the TT+ATT and LT+STT groups, before and after completion surgery, in terms of tumor size, multicentricity, bilaterality, and T and N staging. Completion surgery in the TL+STT group was not followed by a significant increase of tumor number, multi-focality, bilaterality, tumor size or extra-thyroidal extension, (T3 PMC's). All the patients with tumors  $\leq 5$  mm and no capsular invasion (T1a,  $\leq 5$  mm) were V0, L0, N0 (Table 1).

In the ATT + TT group, lymphadenectomy in twelve patients with lymph nodes with features suggestive of malig-

nancy on postoperative US (three central compartment nine selective lateral lymphadenectomy of the involved side) resulted in a significant increase of lymph node positive patients ( $p<0.01$ ). Prophylactic central compartment lymphadenectomy in 38 out of 42 patients of the LT+STT group resulted in 35N0 and 3N1a, a not statistically significant ( $p=0,13$ ) increase of node positive patients (Table 1).

Table 2 summarizes the main postoperative complications, RLN injury and hypoparathyroidism. There were no significant differences in postoperative complication between the patients with TL+STT and ATT + TT at the first operation (Table 3). Completion surgery in patients with LT and STT was not followed by a significant increase of complications incidence. Bilateral central compartment lymphadenectomy resulted in a significant increase of the incidence of temporary hypoparathyroidism ( $p<0.01$ ).

Radioiodine ablation was omitted in 82 patients with unifocal or multicentric  $\leq 5$  mm PMC after TT, ATT or completion, with favorable histology, no extrathyroidal extension and no high-risk history. In 105 patients, after individual dosimetry, the administered I-131 varied between 30 and 150 mCi (1.1 – 5.5 GBq).

After a mean follow-up of 42 months (limits 12-131 months), all but one patient are in complete remission, and none of the patients developed distant metastases. The patient with local recurrence is a 36 year-old male, with ATT at the first intervention and unifocal PMC T1a (9 mm) N1b M0 on multinodular goiter, incidentally discovered on permanent sections. On completion surgery, bilateral central compartment and right lateral selective lymphadenectomy was performed, followed by radioiodine therapy. The local central compartment recurrence was diagnosed 14 months after therapy, with Tg 8.35 ng/mL (N.V.  $<0.1$  ng/mL) and abnormal central neck intake on post-therapy I-131 whole body scan. The relapse was treated with a total activity of 120 mCi(4.4 GBq) and after 12 months the patient is in complete remission (Tg  $<0.1$  ng/mL).

**Table 2.** Postoperative complications (RLN injury and hypoparathyroidism) in 187 thyroidectomies plus 50 completion thyroidectomies (CTT)

| Surgical procedure   | No. of patients | Temporary unilateral RLN injury*<br>No. of patients (%) | Permanent unilateral RLN injury*<br>No. of patients (%) | Temporary hypoparathyroidism<br>No. of patients (%) | Permanent hypoparathyroidism<br>No. of patients (%) |
|--|-----------------|---|---|---|---|
| TT + ATT   |                 |   |   |   |   |
| Patients with one surgical procedure                                   | 133             | 2 (1.5%)  | 1(0.75%)  | 3(2.2%)   | 0   |
| Patients with therapeutic lymphadenectomy                              | 12              | 0   | 0   | 3(25%)  | 0   |
| LT + STT   |                 |   |   |   |   |
| Patients with one surgical procedure (STT)                             | 4               | 0   | 0   | 0   | 0   |
| Patients with CTT and prophylactic central compartment lymphadenectomy | 38              | 1(2.6%)   | 0   | 8(21%)  | 0   |
| TOTAL  | 187             | 3(1.6%)   | 14(7.5%)  | 0   |   |

\*Data based on the indirect laryngoscopy performed in patients with vocal changes

## Discussion

Patients with thyroid benign conditions are addressed to surgery because of compression, hyperfunction or aesthetic reasons. There is also a certain number of patients with thyroid nodules and clinical and imagistic suspicion of malignancy and non-diagnostic FNAC. Incidental identification of PMC on permanent sections, in thyroids removed for reasons other than cancer is common. We found 187 PMC in 2156 patients (8.67%), figure close to the reported incidence in a similar study (26). A third of the PMCs were multifocal and 16.5% bilateral, similar to other published series (27). Of the 255 PMC, 200 were  $\leq 5$  mm, and 55 tumors were 6-10 mm in greatest dimension. The mean tumor size was 3.67 mm.

In patients operated for benign thyroid condition less than TT or ATT are common, and in the vast majority of the patients, lymph node resection is not attempted. When cancer is detected on permanent sections, the issue of completion surgery arises. Incidental PMC is often perceived by patients and doctors as a diagnosis and therapy failure and even more as completion surgery is necessary (28). Of the 187 patients with PMC on permanent section 42 (22.46%) had LT or STT and only 12 (6.4%) had central compartment lymphadenectomy at the first intervention (intraoperative clinically involved lymph nodes).

When comparing the two groups of patients, with ATT / TT and respectively TL / STT at the first operation, before and after completion surgery, we found no significant differences regarding the number of tumors, multifocality, bilaterality, mean tumor size, number of tumors 1-5 mm or 6-10 mm on the greatest dimension, and extra-thyroidal extension, invasion (T3) or lymphatic (N1). None of the patients with tumors 1-5 mm in the greatest dimension and without extra-thyroidal extension (T1a) had clinically involved lymph nodes or lymph node metastases on the final pathological staging.

Completion surgery proponents (5,11,13,29) believe that completeness of surgical resection is an important determinant of outcome, while residual metastatic lymph nodes represent the most common site of disease persistence and recurrence. Moreover, complete resection permits accurate staging of the disease, facilitates postoperative treatment with radioactive

iodine, where appropriate, and permits accurate long-term surveillance for disease recurrence, as both RAI whole-body scanning (WBS) and measurement of serum Tg are affected by residual normal thyroid tissue.

On the other hand, incidentally detected PMC, even when multifocal, is a biologically indolent tumor with a very good prognosis (30,31). In a study of Ito et al (15), none of the 317 patients with STT for presumed benign thyroid pathology underwent further surgery such as completion total thyroidectomy and node dissection. Seven patients (2.2%) have had recurrences, 6 locoregional and one bone metastasis and none of the patients have died of thyroid carcinoma. In another recent study published by the same group (32), 340 patients with PMC without unfavourable features (location adjacent to the trachea or on the dorsal surface of the thyroid possibly invading the RLN, clinically apparent nodal metastasis, or high-grade malignancy on FNAB) underwent observation for periods ranging from 18 to 187 months (average 74 months). The proportions of patients whose PMC showed enlargement by 3 mm or more were 6.4 and 15.9% on 5-year and 10-year follow-up, respectively. Novel nodal metastasis was detected in 1.4% at 5 years and 3.4% at 10 years. After observation 109 of the 340 patients underwent surgery for various reasons, and none of those patients showed carcinoma recurrence.

In the ATT / TT group, therapeutic lymphadenectomy performed when there were involved lymph nodes on the US resulted in a significant increase of lymph node positive patients. This finding supports the recommendation to perform systematic lymph node dissection of the lateral and central compartment in the case of clinically pathological findings in cervical lymph nodes (33).

In our study, completion surgery in the TL / STT group did not result in a significant increase of tumor number, multifocality, bilaterality, tumor size or extra-thyroidal extension, (T3 PMCs). In the same group of patients, prophylactic central compartment dissection wasn't followed by a statistically significant increase of node positive patients. This is in accordance with recently published data) (33).

Because in different studies the extent of surgery did not influence the mortality in patients with PMC, which remains extremely low (15,31,34), the main concern will be morbidity.

**Table 3.** Postoperative complications (RLN injury and hypoparathyroidism): The operative risk related to extension of surgery and central compartment lymphadenectomy

|   | Temporary unilateral<br>RLN injury | Permanent unilateral<br>RLN injury | Temporary<br>hypoparathyroidism | Permanent<br>hypoparathyroidism |
|---|------------------------------------|------------------------------------|---------------------------------|---------------------------------|
| TT+ATT<br>versus<br>LS+ST<br>(initial surgery)                              | p=0.94                             | p=0.97                             | p=0.91                          | -                               |
| TT+ATT<br>versus<br>LS+ST<br>(after completion)                             | p=0.76                             | -                                  | p=0.52                          | -                               |
| Patients with limphadenectomy<br>versus<br>Patients without limphadenectomy | p=0.60                             | p=0.73                             | p<0.01                          | -                               |

The indication for reoperation in PMC incidentally found after TL or STT should be weighted in terms of benefits of local recurrence versus risk for complications. Moreover, reoperation might be postponed until local or lymphatic recurrence, if the surgery can be done well and the risk for distant metastases is not increased.

In this study we found no statistical difference of temporary or permanent RLN palsy and temporary hypoparathyroidism between patients with TL+STT and ATT + TT at the first operation. Systematic exposure of the nerve during operation was shown to reduce the risk of RLN lesions (35). Temporary hypoparathyroidism is more common in patients with TT when compared with STT patients. As a consequence, some authors recommend ATT as an alternative to TT (7,36-38). The good results of CTT are to be expected when surgery is performed by experienced surgeons and surgery is performed within 7 days of the primary operation (39,40).

In accordance with most published data (24,41), in our patients, central compartment lymphadenectomy resulted in a significant increase of temporary hypoparathyroidism ( $p < 0.01$ ) when compared to patients in whom lymphadenectomy was omitted. There was no significant increase of RLN injury in patients with lymphadenectomy.

The large series of patients with partial resection followed for a long time confirms the low malignant potential of PMC. That means that in most of the patients the CTT and lymphadenectomy will be an overtreatment (42). If overtreatment with initial surgery can be accepted (in experienced hands the complication for TT and lymphadenectomy being low), it would be more difficult to sustain it in patients with less than ATT or TL at the first operation.

Although PMC is generally associated with an excellent prognosis, a small number of patients experience local recurrence or may die of PMC. In these cases, early detection and aggressive treatment, surgery and radioiodine therapy, are mandatory (43). The presence of risk factors associated with cancer-related mortality can help identify patients who should be considered for more aggressive management (44). Age greater than 45 years (44), male gender (45), tumor size (greater than 5 mm) (46), multicentricity/bilaterality (45,47,48) [contested by some authors (46)], capsular invasion (48), extrathyroidal invasion, (44,45), lymph node metastases (30,49), and distant metastases(30) were considered to be significant risk factors for overall survival. Other pathological parameters, such as vascular and lymphatic invasion and peritumoral desmoplasia are indicators of PMC invasive behaviour (50,51). The BRAF (V600E) mutation can be used as a potential prognostic factor in PMC patients (49,52,53), as well as a target for adjuvant treatment in metastatic disease (54).

## Conclusions

In patients with less than total thyroidectomy and incidentally found PMC on resection specimens, 1-5 mm in greatest dimension and without extrathyroidal extension, completion surgery was not followed by a significant increase of pathological features associated to cancer related morbidity and mortality. In

patients with lymph node involvement on postoperative US examination lymphadenectomy resulted in a significant increase of lymph node positive patients. Prophylactic central compartment was not followed by a statistically significant increase of node positive patients and resulted in increased temporary hypoparathyroidism.

In patients with high risk history, PMC's >5 mm, unfavourable histology or extra-thyroidal extension, completion surgery facilitates accurate treatment and long-term surveillance for disease recurrence.

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