Comparison of the prevalence of incidental and non-incidental papillary thyroid microcarcinoma during 2008–2016: a single-center experience

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Abstract

Background: The incidence of papillary thyroid microcarcinoma (PTMC) is increasing; however, it is not clear whether this reflects an increase in the incidence of incidental or in that of non-incidentally (presurgically) discovered PTMC (IPTMC vs. NIPTMC). We assessed the incidence of IPTMC and NIPTMC over the past 9 years, to discern whether the increase in PTMC incidence is due to improved diagnostics or to a real increase in the incidence.

Methods: We performed a retrospective chart review of 4327 patients who were consecutively admitted to and surgically treated for thyroid pathology at a single institution. As a main presurgical diagnostic test, all patients underwent ultrasound-guided fine-needle aspiration biopsy (UG-FNAB). The analyzed time frame was divided into three equal periods (I: 2008–2010, II: 2011–2013, III: 2014–2016), and IPTMCs and NIPTMCs were assessed and compared in each period.

Results: We evaluated 393 (9.08%) patients with thyroid malignancy, of which 156 (3.60% of all thyroid tumors [TTs]; 39.69% of all thyroid cancers [TCs]) were diagnosed as PTMC. The prevalence of NIPTMC among all TCs increased from 16.66% in 2008 to 33.75% in 2016, while that of IPTMC decreased from 20.83% in 2008 to 13.75% in 2016. The incidence rates of NIPTMC and IPTMC in period III differed statistically significantly (p < 0.0001). The prevalence rate of NIPTMC in period III was higher than that in period II, yet comparable to that in period I (p = 0.0014; p = 0.2804, respectively).

Conclusions: The prevalence of NIPTMC, rather than that of IPTMC, is escalating; this may be due to better presurgical diagnosis.

Keywords: Incidental, Non-incidental, Papillary thyroid microcarcinoma

Background

Thyroid carcinoma (TC) is the most common malignant tumor of the endocrine system [1]. It constitutes approximately 1% of all human malignancies and is the main cause of death among endocrine tumor-related deaths [2]. In 2010, Jemal et al. reported 44,700 new cases of thyroid cancers per year, worldwide, and 1700 deaths due to this condition occurred annually [3]. An annual increase of 5.3% in TC incidence was reported by Magreni et al. in 2015 [4].

Papillary thyroid cancer (PTC), which is the main type of TC, accounts for 80% of all thyroid malignancies [5]. The prognosis of PTC is generally favorable; however, for some subtypes, prognosis may depend on the cancer stage at the time of diagnosis. For early stages, the 10-year survival rate reaches 90%, whereas for later stages, the 10-year survival rate is not as high [5].

A clinically important type of PTC is a tumor with a small size (diameter ≤ 1.0 cm), regardless of whether...
lymph node and local invasion, as well as distant metastases, has occurred. The World Health Organization (WHO) defines these tumors as a papillary thyroid microcarcinoma (PTMC) [6]. PTMCs account for approximately 30% of all PTCs [7]. Some authors have described PTMCs as tumors with low malignancy, which are slow-growing, minimally invasive, and associated with low mortality [8]. Based on autopsy studies, Solares et al. have confirmed that up to 36% of PTMCs had low aggressiveness [9]. Other reports have also described these tumors as common and typical findings, with a favorable prognosis [10]. However, very aggressive forms of PTMC have also been described [11]. Therefore, Gao et al. stated that PTCs with a small size (≤ 1.0 cm in diameter) do not always behave as indolent tumors [12].

To date, the diagnosis of PTMC has been highly reliant on a high-frequency ultrasonography examination and ultrasound-guided fine-needle aspiration biopsy (UG-FNAB), which remains the standard diagnostic procedure for the evaluation of thyroid nodules. The main purpose of UG-FNAB is to distinguish between malignant and benign tumors and to identify patients requiring surgical treatment [13].

The accuracy of diagnostic procedures for thyroid nodules has improved over the last few years, and the ease of access to such diagnostic modalities may be the reason for the higher prevalence of thyroid tumors. However, the exact cause of this increase is still debated. As we have observed a continuous increase in the PTMC incidence over a number of years, we have contemplated various reasons for this phenomenon. Although improvements in the imaging tools, availability of UG-FNAB, and easier access to diagnostic thyroid pathology may play a role, some changes in the environment may also have caused a real increase in the morbidity rate.

The purpose of this study was to assess and compare the incidence of PTMC over the last 9 years and to identify whether there is a difference in the number of presurgically discovered (non-incidental) and non-discovered (incidental) PTMCs, to determine whether the increased incidence in PTMC is due to improved diagnostics (mainly UG-FNAB).

All patients underwent UG-FNAB as the main presurgical diagnostic test. The same equipment and ultrasonography set in all biopsies were used. A 10-MHz linear probe of ultrasonography set has been applied. The UG-FNAB was performed using 0.5-mm gauge needles and 10-cc syringes for each procedure. Clinical and pathological classification was performed according to the TNM classification criteria (7th Edition, 2015) by the American Joint Committee on Cancer (AJCC) [14]. All of the patients underwent total thyroidectomy by the same team of surgeons experienced in thyroid surgery, and all histopathological specimens were examined by the same two pathologists, who were both experienced in diagnosing thyroid malignancy.

Statistical analysis
Statistical analysis was conducted with the use of Statistics vs. 12 (StatSoft, Inc., Tulsa, OK, USA; 2014). The following statistical measures were used: arithmetical mean (x), median and standard deviation (SD), and ranges of determined parameters in study groups.

The Shapiro-Wilk test was used to confirm the normality of data distribution. As data demonstrated a normal distribution, t tests were used to assess the significance of differences. Intergroup frequency assessment was performed using a chi-squared test. Yate’s correction was applied when the expected frequency was less than 5 or the total count was less than 50.

P values < 0.05 were taken as indicating statistically significant differences, while p values from 0.05 to < 0.10 were considered as indicating borderline statistical significance.

Results
From 4327 patients diagnosed for thyroid pathology at our institute during the study period, we evaluated 393 (9.08%) patients with thyroid malignancy, of whom 156 (3.60%) of total thyroid pathology; 39.69% of TC patients) were diagnosed with PTMC. In this homogenous group, there were 52 (33.33%) patients with IPTMC and 104 (66.67%) with NIPTMC. There were 45 (89.18%) females and 7 (10.82%) males in the IPTMC group and 98 (95%) females and 6 (5%) males in the NIPTMC group (p = 0.1013). The mean age of all patients with PTMC was 48.6 (± 14.6), and 44.6 (± 15.9) and 49.0 (± 14.5) for males and females, respectively (p = 0.1390; Table 1).

The prevalence of PTMC increased over the 9-year period, from 37.5% in 2008 to 47.5% in 2016 (p = 0.0414). The prevalence of NIPTMC increased from 16.66% of all TCs in 2008 to 33.75% in 2016, but IPTMC decreased from 20.83% in 2008 to 13.75% in 2016 (Table 2). In the years 2009, 2015, and 2016, we observed more patients with NIPTM than with IPTMC (Table 3; Fig. 1a, b and c). Moreover, we noticed a
statistically significant predominance of NIPTMC over IPTMC in periods I (2008–2010) and III (2014–2016), but not in period II (2011–2013), \( p = 0.0216; p < 0.0001; p = 0.6176 \), respectively; Table 4, Fig. 1d, e, and f). Furthermore, there was an increase in the prevalence of NIPTMC in period III as compared to period II \( p = 0.0014 \), but not as compared to period I \( p = 0.2804 \) (Table 5).

**Discussion**

The incidence of PTMC has been increasing worldwide. In our study, we observed that the prevalence of this tumor has increased more than four times, from 1.86% of all thyroid tumors in 2008 to 7.97% in 2016. Although it is typically minimally invasive, Gao et al. described PTMC as a public health concern because of its tremendous increase in the past few decades [12]. Additionally, it has been suggested that if any additional factors, such as extrathyroidal invasion, lymph node metastases, or the \( BRAFT V600E \) mutation, are found, PTMC should be treated as a "larger" papillary thyroid cancer [15].

**Postoperatively,** PTMC is often found in multinodular goiter (MNG) and it is then diagnosed as IPTMC [16]. In our study, the prevalence of IPTMC increased from 1.03% of all thyroid tumors in 2008 to 2.31% in 2016, together with the increase of all PTMCs (from 1.86% in 2008 to 7.97% in 2016). In terms of total PTMC, the prevalence of IPTMC has decreased approximately by half: from 20.83% in 2008 to 13.75% in 2016. Li et al. reported that IPTMC is undetectable before surgery, due to its coexistence with MNG, its small size, and its deep localization within thyroid gland [17]. For that reason, in MNG, every nodule should be assessed by ultrasound examination to determine the risk of cancer. In our previous study, we revealed that the assistance of a radiologist in UG-FNAB procedures increases the value of the procedure [18].

It was suggested that pre-operative diagnosis of PTMC is difficult and therefore rare, because of its slow growth rate, absence of specific symptoms, clinical characteristics, and potential co-occurrence with benign thyroid

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**Table 1** Demographic characteristics of patients with a diagnosis of papillary thyroid microcarcinoma (PTMC)

| Parameter          | PTMC \((n = 156)\) |
|--------------------|--------------------|
| Gender             |                    |
| Male               | 13 (8.3%)          |
| Female             | 143 (91.7%)        |
| Age (years)        |                    |
| All patients       | 48.6 ± 14.6        |
| Male               | 44.6 ± 15.9        |
| Female             | 49.0 ± 14.5        |

Descriptive data are presented as numbers \((n)\), percentage \(\%\), and mean ± standard deviation \((± SD)\).

**Table 2** The prevalence of incidental and non-incidental papillary thyroid microcarcinoma (IPTMC and NIPTMC) according to all thyroid tumors and all thyroid cancers in years 2008–2016

| Year | IPTMC | NIPTMC | PTMC | All thyroid cancers | All thyroid tumors |
|------|-------|--------|------|--------------------|-------------------|
| 2008 | 5 (1.03%) | 4 (0.83%) | 9 (1.86%) | 24 (4.96%) | 484 (100%) |
| 2009 | 3 (0.79%) | 10 (2.62%) | 5 (1.04%) | 26 (6.18%) | 382 (100%) |
| 2010 | 3 (0.71%) | 9 (2.13%) | 12 (2.84%) | 36 (8.51%) | 423 (100%) |
| 2011 | 4 (0.83%) | 5 (1.04%) | 18 (3.31%) | 29 (6.00%) | 483 (100%) |
| 2012 | 9 (1.86%) | 9 (1.66%) | 16 (3.16%) | 51 (9.39%) | 543 (100%) |
| 2013 | 13 (3.40%) | 9 (1.66%) | 10 (2.66%) | 53 (9.38%) | 565 (100%) |
| 2014 | 9 (1.86%) | 9 (1.66%) | 16 (2.83%) | 53 (9.38%) | 576 (100%) |
| 2015 | 6 (1.01%) | 25 (4.21%) | 31 (5.22%) | 62 (10.44%) | 608 (100%) |
| 2016 | 11 (2.31%) | 27 (5.66%) | 38 (7.97%) | 31 (5.22%) | 639 (100%) |

**Table 3** The prevalence of incidental and non-incidental papillary thyroid microcarcinoma in each year

| Year | Incidental | Non-incidental | Total | \( p \) |
|------|------------|----------------|-------|--------|
| 2008 | 5 (1.03%) | 4 (0.83%) | 9 (1.86%) | 0.7115 |
| 2009 | 3 (0.79%) | 10 (2.62%) | 13 (3.40%) | 0.0261 |
| 2010 | 3 (0.71%) | 9 (2.13%) | 12 (2.84%) | 0.0578 |
| 2011 | 4 (0.83%) | 5 (1.04%) | 9 (1.86%) | 0.7169 |
| 2012 | 9 (1.66%) | 9 (1.66%) | 18 (3.31%) | 0.0001 |
| 2013 | 7 (1.42%) | 9 (1.59%) | 16 (2.83%) | 0.5874 |
| 2014 | 4 (0.83%) | 6 (1.60%) | 10 (2.66%) | 0.4911 |
| 2015 | 6 (1.01%) | 25 (4.21%) | 31 (5.22%) | 0.0001 |
| 2016 | 11 (2.31%) | 27 (5.66%) | 38 (7.97%) | 0.003 |

Statistically significant differences are shown in italics.

*IPTMC* incidental papillary thyroid microcarcinoma, *NIPTMC* non-incidental papillary thyroid microcarcinoma, *PTMC* papillary thyroid microcarcinoma

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nodules [19]. Some authors have stated that the increasing rate of the prevalence of non-incidental thyroid microcarcinoma (NIPTMC) during the past few decades may have been due to the extensive development of high-frequency ultrasonography and the UG-FNAB technique [20]. These observations are in accordance with the results of our study. At the beginning of this trial, in 2008, only 0.83% of all thyroid tumors were NIPTMC, whereas this figure was 5.66% in 2016.

The mortality rate of PTMC has remained unchanged over the last few decades, which additionally supports the hypothesis of increased NIPTMC diagnoses and treatment [21]. At present, even tumors with a 3-mm diameter can be detected by ultrasonography and subsequently qualify for UG-FNAB [15]. For this reason, a large number of very small malignant tumors are found, thus increasing the rate of NIPTMC. Chen et al. suggested that even nodules with a dimension of

![Fig. 1](image-url)

**Fig. 1** a The percentage of incidental and non-incidental papillary thyroid microcarcinomas in the period 2008–2016. b The percentage of incidental and non-incidental papillary thyroid microcarcinomas, and all papillary thyroid microcarcinomas according to total number of thyroid carcinomas in the period 2008–2016. c The percentage of incidental and non-incidental papillary thyroid microcarcinomas, total papillary thyroid microcarcinomas, and total thyroid carcinomas according to total number of thyroid tumors in the period 2008–2016. d The percentage of incidental and non-incidental papillary thyroid microcarcinomas in three equal time-periods. e The percentage of incidental, non-incidental papillary thyroid microcarcinomas, and total papillary thyroid microcarcinomas according to total number of thyroid carcinomas in three equal time-periods. f The percentage of incidental and non-incidental papillary thyroid microcarcinomas, total papillary thyroid microcarcinomas, and total thyroid carcinomas according to total number of thyroid tumors in three equal time-periods. TMC, thyroid microcarcinoma; TC, thyroid carcinoma

| Table 4 | Patients with incidental and non-incidental papillary thyroid microcarcinoma, all thyroid cancers and all papillary thyroid microcarcinoma cases in three equal time-periods |
|---------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| NIPTMC  | 52 (33.3%)                                                                                                                                                                                      |
| IPTMC   | 104 (66.7%)                                                                                                                                                                                     |
| Period I (2008–2010) | Period II (2011–2013) | Period III (2014–2016) |
| NIPTMC  | 23 | 23 | 58 |
| IPTMC   | 11 | 20 | 21 |
| TC      | 86 | 133 | 174 |
| Percentage of PTMC in all TC cases in each period [%] | | | |
| NIPTMC  | 26.74% | 17.29% | 33.33% |
| IPTMC   | 12.79% | 15.04% | 12.07% |
| PTMC    | 39.53% | 32.33% | 45.40% |
| \(p\)   | 0.0216 | 0.6176 | < 0.0001 |

Statistically significant differences are shown in italics

IPTMC incidental papillary thyroid microcarcinoma, NIPTMC non-incidental papillary thyroid microcarcinoma, PTMC papillary thyroid microcarcinoma, TC all thyroid cancers
Period III (2014–2016) but also is a diagnostic tool in thyroid pathology.

Unfortunately, surgery still not only represents a treatment option but also is a diagnostic tool in thyroid pathology. A retrospective study and included a relatively small number of patients. Unfortunately, surgery still not only represents a treatment option but also is a diagnostic tool in thyroid pathology.

Statistically significant differences are shown in italics.

**Table 5** Comparison of the three equal periods of time according to incidence of non-incidental and incidental papillary thyroid microcarcinoma

|        | Period I (2008–2010) | Period II (2011–2013) | Period III (2014–2016) |
|--------|----------------------|------------------------|------------------------|
|   −    |                       | 0.0882                 | 0.2804                 |
| Period I (2008–2010) | 0.0882 | −                      | 0.0014                 |
| Period II (2011–2013) | 0.2804 | 0.0014 | −                      |

**Conclusions**

The proportion of IPTMC and NIPTMC of all thyroid tumors is relatively high and is increasing. However, in terms of total TCs, only the prevalence of NIPTMC, but not that of IPTMC, is increasing; this may be explained by better presurgical diagnostic processes.

**Abbreviations**

IPTMC: Incidental papillary thyroid microcarcinoma; MNG: Multinodular goiter; NIPTMC: Non-incidental papillary thyroid microcarcinoma; PTC: Papillary thyroid cancer; PTMC: Papillary thyroid microcarcinoma; TC: Thyroid cancer; TT: Thyroid tumor; UG-FNAB: Ultrasound-guided fine-needle aspiration biopsy

**Availability of data and materials**
Not applicable.

**Authors’ contributions**

KK is responsible for the conceptualization, investigation, methodology, project administration, resources, writing the original draft, and reviewing and editing the manuscript. KK, PK, JM, AK, and OK obtained the data. KK and AZK did the formal analysis, supervision, and validation. All authors read and approved the final manuscript.

**Ethics approval and consent to participate**

All research was carried out in compliance with the Helsinki Declaration. This study was approved by the Ethics Committee of Wroclaw Medical University (number: KB-27/2018). The data were analyzed anonymously and retrospectively on the basis of medical records. The authors did not have access to any identifying patient information and did not have any direct access to the study participants.

**Consent for publication**
Not applicable.

**Competing interests**

The authors declare that they have no competing interest.

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