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Evolution of Differentiated Thyroid Cancer: A Decade of Thyroidectomies in a Single Institution

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Key Words

Thyroidectomies · Thyroid cancer · Incidence

Abstract

Background: Numerous studies have shown an increase in the incidence of thyroid cancer (TC) in recent years. ***Objectives:*** In this paper, we reviewed the incidence of TC in a series of patients undergoing thyroid surgery at a single institution over a 10-year period. ***Patients and Methods:*** The cohorts were divided into two periods (2001–2005 and 2006–2010) with the purpose of comparing various clinicopathologic variables. ***Results:*** A total of 1,263 patients were included. A significant increase in the number of malignancies was shown in the second period, namely 90 cases in 2001–2005 (15.2% of all interventions) compared to 163 cases in 2006–2010 (24.3%) ($p < 0.001$). These differences were attributed to an increase in papillary thyroid carcinoma (PTC), as there were 66 PTC cases in the first period (11.13% of thyroidectomies performed) compared to 129 cases in the second period (19.25%). There were no clinicohistological differences among PTC cases in these two periods. ***Conclusions:*** Over the last decade, there has been an increase in the incidence of TC in patients undergoing thyroid surgery. This increase is exclusively due to increases in PTC. Our study verifies the existence of this trend in our geographical area, similar to that noted in other parts of the world.

Introduction

Numerous studies have shown a worldwide increase in the incidence of thyroid cancer (TC) in recent years [1] due to the increased frequency of papillary thyroid carcinoma (PTC). The reason for this increase is not well understood, although some authors argue that excessive medicalization, sometimes called 'overdiagnosis' [2] or 'screening effect' is to blame [3]. Thus, a greater number of ultrasound scans (US) and other imaging techniques, along with an increase in the number of thyroidectomies for benign conditions and better histological examination

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of surgical specimens, have led to the diagnosis of PTC cases with low clinical impact [4–9]. This argument is corroborated by epidemiological data which suggest that the increase in the diagnosis of PTC is at the expense of smaller tumors, especially microcarcinomas (PTC <1 cm) [10, 11]. Other authors, however, point to a real increase in the incidence of PTC [12, 13], which could be related to the effect of ionizing radiation or iodine supplementation in the general population [14–16]. Other reasons, such as hormonal factors [17], the increased incidence of obesity [18], environmental toxins such as polybrominated diphenyl ethers [19], or changing histological criteria for PTC [20] have also been postulated.

The aim of this study was to retrospectively analyze a series of thyroidectomies performed at our center over the course of a decade (2001–2010) and to determine the incidence of TC in these cases.

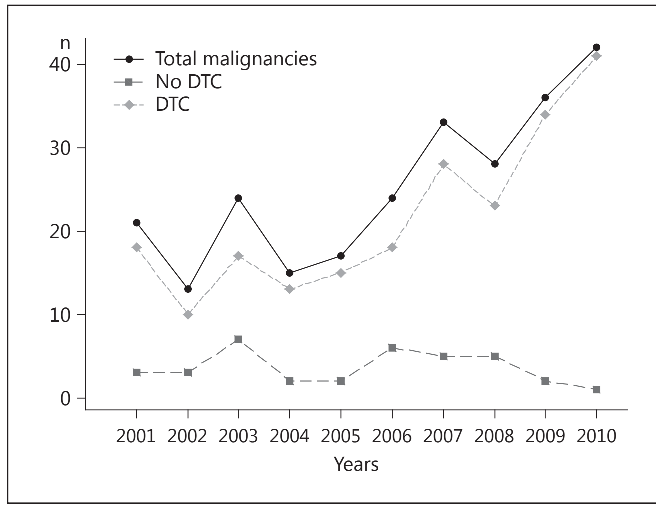

Fig. 1. TC in patients undergoing thyroid surgery during the period 2001–2010 (see text for details).

Material and Methods

Between January 2001 and December 2010, a total of 1,323 subjects underwent thyroid surgery. Patients with previous thyroid surgery or incomplete clinical information were excluded. All included patients had a solitary nodule or a multinodular goiter detected by clinical examination, US, or both. Preoperatively, an US confirmed nodular thyroid disease in all cases. A fine-needle aspiration biopsy (FNAB) was performed for thyroid nodules >1 cm and for nodules <1 cm with suspicious US features. Thyroidectomy was prescribed for patients with malignant, suspicious, or repetitive indeterminate nodules according to FNAB results. Moreover, surgery was indicated for benign disease when local symptoms were present or for esthetic reasons.

Total cohorts were separated into two groups: group 1 included patients operated on between 2001 and 2005, whereas group 2 included patients operated on between 2006 and 2010. In both groups, demographic characteristics, type of surgery (total thyroidectomy vs. non-total thyroidectomy), preoperative serum levels of thyrotropin (TSH), presence of thyroid antibodies, and incidence of TC according to histological types were compared. Histological variants were classified as differentiated TC (DTC), including PTC and follicular thyroid carcinoma (FTC), and non-DTC, which included all other types of malignancies (medullary carcinoma, undifferentiated carcinoma, metastatic thyroid, and lymphoma). Finally, we compared the characteristics of PTC detected in both periods in relation to the following variables: age, preoperative TSH value, tumor size, percentage of microcarcinomas, mutlifocality, lymph node metastases, associated thyroiditis, and mode of diagnosis (incidental vs. non-incidental). We defined an incidental diagnosis as PTC diagnosed at final histology in a patient whose reason for intervention was benign thyroid disease. Quantitative variables were expressed as mean and standard deviation, and categorical variables were expressed as frequencies and proportions. Statistical analysis was performed using the χ^2 test for categorical variables and the Student t test for quantitative variables. p values ≤0.05 were considered statistically significant.

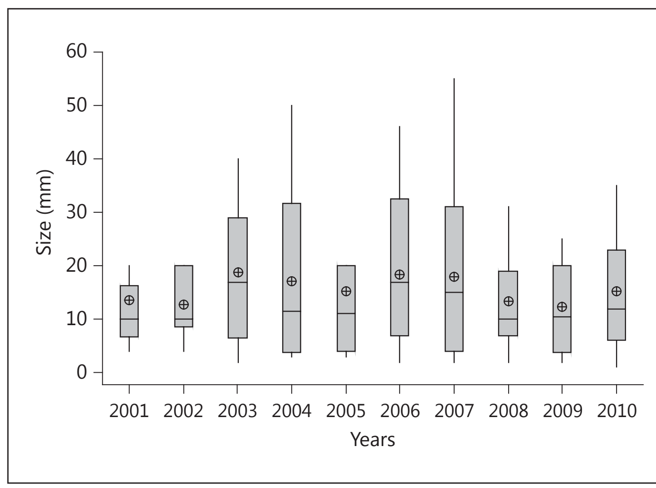

Fig. 2. Mean size distribution of PTC over the decade.

Results

A total of 1,263 cases, 1,023 women and 240 men (average age of 51.9 years), were included retrospectively. Previous to surgery all patients underwent FNA. Thyroidectomy was prescribed for malignancy or suspicious of malignancy in 221 patients (17.5%). Final histological examination revealed the presence of TC in 253 cases (20%), and of these, 216 patients had DTC (195 PTC cases, 21 FTC cases) (fig. 1). The mean size of the PTC was 15.4 (±12.6) mm, and no significant differences in size were observed over the 10 years (fig. 2).

Table 1. Characteristics of the PTC cases in both periods (2001–2005 and 2006–2010)

	PTC (2001–2005)	PTC (2006–2010)	p
Age (mean ± SD), years	46.2 ± 12.9	49.2 ± 15.3	0.15
TSH (mean ± SD), mU/l	1.78 ± 2.0	2.22 ± 2.5	0.26
Size (mean ± SD), mm	15.7 ± 13.1	15.2 ± 12.4	0.79
Microcarcinomas, %	48.5	45.7	0.71
Multifocality, %	44	46.5	0.73
Bilaterality, %	17	27	0.09
Lymph node M1, %	26	36	0.10
Thyroiditis, %	31	32	0.85
Incidental diagnosis, %	47	41	0.43

Group 1 included 593 cases (487 women and 106 men) with a mean age of 51.8 (±14.2) years. In group 2, there were 670 subjects (536 females and 134 males) with a mean age of 51.9 (±16.3) years. There were no significant differences in gender or age in both groups. However, there was a significant increase in the number of malignancies in the second period: 90 TC cases (15.2% of all interventions) in group 1 compared to 163 cases (24.3%) in group 2 ($p < 0.001$). Differences were due to a significant increase in the number of DTC cases: 73 (12.1%) in the first half of the decade versus 143 (21.3%) in the second half ($p < 0.001$). Within DTC cases, there was no significant variation in the number of FTC cases: 7 (1.2%) in group 1 compared to 14 (2%) in group 2 ($p = 0.29$). Thus, the observed increase in the incidence of TC was due solely to an increase in PTC: 66 cases between 2001 and 2005, accounting for 11.13% of all thyroidectomies performed, compared to 129 cases between 2006 and 2010, which accounted for 19.25% of all surgical interventions. Non-DTC thyroid malignancies included 13 and 11 medullary TCs, 5 and 3 anaplastic TCs, and 1 and 6 other tumors (secondary metastasis and primary thyroid lymphoma) in groups 1 and 2, respectively.

There were no significant differences in variables analyzed between the two 5-year periods. The preoperative TSH value was 1.8 (±5.9) mU/dl in group 1 patients and 1.5 (±1.9) mU/dl in group 2 patients. Although not statistically significant, there was an increase in the number of total thyroidectomies in the second half of the decade: 409 cases (69%) between 2001 and 2005 compared to 494 cases (73.7%) between 2006 and 2010 ($p = 0.06$). In both groups, 73% of patients had no thyroid antibodies.

Table 1 summarizes the characteristics of the PTC cases in both periods. It can be seen that there were no differences in any of the observed variables, which included age, preoperative TSH value, tumor size, percentage of microcarcinomas, multifocality, metastatic disease, thyroiditis, and mode of diagnosis. Thus, there were a total of 84 incidental cancers, 31 in the first period (47%) and 53 in the second period (41%) ($p = 0.43$). These numbers represented 7.6% of the patient cohort with total thyroidectomies in group 1 and 10.7% of the patient cohort with total thyroidectomies in group 2 ($p = 0.1$).

In addition, only 6 cases (9%) in the first period and 12 cases (9%) in the second period were non-incidental microcarcinomas.

Discussion

This study supports, in our environment, the trend of increased incidence of TC, due to an increase in PTC, during the first decade of the century in the cohort of patients who underwent thyroid surgery. The percentage of PTC increased by almost 10% between 2006 and 2010 compared to 2001 and 2005.

One presumed reason for this increase in the incidence of PTC is the screening effect, namely the higher and better performance of various tests in the general population, such as US and FNABs of thyroid nodules [5–9], which has led to increased diagnosis of PTC. This argument is corroborated by epidemiological data suggesting an increase in PTC diagnosis at the expense of smaller PTCs, especially microcarcinomas [10, 11, 21]. These tumors are of unknown clinical significance. It has been hypothesized that if the entire pool of occult PTC were identified antemorten, the resulting ascertainment bias could result in a 50-fold increase in the apparent incidence of PTC [22]. In our study, we did not observe an increase in microcarcinomas, and the average size of PTC did not change over the decade. Furthermore, although it is postulated as being more frequent, not all reports found that the increase in PTC was only at the expense of smaller PTCs [23, 24]. Davies and Welch [10] found, based on data from the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) Program, that between 1988 and 2002, the largest percent increases in PTC were in tumors <2 cm. Hughes et al. [2] also analyzed the SEER registry and found that the greatest increase in PTC occurred in patients older than 45 years with microcarcinomas; the authors attributed these findings to overdiagnosis. However, using the same database, Zhu et al. [25]

found that the rate of the age-adjusted incidence showed a significant increase in PTC for all tumor sizes between 1988 and 2003. In a detailed analysis conducted by Enewold et al. [13] on the same SEER program, the authors found that PTCs >5 cm increased 222% (similar to the 248% in tumors <1 cm) in American white women. Similarly, Yu et al. [26] compared the incidence of PTC in two different periods (1992–1996 and 2000–2004) and found a significant increase in all tumor sizes. Also, in an Italian study that compared the most recent periods (1998–2003 and 2004–2009), the authors did not find differences in the percentage of microcarcinomas [27]. Finally, Morris and Myssiorek [12] reported a similar increase in the percentage of cases with extrathyroidal extension, a factor that does not support the screening effect as the cause of the observed changes.

Similar to other studies on the incidence of neoplasms, data are recorded in relation to the reference population (usually per 100,000 population). Since a high percentage of PTC cases are incidentally diagnosed after thyroidectomies for benign disease, the population incidence of thyroid interventions and the extent of the thyroidectomy may influence this kind of malignancy [28–31]. In a recent report, Sassolas et al. [32] found that 64% of microcarcinomas are diagnosed incidentally; in a study by Alevizaki et al. [33], this figure rose to 88%. In the present study, the frequency of TC was not related to the general population, but to cases of thyroidectomies performed. We observed an increment in the percentage of interventions that were positive for malignancy, reaching 24.3% in the second period. Using a similar design, Sassolas et al. [34] found that 22% of all thyroid interventions for any cause were related to TC.

It has been proposed that the increase in PTC may be due to an improvement in the selection of patients referred for surgery [3]. However, the fact that incidental and non-incidental cases increased in parallel does not support this hypothesis. In the present study, the percentage of incidental PTC cases showed no differences in the two periods analyzed. The combination of lack of specific increasing trends of smaller tumors and stability in the percentage of cases incidentally diagnosed seems to favor a true increase in the incidence of PTC. Moreover, in most recent years, there have been no substantial changes in the diagnosis and therapeutic management of patients with nodular thyroid disease. Thus, it appears that the increase in PTC is due to both improvements in diagnostic techniques and their high use (overdiagnosis), and a real increase in the incidence of PTC. The etiology of this globally verified phenomenon has not been established.

There are some limitations to our study. The study population is not representative of the general population nor is it a population with thyroid disease. Rather, as was mentioned above, it contains patients who have been thyroidectomized. Therefore, we cannot rule out bias caused by changes in social or demographic parameters in the reference population. Moreover, the comparison periods were two successive 5-year periods, a very short time interval for the identification of significant changes in incidence trends. However, the relatively short study period also reduced the likelihood of changes in socio-demographic status, referral criteria, surgical indications, and diagnostic (clinical and histological) and therapeutic protocols. Therefore, this variability could be higher in studies that compare longer periods and thus produce greater bias.

In conclusion, this study suggested an increase in the number of TC cases in the first decade of the century in patients undergoing thyroid surgery.

Disclosure Statement

The authors have no conflicts of interest to disclose.

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