Received: 22 August 2020 | Revised: 14 October 2020 | Accepted: 13 November 2020

DOI: 10.1002/lio2.504

ORIGINAL RESEARCH

Laryngoscope Investigative Otolaryngology

A shift to more targeted thyroidectomies increased the detection of thyroid cancer and in particular low-risk papillary tumors in Southwestern Greece the decade 2007 to 2016

Georgios K. Markantes PhD[1] | Stylianos Tsochatzis MD[2] | Konstantinos Panagopoulos PhD[2] | Maria Melachrinou PhD[3] | Venetsana E. Kyriazopoulou PhD[1] | Kostas B. Markou PhD[1] | Marina A. Michalaki PhD[1]

[1]Division of Endocrinology, Department of Internal Medicine, University of Patras School of Health Sciences, Patras, Greece

[2]Department of General Surgery, University of Patras School of Health Sciences, Patras, Greece

[3]Department of Pathology, University of Patras School of Health Sciences, Patras, Greece

Correspondence
Marina A. Michalaki, Division of Endocrinology, Department of Internal Medicine, University of Patras School of Health Sciences, Patras, PC 26500, Greece.
Email: mixmar@upatras.gr

Abstract

Objectives: Data regarding thyroid cancer (TC) epidemiology in Greece in the last decade are scarce, so we investigated the trends in TC detection during 2007 to 2016.

Methods: We retrospectively studied 2040 pathology reports of total thyroidectomies performed at our institution from 2007 to 2016.

Results: A number of 478 cases of TC were identified in the studied decade. The overall incidence of TC among thyroidectomies rose over the years. The proportion of papillary T1 tumors among thyroidectomies increased in the second period of our study (2012-2016), while that of papillary T2 to T4 tumors and other TC subtypes remained unchanged. Papillary T1 tumors represented 63.6% of all TC cases and 75.3% of them were low-risk microcarcinomas (papillary thyroid microcarcinoma). The strategy of fine needle aspiration (FNA) prior to surgery in the management of thyroid nodules was adopted by more clinical endocrinologists in the area of Southwestern (SW) Greece in the second period of our study (2012-2016:29.7% vs 2007-2011:18.4%, $P < .001$). Consequently, the indication for thyroidectomy was set by FNA more frequently in 2012 to 2016 than in 2007 to 2011 (42.5% vs 26.4% of cases, $P < .001$).

Conclusions: The wider use of FNA in the triage of thyroid nodules led to increased rates of TC in thyroidectomies performed in SW Greece during the decade 2007 to 2016; low-risk, small papillary tumors represented the majority of TC cases.

KEYWORDS

FNA, Greece, incidence, papillary microcarcinoma, thyroid cancer

1 | INTRODUCTION

Thyroid cancer (TC) is the most common endocrine malignancy accounting for 88% of all endocrine carcinomas and 3% of all human cancers.[1,2] TC represents 1.5% of new cancer diagnosis in Europe[3] and 1% in the United States.[4] Primary TC is categorized into differentiated thyroid carcinoma (namely, papillary thyroid carcinoma [PTC] and follicular thyroid carcinoma [FTC]), undifferentiated anaplastic carcinoma and the C-cell origin medullary thyroid carcinoma (MTC).[5]

Over the last two decades, a rising incidence of TC is observed worldwide that can be attributed almost entirely to PTC.[3,6,7] PTC accounts for 84% of all TC and is considered an indolent tumor with a low mortality rate of around 0.5/100.000 person-years in most countries, and in both sexes.[4,8] The observed universal rise in PTC incidence rates is probably due to overdiagnosis, since only the incidence of small PTC cancers increases, while mortality remains stable or even decreases.[8] The widespread use of thyroid ultrasonography has led to increased incidental diagnosis of TC in asymptomatic individuals.[6,9] Moreover, it has been shown that TC (especially PTC) is a very common autopsy finding, affecting 10% to 33% of people not known to have such a disease during their lifetime.[10,11] Hence, there is a substantial reservoir of subclinical, nonlethal disease. In contrast, a number of studies have recorded an increased detection of advanced PTC accompanied with increased mortality rates, indicating a true rise of TC incidence.[4,12,13]

In Greece, which is an iodine sufficient country for almost 30 years,[14,15] TC is the third most common malignancy in women and among the 10 commonest in men, according to recently published data from a national pathology-based cancer registry.[16] As specified in this work, there were about 12 000 new cases of TC in Greece during the period 2009 to 2013; however, neither the incidence and mortality rates nor the histological characteristics were recorded,[16] while data regarding the trends in TC incidence over the last decade are missing. The aim of the present study was to describe and interpret the recent trends in TC incidence (in general and by subtype) in the area of Southwestern (SW) Greece. To do so, we recorded the cases of TC among thyroidectomies performed between 2007 and 2016 at the University Hospital of Patras, which is a tertiary referral center in SW Greece and analyzed its pathological characteristics.

2 | MATERIALS AND METHODS

We retrospectively studied the pathology reports of all thyroidectomies (n = 2040) performed from January 2007 to December 2016 in the University Hospital of Patras. Of note, the standard practice in our center is to perform total thyroidectomy instead of lobectomy, even in cases of small and apparently low-risk thyroid tumors or suspicious nodules. Lymph node dissection was performed only when indicated. Our hospital is an academic, tertiary hospital, a referral center for TC in SW Greece. The databases of the Departments of Pathology and of General Surgery were used for data extraction.

Our practices regarding the extent of surgery remained similar during the studied decade, so we arbitrarily divided the decade into two 5-year periods: 2007 to 2011 (period 1) and 2012 to 2016 (period 2). For each patient the following characteristics were recorded: indication for thyroidectomy, sex, age at diagnosis, diagnostic category of fine needle aspiration (FNA; if performed) according to the Bethesda system[17] and histological diagnosis. In case of cancer, further information such as the type (PTC, FTC, MTC, anaplastic, lymphoma, other), tumor size, presence, and degree of extra-thyroidal extension and number of infiltrated lymph nodes, if any, were collected. All tumors were staged according to the American Joint Committee on Cancer (AJCC) eighth edition/Tumor-Node-Metastasis (TNM) classification system.[18] We defined as "papillary thyroid microcarcinoma (PTMC)," a papillary tumor with diameter 1 cm or less.[19] We also identified the cases of noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP), formerly referred to as encapsulated follicular variant of PTC (EFVPTC).[20]

The data were analyzed anonymously, and approval was obtained by the University Hospital of Patras Ethics Committee, while informed consent was obtained from all participants included in the study.

2.1 | Statistical analysis

Descriptive and inferential statistics were used to analyze the data. Independent sample *t* test (Student's *t* test) was used for comparisons between groups when studying continuous variables, while chi-square test (chi-square test for independence) was used in case of categorical variables. The chi-square test was used to detect overall statistically significant differences among the years of the decade under study and partitioning of chi-square test was used as post hoc analysis to detect between which particular years or group of years (periods) the statistically significant differences occurred. Data were presented as mean ± SD (continuous data) or as percentage (discrete data). The level of statistical significance was set at 0.05 (two tailed). Statistical procedures were performed using SPSS 25.0 for Windows (SPSS Inc., Chicago, Illinois).

3 | RESULTS

In the decade 2007 to 2016, 2040 total thyroidectomies were performed in the University Hospital of Patras. TC was identified in 478 (23%) cases, whereas the remaining 1562 (77%) samples represented benign conditions such as multinodular goitre (MNG), Graves' disease, and follicular adenoma. Out of the 478 cases of TC, 425 were PTC (88.9%), 32 were FTC (6.7%), 10 were MTC (2.1%), and 11 were other cancers (2.3%). T1 PTC represented 63.6% of all TC cases; PTMC constituted 53.3%, and T1b 15.7% of all TC, respectively.

There was a significant variation in the percentage of TC cases per thyroidectomy among the years of the studied decade ($P < .001$); post hoc analysis revealed that from 2007 to 2012 the percentage of TC per thyroidectomy remained stable and an increase was observed

TABLE 1 Number of thyroidectomies, cases of thyroid cancer, and histologic subtype for each year of the study

	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	Total
Thyroidectomies	231	203	236	194	199	204	197	195	195	186	2040
Thyroid cancer	41 (17.8%)	38 (18.7%)	44 (18.6%)	46 (23.7%)	43 (21.6%)	37 (18.1%)	57 (28.9%)	62 (31.8%)	48 (24.6%)	62 (33.3%)	478 (23.4%)
PTC	35 (15.2%)	32 (15.8%)	42 (17.8%)	41 (21.1%)	38 (19.1%)	34 (16.7%)	50 (25.4%)	53 (27.2%)	43 (22.1%)	57 (30.6%)	425 (20.8%)
PTMC	19 (8.2%)	22 (10.8%)	25 (10.6%)	27 (13.9%)	22 (11.1%)	21 (10.3%)	32 (16.2%)	29 (14.9%)	24 (12.3%)	34 (18.3%)	255 (12.5%)
PTC T1b	7 (3%)	4 (2%)	5 (2.1%)	6 (3.1%)	8 (4%)	7 (3.4%)	9 (4.6%)	14 (7.2%)	6 (3.1%)	9 (4.8%)	75 (3.7%)
PTC T2-T4	10 (4.3%)	7 (3.5%)	15 (6.4%)	16 (8.3%)	10 (5%)	6 (2.9%)	11 (5.6%)	11 (5.6%)	17 (8.7%)	18 (9.7%)	121 (5.9%)
FTC	5 (2.2%)	2 (1%)	2 (0.8%)	2 (1%)	2 (1%)	1 (0.5%)	2 (1%)	7 (3.6%)	5 (2.6%)	4 (2.2%)	32 (1.6%)
MTC	1 (0.4%)	1 (0.5%)	0	0	3 (1.5%)	1 (0.5%)	1 (0.5%)	2 (1%)	0	1 (0.5%)	10 (0.5%)
Other Ca	0	3 (1.5%)	0	3 (1.5%)	0	1 (0.5%)	4 (2%)	0	0	0	11 (0.5%)

Note: Percentages are % of the total number of thyroidectomies for the respective year.
Abbreviations: FTC, follicular thyroid carcinoma; MTC, myeloid thyroid carcinoma; PTC, papillary thyroid carcinoma; PTMC, papillary thyroid microcarcinoma.

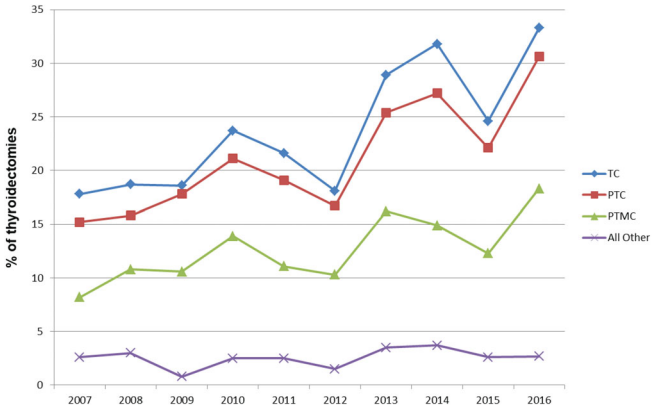

FIGURE 1 Cases of thyroid cancer (all types-TC), papillary thyroid carcinoma (PTC), papillary thyroid microcarcinoma (PTMC), and all other types of TC except papillary (All Other), presented as percentage of the total number of thyroidectomies per year during the decade 2007 to 2016

from 2012 to 2013 ($P < .01$), which was sustained thereafter. The same pattern was observed for PTC ($P < .001$), while the incidence of all other types of TC was unaltered during the study period (Table 1, Figure 1). Studying the different T stages of PTC, we found that the incidence of T1b and T2 to T4 tumors was unchanged, while the incidence of PTMC had a trend to increase over time, although this did not reach statistical significance ($P = .06$).

Comparisons between the two periods of our study (2007-2011 vs 2012-2016) are shown in Table 2. No difference was found between the two study periods regarding the mean age at diagnosis of cancer, the female to male ratio, the ratio of PTC to FTC or the mean PTC size. The rate of TC, PTC, PTMC, and PTC T1b per thyroidectomy was increased in period 2 (TC: 27.2% vs 19.9%, $P < .001$, PTC: 24.3% vs 17.7%, $P < .001$, PTMC: 14.3% vs 10.8%, $P < .01$, PTC T1b: 4.6% vs 2.8%, $P < .05$). The number of thyroidectomies tended to decrease in period 2 (195.4 ± 6.4 vs 212.6 ± 19.4, $P = .09$). The numbers of TC and PTC cases per year showed an increasing trend but the significance of this finding was marginal (53.2 ± 10.7 vs 42.4 ± 3.1, $P = .06$ for TC, and 47.4 ± 9.1 vs 37.6 ± 4.2, $P = .05$ for PTC). There was no difference in the mean number of PTMC, T1b, and T2 to T4 PTC per year between the two periods.

The indication for thyroidectomy was set by FNA biopsy (diagnostic category of III-VI according to the Bethesda system) prior to operation in only 35.4% of cases and more frequently in study period 2 than 1 (42.5% vs 26.4%, $P < .001$). Thus, 293 TCs out of 478 (61.3%) were incidentally discovered, namely, in the absence of either an FNA result raising concern for a possible malignancy or high circulating calcitonin levels (Table 2). Surgical treatment of large and/or compressive MNG (46%), Graves' disease (6.9%), or clinically suspicious solitary nodules with benign/nondiagnostic/nonavailable FNA results (8.4%) were the indications for thyroidectomy in these patients. Among these 293 TCs, 95% were PTC and 5% were FTC; 66.6% were staged as T1a, 15.7% as T1b, 4.1% as T2 and 13.7% as T3.

From a total of 255 PTMC, 209 (82%) were incidentally discovered (Table 2) and all of them were intrathyroidal, without aggressive histology. Of the 46 remaining, nonincidentally identified PTMCs, only 26 were characterized by invasion into perithyroidal tissues and/or local lymph nodes or aggressive histology. Hence, the majority (89.8%) of PTMCs comprised low-risk tumors. Notably, the incidence of incidentally identified TC, PTC, and PTMC was less in the second period of the study (Table 2).

Furthermore, out of 425 PTC, 17 (4%) were NIFTP. The mean NIFTP size was 2.19 cm and four were microcarcinomas.

4 | DISCUSSION

In this retrospective study covering the decade 2007-2016, we evaluated TC incidence and pathology characteristics among thyroidectomies performed in SW Greece. Our population consists mainly of middle-aged women. We found that TC rates increased over time, probably due to the wider use of FNA in the triage of thyroid nodules,

TABLE 2 Comparison between the two study periods (2007–2011 vs 2012–2016) regarding patient demographics, TC types, tumor T-classification and frequency of incidentally discovered TC, PTC, and PTMC

	Entire study	Period 1	Period 2	Period 1 vs 2
Mean age at diagnosis of cancer ± SD (years)	47.88 ± 14.9	47.81 ± 13.8	47.93 ± 15.9	ns
Female to male ratio	3.3	2.9	3.7	ns
PTC to FTC ratio	13.3	14.5	12.5	ns
Mean PTC size ± SD (cm)	1.08 ± 1.2	1.06 ± 1.29	1.09 ± 1.15	ns
Thyroidectomies per year (mean ± SD)	204.0 ± 16.4	212.6 ± 19.4	195.4 ± 6.4	ns
TC cases per year (mean ± SD)	47.8 ± 9.4	42.4 ± 3.1	53.2 ± 10.7	0.06
PTC cases per year (mean ± SD)	42.5 ± 8.4	37.6 ± 4.2	47.4 ± 9.1	0.05
PTMC cases per year (mean ± SD)	25.5 ± 4.9	23.0 ± 3.1	28.0 ± 5.4	ns
PTC T1b cases per year (mean ± SD)	7.5 ± 2.8	6.0 ± 1.6	9.0 ± 3.1	ns
PTC T2-T4 cases per year (mean ± SD)	12.1 ± 4.2	11.6 ± 3.8	12.6 ± 4.9	ns
TC per thyroidectomy	23.4%	19.9%	27.2%	<0.001
PTC per thyroidectomy	20.8%	17.7%	24.3%	<0.001
All other types of TC per thyroidectomy	2.6%	2.2%	2.9%	ns
PTMC per thyroidectomy	12.5%	10.8%	14.3%	<0.01
PTC T1b per thyroidectomy	3.7%	2.8%	4.6%	<0.05
PTC T2-T4 per thyroidectomy	5.9%	5.5%	6.5%	ns
FNA performed prior to thyroidectomy	23.8%	18.4%	29.7%	<0.001
Thyroidectomy based on FNA	35.4%	26.4%	42.5%	<0.001
Incidentally discovered				
TC	293 (61.3%)	146 (68.9%)	147 (55.2%)	<0.01
PTC	279 (65.6%)	139 (74%)	140 (59.1%)	<0.01
PTMC	209 (82%)	103 (89.6%)	106 (75.7%)	<0.01

Note: Data are presented as mean ± SD (continuous data) or as percentage (discrete data) and analyzed with t-test and chi-square test, respectively.
Abbreviations: FTC, follicular thyroid carcinoma; PTC, papillary thyroid carcinoma; PTMC: papillary thyroid microcarcinoma; TC, thyroid cancer.

which led to more targeted thyroidectomies. Notably, the majority (63.6%) of TC were T1 papillary tumors, while the incidence of stage T2 to T4 PTC as well as of all other types of TC remained unchanged. Almost 90% of PTMC detected were low-risk tumors.

Over the last five decades, there is a well-established, sustained, worldwide increase in TC incidence. There is considerable variability regarding the magnitude of this increase in different geographic areas: the annual percent change is 3.6% in the United States (1974-2013)[4] and 27.1% in South Korean males (1996-2010),[21] while ranging between 2% and 10% in most European countries.[3] TC affects more women than men, but increased incidence is reported in both sexes. Furthermore, the major part of relevant reports conclude that increased detection of PTC is the culprit behind the rise in TC cases.[3]

There is a rigorous scientific debate as to whether the reported detection of more cases of TC is due to a true increase in its occurrence or it is simply a result of overdiagnosis or underdiagnosis in the past studies. In an era of widespread use of ultrasound examination and FNA, our capability to detect small subclinical tumors is undoubtedly increased. Moreover, increased scrutiny during pathologic examination of surgical specimens has led to increased discovery of occult tumors. These observations are in accordance with our findings. However, an increase in advanced-stage PTC detection and TC mortality (compatible with a true increase in TC occurrence) has been reported in a few studies.[4,12,13,22]

Unfortunately, a nationwide epidemiological study on TC in Greece is missing and the few existing studies are regional, single center and provide data up to 2010.[23-26] In these studies of previous decades, an increasing incidence of TC and in particular PTC was described. The reported mean PTC size (range: 1.04-1.81 cm), mean age at diagnosis of TC (range: 42.4-49.5 years), and female to male ratio (range: 3.8-4)[23-26] were similar to ours (1.08 ± 1.2 cm, 47.88 ± 14.9 years, and 3.3, respectively). An isolated rise of small T1 tumors was found in two of these studies,[24,25] while the third reported an increased incidence across all stages of differentiated TC.[23] In our study, there was an indisputable rise in T1 PTC in the period 2012 to 2016, while the incidence of T2 to T4 tumors remained unchanged. PTMC accounted for 60% of all our PTC cases, which is in accordance with previous studies of Alevizaki et al[25] and Griniatsos et al[24] who reported percentages of 51.6% and 63.7%, respectively. However, our finding that 89.8% of PTMC were intrathyroidal without aggressive histology comes in contrast with available domestic data: Alevizaki et al showed that 29.9% of PTMC

presented with capsular invasion and 11.8% with lymph node metastasis,[25] whereas Pazaitou-Panayiotou et al found that unifocal, intrathyroidal PTMC without lymph node invasion accounted for only half of sub-centimeter TC.[23]

We hypothesize that the wide use of high-resolution thyroid gland ultrasonography in our country from 2000[27] has led to increased identification of asymptomatic thyroid nodules. According to our data, it seems that prior to 2012 the majority of clinical endocrinologists in the area of SW Greece did not use diagnostic FNA biopsy when evaluating patients with thyroid nodules. Thus, only 18.4% of patients underwent FNA biopsy prior to thyroidectomy. Thereafter, the Greek financial crisis which limited the access of patients to health care providers, in combination with more expanded use of FNA in clinical practice led to less and more targeted thyroidectomies. Indeed, in period 2 of our study the indication for thyroidectomy was set by the FNA result in 42.5% of cases (vs 26.4% in period 1). Consequently, the proportion of TC per thyroidectomy increased. Notably, virtually all the extra TC cases found in period 2 were small papillary tumors. Unfortunately, we do not have the information whether the FNA biopsies that eventually led to thyroidectomies in our patients were performed in nodules which were symptomatic or detected during screening procedures. Hence, some of these "targeted" thyroidectomies might have been performed for incidentally discovered, subclinical disease.

To the best of our knowledge, during the studied decade (2007-2016), there is no evidence of major alterations in environmental factors predisposing to thyroid malignancy in Greece. Iodine deficiency has been linked to increased FTC and anaplastic TC,[8,28-30] while iodine supplementation is associated with increased PTC prevalence.[28,31] Although in the past Greek population was severely iodine deficient, after the 1990s Greece should be considered an iodine sufficient country.[14,15] The transition from iodine deficiency to adequate dietary iodine intake over the last decades is reflected in the rise in the ratio of PTC/FTC from 3.3 in the period 1963 to 1982[25] to 13.2 to 14.4 in the 2000s.[24,25] Since then, the ratio has remained stable, as in our study it was found to be 13.3. Therefore, it seems that the increasing incidence of PTC observed in our study could not be attributed to the long-standing iodine supplementation.

Recently, it was proposed that the EFVPTC should be renamed "non-invasive follicular thyroid neoplasm with papillary-like nuclear features" (NIFTP), thus reflecting its extremely low malignant potential and favorable outcomes while raising doubt regarding the necessity of its surgical resection.[20] There is considerable variability regarding the reported incidence of NIFTP worldwide, with European and American studies reporting rates of 15% to 28% of PTCs,[20,32] while Asian ones providing much lower rates (0.2%-4.7% of PTCs).[32] In our study, the first in Greece to examine the incidence of this variant, NIFTPs accounted for 4% of all PTCs.

Our study has two important limitations. First, our data are derived from a single tertiary hospital and, therefore, it is not a nationwide study that would help to draw conclusions that apply to the whole Greek population. Second, as we used pathology reports for data collection, we do not have information regarding distant metastases or follow up (persistence, recurrence, mortality), which would be helpful for the estimation of the aggressiveness of these tumors.

In conclusion, the increasing TC detection during the decade 2007 to 2016 in SW Greece can be almost entirely attributed to a rise in low-risk T1 PTC and is at least in part due to the more targeted thyroidectomies performed. Nevertheless, a true increase in the occurrence of small PTC due to an unidentified environmental/other factor cannot be safely excluded based solely on our findings.

ACKNOWLEDGMENT

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

ETHICS STATEMENT

All procedures performed in this study involving human participants were in accordance with the ethical standards of the University Hospital of Patras Ethics Committee and with the 1964 Helsinki declaration and its later amendments. Written informed consent was obtained from all participants.

ORCID

Marina A. Michalaki https://orcid.org/0000-0003-2073-8523

BIBLIOGRAPHY

1. Van der Zwan JM, Mallone S, Van Dijk B, et al. Carcinoma of endocrine organs: results of the RARECARE project. *Eur J Cancer*. 2012;48:1923-1931.
2. Malaguarnera R, Vella V, Pellegriti G, Belfiore A. Editorial: clinical and molecular epidemiology of thyroid cancer of follicular origin. *Front Endocrinol*. 2018;9:1-2.
3. Wiltshire J, Drake T, Uttley L, Balasubramanian B. Systematic review of trends in the incidence rates of thyroid cancer. *Thyroid*. 2016;26:1541-1552.
4. Lim H, Devesa S, Sosa J, Check D, Kitahara C. Trends in thyroid cancer incidence and mortality in the United States, 1974-2013. *JAMA*. 2017;317:1338-1348.
5. Fagin JA, Wells SA Jr. Biologic and clinical perspectives on thyroid cancer. *N Engl J Med*. 2016;375:1054-1067.
6. Davies L, Welch HG. Increasing incidence of thyroid cancer in the United States, 1973-2002. *JAMA*. 2006;295:2164-2167.
7. Pellegriti G, Frasca F, Regalbuto C, Squatrito S, Vigneri R. Worldwide increasing incidence of thyroid cancer: update on epidemiology and risk factors. *J Cancer Epidemiol*. 2013;2013:1-10.
8. Li M, Brito JP, Vaccarella S. Long-term declines of thyroid cancer mortality: an international age-period-cohort analysis. *Thyroid*. 2020;30:25–33. https://doi.org/10.1089/thy.2019.0684.
9. Russ G, Leboulleux S, Leenhardt L, Hegedüs L. Thyroid incidentalomas: epidemiology, risk stratification with ultrasound and workup. *Eur Thyroid J*. 2014;3:154-163.
10. Harach HR, Franssila KO, Wasenius VM. Occult papillary carcinoma of the thyroid: a "normal" finding in Finland. *Cancer*. 1985;56:531-538.
11. Furuya-Kanamori L, Bell KJL, Clark J, Glasziou P, Doi SAR. Prevalence of differentiated thyroid cancer in autopsy studies over six decades: a meta-analysis. *J Clin Oncol*. 2016;34:3672-3679.

12. Morris LG, Myssiorek D. Improved detection does not fully explain the rising incidence of well-differentiated thyroid cancer: a population-based analysis. *Am J Surg*. 2010;200:454-461.
13. Pandeya N, McLeod DS, Balasubramaniam K, et al. Increasing thyroid cancer incidence in Queensland, Australia 1982-2008—true increase or overdiagnosis? *Clin Endocrinol (Oxf)*. 2016;84:257-264.
14. Markou KB, Koukkou EG. The Greek population is iodine sufficient and not at risk of iodine-induced hyperthyroidism. *J Nutr*. 2012;142:1611.
15. Markou K, Michalaki M, Makri M, Georgopoulos NG, et al. Iodine intake and thyroid function in villagers and city dwellers in south-western Greece. *Thyroid*. 1996;1:S79.
16. Patsea E, Kaklamanis L, Batistatou A. The first report of a 5-year period cancer registry in Greece (2009-2013): a pathology-based cancer registry. *Virchows Arch*. 2018;472:677-682.
17. Cibas ES, Ali SZ. The Bethesda system for reporting thyroid cytopathology. *Thyroid*. 2009;19:1159-1165.
18. Tuttle RM, Haugen B, Perrier ND. Updated American Joint Committee on cancer/tumour-node-metastasis staging system for differentiated and anaplastic thyroid cancer (eighth edition): what changed and why? *Thyroid*. 2017;27:751-756.
19. Haugen BR, Alexander EK, Bible KC, et al. 2015 American Thyroid Association Management Guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: the American Thyroid Association Guidelines Task Force on thyroid nodules and differentiated thyroid cancer. *Thyroid*. 2016;26:1-133.
20. Nikiforov YE, Seethala RR, Tallini G, et al. Nomenclature revision for encapsulated follicular variant of papillary thyroid carcinoma: a paradigm shift to reduce overtreatment of indolent tumours. *JAMA Oncol*. 2016;2:1023-1029.
21. Kweon SS, Shin MH, Chung IJ, Kim YJ, Choi JS. Thyroid cancer is the most common cancer in women, based on the data from population-based cancer registries, South Korea. *Jpn J Clin Oncol*. 2013;43:1039-1046.
22. Enewold L, Zhu K, Ron E, et al. Rising thyroid cancer incidence in the United States by demographic and tumour characteristics, 1980-2005. *Cancer Epidemiol Biomarkers Prev*. 2009;18:784-791.
23. Pazaitou-Panayiotou K, Iliadou PK, Chrisoulidou A, et al. The increase in thyroid cancer incidence is not only due to papillary microcarcinomas: a 40-year study in 1,778 patients. *Exp Clin Endocrinol Diabetes*. 2013;121:397-401.
24. Griniatsos J, Tsigris C, Kanakis M, et al. Increased incidence of papillary thyroid cancer detection among thyroidectomies in Greece between 1991 and 2006. *Anticancer Res*. 2009;29:5163-5170.
25. Alevizaki M, Papageorgiou G, Rentziou G, et al. Increasing prevalence of papillary thyroid carcinoma in recent years in Greece: the majority are incidental. *Thyroid*. 2009;19:749-754.
26. Ilias I, Alevizaki M, Lakka-Papadodima E, Koutras DA. Differentiated thyroid cancer in Greece: 1963-2000. Relation to demographic and environmental factors. *Hormones (Athens)*. 2002;1:174-178.
27. Vlassopoulou V, Vryonidou A, Paschou SA, et al. No considerable changes in papillary thyroid microcarcinoma characteristics over a 30-year time period. *BMC Res Notes*. 2016;9:252.
28. Busnardo B, De Vido D. The epidemiology and etiology of differentiated thyroid carcinoma. *Biomed Pharmacother*. 2000;54:322-326.
29. Delange F, Lecomte P. Iodine supplementation: benefits outweigh risks. *Drug Saf*. 2000;22:89-95.
30. Lawal O, Agbakwuru A, Olayinka OS, Adelusola K. Thyroid malignancy in endemic nodular goitres: prevalence, pattern and treatment. *Eur J Surg Oncol*. 2001;27:157-161.
31. Harach HR, Williams ED. Thyroid cancer and thyroiditis in the goitrous region of Salta, Argentina, before and after iodine prophylaxis. *Clin Endocrinol (Oxf)*. 1995;43:701-706.
32. Bychkov A, Jung CK, Liu Z, Kakudo K. Noninvasive follicular thyroid neoplasm with papillary-like nuclear features in Asian practice: perspectives for surgical pathology and cytopathology. *Endocr Pathol*. 2018;29:276-288.

How to cite this article: Markantes GK, Tsochatzis S, Panagopoulos K, et al. A shift to more targeted thyroidectomies increased the detection of thyroid cancer and in particular low-risk papillary tumors in Southwestern Greece the decade 2007 to 2016. *Laryngoscope Investigative Otolaryngology*. 2020;5:1260–1265. https://doi.org/10.1002/lio2.504