Incidental thyroid carcinoma after thyroidectomy for benign thyroid disease in Suez Canal region

Mohammed Faisal[a], Hamada Fathy[a], Ahmed Risk[a], Maha M. Atwa[b]

Departments of [a]Surgery, [b]Pathology, Faculty of Medicine, Suez Canal University Hospital, Ismailia, Egypt

Correspondence to Mohammed Faisal, MD of Surgery, Department of Surgery, Faculty of Medicine, Suez Canal University Hospital, km 4.5 Ring Road, 41522, Ismailia, Egypt. Tel: +20 122 616 1340; fax: 0643565662; e-mail: m.faisal@med.suez.edu.eg

Received 27 February 2018
Accepted 11 March 2018

The Egyptian Journal of Surgery
2018, 37:361–367

Background
The term 'incidental' thyroid cancer is a term applied to a very small, unsuspected cancer identified incidentally on pathologic examination of thyroid tissue removed for benign disease.
Aim
The aim was to evaluate the prevalence of incidental thyroid carcinoma (ITC) after thyroidectomy for benign thyroid lesions with its different pathological types.
Patients and methods
The study population was selected by comprehensive sampling. All the patients attended the General Surgery Department in the Suez Canal University hospital for thyroidectomy of previously diagnosed benign thyroid diseases within the period between 1 July 2009 and 31 December 2014 and fulfilled the inclusion criteria.
Results
In this study, 211 patients underwent thyroidectomy. The female (n=179) to male (n=32) ratio was 5.6 : 1, and the age ranges from 18 to 75 years. The highest age incidence was found to be in the fifth decade of life (60 patients). In this study, the incidental carcinoma was found in 22 (10.4%) patients. The frequency of papillary carcinoma was 8.5% of all thyroid diseases and 81.8% of ITC (18/22). Moreover, the frequency of follicular carcinoma was 1.4% of all thyroid diseases (three cases) and 13.6% of ITC.
Conclusions
A correct preoperative assessment, with a careful selection of nodules for fine-needle aspiration cytology on the basis of ultrasound pattern, could better address the choice of surgical procedure.

Keywords:
fine-needle aspiration cytology, incidental, microcarcinoma, occult, thyroid swelling

Egyptian J Surgery 37:361–367

1110-1121

Introduction

Thyroid cancer is the most common endocrine carcinoma, as it accounts for almost 90% of all endocrine malignancies. The incidence of thyroid carcinoma is ~1–3 cases in every 100 000 population. During the past 30 years, the rate of thyroid cancer incidence has increased worldwide [1]. The increased incidence of thyroid carcinoma seems to be related to an improvement in the diagnostic approach. The more widespread employment of ultrasonographic and cytological techniques ensures the early diagnosis of occult thyroid nodules [2].

The term 'occult thyroid carcinoma' was introduced by Graham in 1928 to describe thyroid tumors that are clinically hidden but suspicious because of the presence of metastatic laterocervical nodes. Later, the term 'occult' was extended to cover all thyroid cancers less than 15 mm in diameter irrespective of their clinical presentation [3].

Nowadays, the term 'incidental' thyroid cancer is a term applied to a very small, unsuspected cancer identified incidentally on pathologic examination of thyroid tissue removed for benign disease [4]. The incidence of incidental thyroid carcinoma (ITC) ranges from 3 to 16% in different series with the highest frequency in patients affected by multinodular goiter [5]. These tumors, even if small, can metastasize to regional cervical nodes, but the potential they have to cause significant morbidity and mortality is nowadays controversial [6]. The etiology of these cancers is still debatable, and several authors have suggested that iodization will cause a rise in the incidence of thyroid cancers, especially papillary carcinomas [7]. The mean false-positive and false-negative rates of the fine-needle aspiration cytology (FNAC) are reported as less than 5%. The main limitations of FNAC are the inability of cytology to distinguish follicular and Hürthle cell carcinomas from the respective benign adenomas, the requirement of an experienced prober to avoid

nondiagnostic punctures, and the presence of multiple nodules in a goiter [8].

The purpose of this study was to evaluate the prevalence of ITC after thyroidectomy for benign thyroid lesions with its different pathological types.

Patients and methods

Study type

A cross-sectional descriptive retrospective and prospective clinical study after the approval of the Research Ethical Committee (REC), Faculty of Medicine-Suez Canal University was obtained.

Study site

The study was conducted in General Surgery Department at Suez Canal University hospital in Ismailia.

Target population

The retrospective part

All files of patients submitted for thyroidectomy for benign thyroid disease at the Department of General Surgery in the Suez Canal University hospital within the period between 1 July 2009 and 30 June 2014 were reviewed and included in the study.

The prospective part

All patients submitted for thyroidectomy for benign thyroid disease at the Department of General Surgery in the Suez Canal University hospital during the period of 1 July 2014 to 31 December 2014 were included in this study.

Inclusion criteria

All patients attending the General Surgical Department for thyroidectomy of benign thyroid diseases in the Suez Canal University hospital were selected according to the following criteria:

(1) Male and female patients.
(2) Patients who underwent thyroidectomy for benign thyroid diseases.
(3) The histopathologic examination of the thyroidectomy specimens were examined at Pathology Department in the Suez Canal University hospital.

Exclusion criteria

The following were the exclusion criteria:

(1) History of head and/or neck radiation.
(2) Clinical or cytological suspicion or diagnosed thyroid malignancy.
(3) In retrospective part: patients with medical records lacking critical data to complete the survey.

Sample size

The study population was selected by comprehensive sampling.

(1) All the patients attending the General Surgery Department in the Suez Canal University Hospital for thyroidectomy of previously diagnosed benign thyroid diseases within the period between 1 July 2009 and 31 December 2014 and fulfilled the inclusion criteria were included.

Data collection:

The study has a retrospective and a prospective view:

(1) The retrospective data were collected from the medical records of the patients saved at the archiving unit in the Suez Canal University hospital.
(2) The prospective data were from patients attending the General Surgery Department in the Suez Canal University hospital in Ismailia.

The required data were collected using a questionnaire designed by the researcher.

Data collected was processed to identify the incidence and different pathological aspects of ITC after thyroidectomy for benign thyroid disease.

Results

The present study included 211 patients subjected to thyroidectomy for benign thyroid disease.

All patients were subjected to preoperative and postoperative evaluations in the form of clinical, biochemical, radiological, operative, and pathological studies. The incidence was much more common in females (179 patients) than males (32 patients), with ratio of 5.6 : 1. The age ranges from 18 to 75 years, with mean age of 40.72 years. The highest age incidence was found to be in the fifth decade of life (60 patients) and next was in the fourth decade (51 patients), and much less below 20 (four patients) years. The incidence was more in rural areas (112 patients) than urban areas (99 patients) (Table 1).

The performed surgical procedures were 42 (20%) hemithyroidectomy, 21 (10%) subtotal thyroidectomy, 32 (15%) near-total thyroidectomy, and 116 (55%) total thyroidectomy (Table 2).

The postoperative histopathological examination of the removed gland showed the presence of ITC in

22 (10.4%) patients of total number of patients; of them, 18 of them had papillary thyroid cancer, three patients had follicular thyroid cancer, and one patient had undifferentiated thyroid cancer. The rest of the 189 (89.6%) patients had benign thyroid disorders (Figs 1 and 2.)

The distribution of ITC according to preoperative diagnosis was 11 (50%) patients with nontoxic multinodular goiter, seven (31.8%) patients with toxic multinodular goiter, two (9.1%) patients with solitary thyroid nodule, and two (9.1%) patients with diffuse goiter (Fig. 3).

Of 22 patients with ITC, 19 patients were female and only three patients were males, and the highest age incidence was found to be in the fourth decade of life (eight patients) (Table 3).

The most frequent postoperative complication was hypoparathyroidism reported in five (2.4%) patients then recurrent laryngeal nerve injury in four (1.9%) patients and the less common was infection reported only in two (0.95%) patients (Table 4).

The incidence of different pathological types of ITC according to preoperative diagnosis is summarized in Table 5: (50%) of papillary thyroid carcinomas were preoperatively diagnosed as nontoxic multinodular goiter, whereas 66.7% of follicular carcinomas preoperatively were diagnosed as nontoxic multinodular, and 100% of undifferentiated carcinomas preoperatively were diagnosed as diffuse goiter (Table 6).

Table 1 Age, sex, and residence distribution of the study population

Items	*n*=211 [*n* (%)]
Sex	
Male	32 (15.2)
Female	179 (84.8)
Female/male ratio	5.6 : 1
Age (years)	
<20	4 (1.9)
20 to <30	43 (20.4)
30 to <40	51 (24.2)
40–50	60 (28.4)
>50	53 (25.1)
Mean±SD	40.72±12.43
Minimum–maximum	18–75
Residence	
Rural	112 (53)
Urban	99 (47)

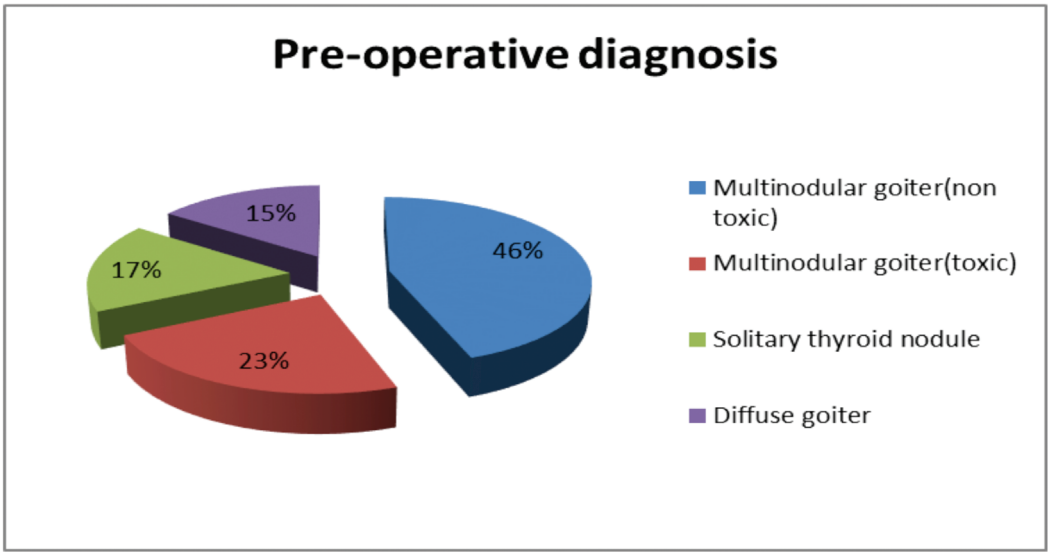
Discussion

The present study included 211 patients subjected to thyroidectomy for benign thyroid disease. All patients were subjected to preoperative and postoperative evaluations in the form of clinical, biochemical, radiological, operative, and pathological studies.

Table 2 Types of the operations done

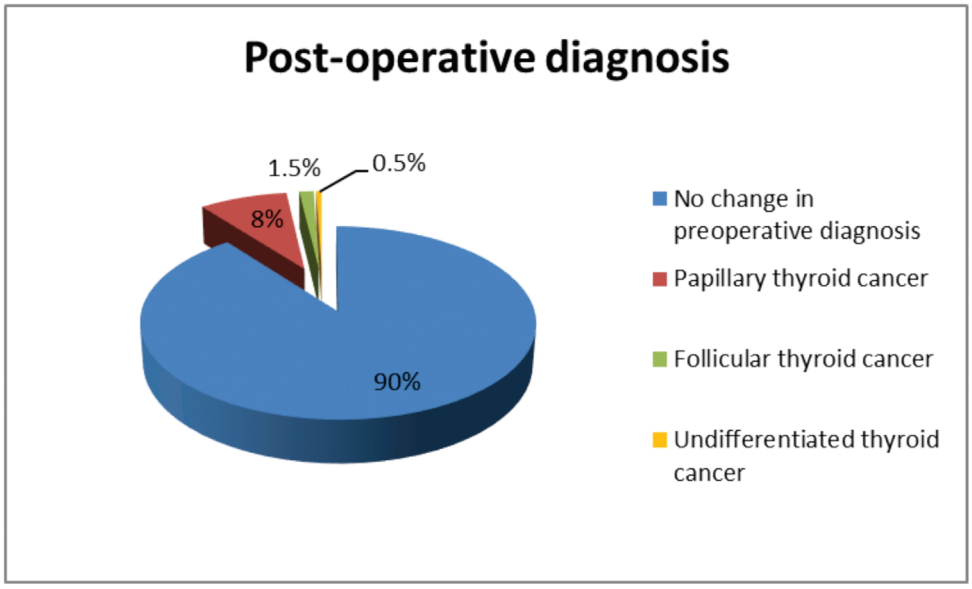
Operation type	*n* (%)
Hemithyroidectomy	42 (20)
Subtotal thyroidectomy	21 (10)
Near-total thyroidectomy	32 (15)
Total thyroidectomy	116 (55)
Total	211 (100)

Figure 1



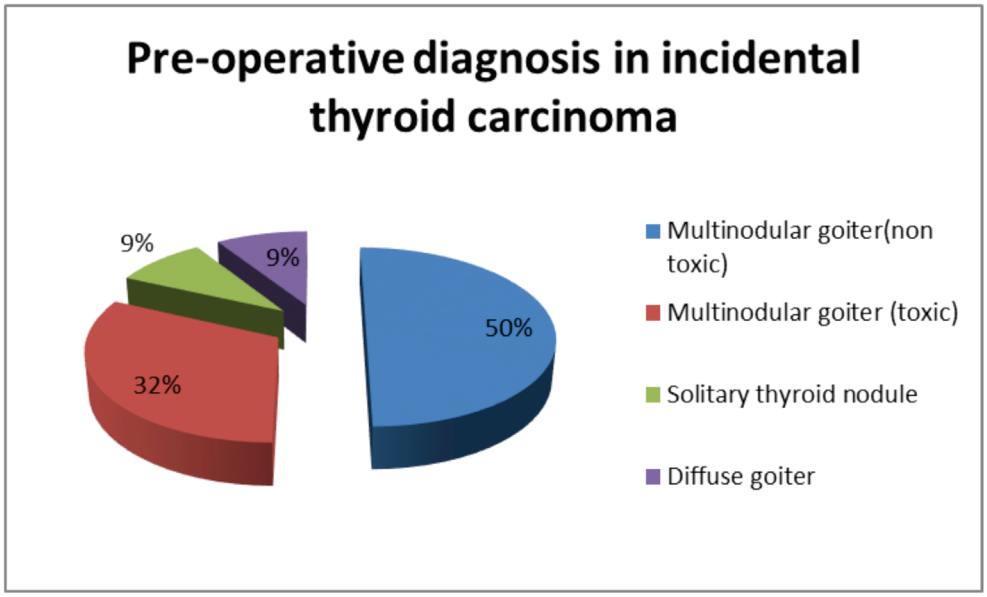
Preoperative diagnosis.

Figure 2



The incidence of the histopathological results of the removed gland.

Figure 3



Frequency of incidental thyroid carcinoma in relation to preoperative diagnosis.

From this study, the female (179) to male (32) ratio for the patients subjected to thyroid surgery was 5.6 : 1, and their age ranges from 18 to 75 years, with mean age of 40.72 years. The highest age incidence was found to be in the fifth decade of life (60 patients) and much less below 20 years of age (four patients). These were similar to the results of Askitis *et al.* [9]. They studied 228 cases of thyroidectomy specimens, which comprised 182 females and 46 males with female : male ratio of 4 : 1, and the age ranged from 11 to 80 years, with a median age of 50 years.

In this study, the incidental carcinoma was found in 22 (10.4%) patients. Nonmalignant thyroid diseases were seen in 189 (89.6%) patients. These results were similar to the results of Miccoli *et al.* [10], which studied 998 patients who underwent thyroidectomy for benign thyroid disease, and the final histology revealed ITC in 104 (10.4%) patients. This group included 71 females and 33 males, with a mean age of 48.5 years (range: 21–79 years). Moreover, Costamagna *et al.* [11] studied 646 patients who underwent thyroid surgery, and the final histology revealed ITC in 53 (9.3%) patients. This group

included 46 women and seven men, with a mean age of 56.7 years (range: 25–82 years).

Different results were obtained by Askitis *et al.* [9] in their study, where 228 patients underwent total thyroidectomy and the final histopathological examination revealed ITC in 33 (14.5%) cases. These small differences may be towing to their selection of patients who underwent only total thyroidectomy.

Our study showed that the incidence of papillary carcinoma in unsuspected cases was 8.5% of all thyroid diseases. Of the 22 patient with ITC, 18 (81.8%) patients had papillary thyroid cancer, and the frequency was high in the fourth decade of life. These results were close to the results of Askitis *et al.* [9], where their study showed that papillary thyroid carcinoma had the highest incidence (27 from 228), representing 11.8% of thyroid diseases and 81.8% of ITC (27/33), and the mean age of the patients at diagnosis was 33 years.

Our study showed that the frequency of follicular carcinoma was 1.4% of all thyroid diseases (three cases), and 13.6% of ITC. Age of patients with follicular carcinoma ranges from 31 to 40 years. These results were close to the results of Askitis *et al.* [9], as they stated that follicular carcinoma was the second most common thyroid malignancy and was observed in four (1.8%) of 228 patients having thyroid diseases and 12.1% of ITC (4/33).

Our study showed that there was only one case that had undifferentiated thyroid cancer (0.5% of thyroid diseases and 4.5% of ITC) in the fourth decade of life, but no cases of anaplastic, medullary thyroid cancer, or lymphoma.

These results were close to the results of Askitis *et al.* [9], as they found two cases had undifferentiated thyroid cancer, representing 6.1% of ITC.

The study by Nanjappa *et al.* [12] included 187 cases that underwent thyroidectomy for benign thyroid disease and found no cases of anaplastic, medullary thyroid cancer, or lymphoma.

As regarding preoperative diagnosis, it was found that 94 (44.5%) patients were diagnosed as having nontoxic multinodular goiter, 49 (23%) patients as toxic multinodular goiter, 36 (17.1%) patients as solitary thyroid nodule, and 32 (15.2%) patients as diffuse goiter.

These results were close to the results of Askitis *et al.* [9], as in their study, of 228 cases, 152 (66.7%) cases were preoperatively diagnosed as nontoxic multinodular goiter, 26 (11.4%) cases as toxic

Table 3 The frequency of malignant cases in relation to preoperative diagnosis

Preoperative diagnosis	Incidental thyroid carcinoma (*n*=22) [*n* (%)]
Multinodular goiter (nontoxic)	11 (50.0)
Multinodular goiter (toxic)	7 (31.8)
Solitary thyroid nodule	2 (9.1)
Diffuse goiter	2 (9.1)

Table 4 Sex and age distribution of the incidental thyroid carcinoma

Items	ITC (*n*=22) [*n* (%)]
Sex	
Male	3 (13.6)
Female	19 (86.4)
Age (years)	
<20	1 (4.5)
20 to <30	0 (0)
30 to <40	8 (36.4)
40–50	6 (27.3)
>50	7 (31.8)
Mean±SD	43.27±11.12
Minimum–maximum	19–63

ITC, incidental thyroid carcinoma.

Table 5 Frequency of complications

Complication	*n* (%)
Hemorrhage	3 (1.4)
Infection	2 (0.95)
Hypoparathyroidism	5 (2.4)
Recurrent laryngeal nerve injury	4 (1.9)
External laryngeal nerve injury	3 (1.4)
Recurrence	3 (1.4)

Table 6 The frequency of malignant cases in relation to preoperative diagnosis

Preoperative diagnosis	Postoperative cancer group (*n*=22) [*n* (%)]		
	Papillary thyroid cancer (*n*=18)	Follicular thyroid cancer (*n*=3)	Undifferentiated thyroid cancer (*n*=1)
Multinodular goiter (nontoxic)	9 (50.0)	2 (66.7)	0 (0)
Multinodular goiter (toxic)	6 (33.3)	1 (33.3)	0 (0)
Solitary thyroid nodule	2 (11.1)	0 (0)	0 (0)
Diffuse goiter	1 (5.6)	0 (0)	1 (100)

multinodular goiter, 34 (14.9%) cases as solitary thyroid nodule, six (2.6%) cases as toxic adenoma, and 10 (4.4%) cases as graves' disease. The study by Nanjappa *et al.* [12] included 187 cases and found 41.2% had MNG, 52.4% had STN, and 6.4% had diffuse goiter.

In this study, 89.9% of ITC were preoperatively diagnosed as multinodular or diffuse goiter and 9.1% of ITC were preoperatively diagnosed as solitary thyroid nodule.

These results were close to the results of Costamagna *et al.* [11], where in their study, 85% of ITC were preoperatively diagnosed as multinodular or diffuse goiter and 15% of ITC were preoperatively diagnosed as solitary thyroid nodule.In this study, 42 (20%) patients were subjected to hemithyroidectomy, 21 (10%) patients to subtotal thyroidectomy, 32 (15%) patients to near-total thyroidectomy, and 116 (55%) patients to total thyroidectomy.

The study by Nanjappa *et al.* [12] included 187 cases, and hemithyroidectomy was performed in 90 (48.1%), subtotal thyroidectomy in 91 (48.7%), near-total thyroidectomy in four (2.1%), and total thyroidectomy in two (1.1%).

Total thyroidectomy is considered the most effective method for achieving complete thyroid malignancy cures. Total thyroidectomy (TT) had no significant effect on the prevalence of permanent postoperative complications in comparison with partial or subtotal thyroidectomy. Furthermore, TT is associated with a reduction in event rates of incidentally diagnosed thyroid cancer, needs of completion thyroidectomy, and redo surgery for disease recurrence [13]. These small cancers have been reported in significant percentages of cases (5–22%) from various surgical studies [9].

The disadvantages of TT may be lifelong replacement therapy. Patients who undergo limited resection may also require replacement therapy with levothyroxine for a shorter period, and even if prolonged, it does not lead to any substantial degradation in the performance and quality of life [12].

Finally, according to our findings of this study, we favors total thyroidectomy as the preferred method in benign thyroid disease for which surgery is indicated when performed by skilled surgeons, but we highly recommend further new long-term RCTs with bigger sample sizes and multicentric studies. The advantages of TT include reduction of recurrence rate, achievement of a permanent cure of thyroid disorders, the avoidance of rare possibilities of transformation from well-differentiated to undifferentiated carcinoma, and avoidance of second operation.

Conclusions

A correct preoperative assessment, with a careful selection of nodules for fine-needle aspiration cytology on the basis of ultrasound pattern, could better address the choice of surgical procedure. The nonirrelevant incidence of ITC, the eventuality of multifocality and bilaterality, and the possible occurrence of relapse support that total thyroidectomy without residuum is a valuable option for treating benign thyroid conditions such as multinodular goiter.

The result of this study confirmed that the frequency of ITC in patients who underwent surgery for benign thyroid diseases is not negligible. Our data also indicated that the possibility of missing a malignant neoplasm existed in patients with large nodules in the context of multinodular goiter. This finding may provide support for the recommendation to perform multiple FNAC not only in dominant nodules but also in all other nodules appearing suspicious at clinical examination or at ultrasound.

When an incidental cancer is diagnosed after hemithyroidectomy, a radicalization with central neck dissection could be considered.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1 Morris LG, Sikora AG, Tosteson TD, Davies L. The increasing incidence of thyroid cancer: the influence of access to care. Thyroid 2013; 23:885–891.

2 Kwang H, Jung H, Boo-Kyung H, Eun Y, Eun S, Soo Y, Joon Y. Incidental thyroid lesions detected on 18F-fluorodeoxyglucose positron emission tomography/CT in patients with non-thyroidal cancer: clinical implications and the value of ultrasound. J Korean Soc Radiol 2014; 71:111–119.

3 Liu H, Lv L, Yang K. Occult thyroid carcinoma: a rare case report and review of literature. Int J Clin Exp Pathol 2014; 7:5210–5214.

4 Vasileiadis I, Karatzas T, Vasileiadis D, Kapetanakis S, Charitoudis G, Karakostas E, Kouraklis G. Clinical and pathological characteristics of incidental and nonincidental papillary thyroid microcarcinoma in 339 patients. Head Neck 2014; 36:564–570.

5 Mehanna H, Al-Maqbili T, Carter B, Martin E, Campain N, Watkinson J, *et al.* Differences in the recurrence and mortality outcomes rates of incidental and nonincidental papillary thyroid microcarcinoma: a systematic review and meta-analysis of 21 329 person-years of follow-up. J Clin Endocrinol Metab 2014; 99:2834–2843.

6 Zheng X, Wei S, Han Y, Li Y, Yu Y, Yun X, *et al.* Papillary microcarcinoma of the thyroid: clinical characteristics and BRAF(V600E) mutational status of 977 cases. Ann Surg Oncol 2013; 20:2266–2273.

7 Zimmermann MB, Galetti V. Iodine intake as a risk factor for thyroid cancer: a comprehensive review of animal and human studies. Thyroid Res 2015; 8:8.

8 Luo J, McManus C, Chen H, Sippel RS. Are there predictors of malignancy in patients with multinodular goiter? J Surg Res 2012; 174:207–210.

9 Askitis D, Efremidou EI, Karanikas M, Mitrakas A, Tripsianis G, Polychronidis A, Liratzopoulos N. Incidental thyroid carcinoma diagnosed after total thyroidectomy for benign thyroid diseases:incidence and association with thyroid disease type and laboratory markers. Int J Endocrinol 2013; 2013: 451959.

10 Miccoli P, Minuto MN, Galleri D, D'Agostino J, Basolo F, Antonangeli L, *et al.* Incidental thyroid carcinoma in large series of consecutive patients operated on for benign thyroid disease. ANZ J Surg 2006; 76:123–126.

11 Costamagna D, Pagano L, Caputo M, Leutner M, Mercalli F, Alonzo A. Incidental cancer in patients surgically treated for benign thyroid disease. Our experience at a single institution. G Chir 2013;34:21–26.

12 Nanjappa N, Kumar A, Swain SK, Aroul TT, Smile SR, Kotasthane D. Incidental thyroid carcinoma. Indian J Otolaryngol Head Neck Surg 2013; 65:37–39.

13 Barczyński M, Konturek A, Stopa M, Cichoń S, Richter P, Nowak W. Total thyroidectomy for benign thyroid disease: is it really worthwhile? Ann Surg 2011; 254:724–730.