

The Prevalence of Incidental Thyroid Carcinoma in Patients Who Underwent Thyroidectomy for Multinodular Goiter

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Abstract The incidence of an incidental carcinoma following surgical treatment for MNG varies from 3 to 16%. The aims of this study are to determine the incidence of an incidental thyroid carcinoma (ITC) in patients with multinodular goiter (MNG) and to evaluate the primary surgical treatment modality for these patients. Between January 2010 and July 2015, a total of 3311 patients who underwent surgery for goiter were retrospectively evaluated. Demographic characteristics of the patients, previous medical history, thyroid hormone profiles, thyroid ultrasonography findings, fine-needle aspiration biopsy (FNAB) findings, thyroid scintigraphy findings, surgical techniques, early postoperative complications, and histopathological diagnoses were recorded. The patients were divided into two groups: those who were incidentally diagnosed with a thyroid carcinoma (ITC group; $n = ?$) and those with MNG (MNG group; $n = ?$). Of 3311 patients, FNAB was performed in 1524 (46%) patients. Of these, 1790 underwent total thyroidectomy (TT) or near total thyroidectomy (NTT), 1066 underwent bilateral subtotal thyroidectomy (BSTT), 354 underwent the Dunhill procedure, and 101 underwent unilateral lobectomy (ULL) due to the presence of unilateral MNG. Postoperative histopathological examinations revealed an incidental thyroid carcinoma (ITC) in 283 (8.54%) patients, papillary carcinoma in 201 patients (201/3311, 6%), follicular cancer in 68 patients (68/3311, 2%), medullary cancer in 13 patients (13/3311, 0.3%), follicular carcinoma in four patients (4/923, 0.4%), and anaplastic cancer in one patient (1/3311, 0.03%). Our study results suggest that TT should be the

primary surgical treatment modality to avoid the complications of a complementary thyroidectomy.

Keywords Incidental · Multinodular goiter · Thyroid cancer · Thyroidectomy

Introduction

Thyroid nodules are common complaints, which affect about 4 to 7% of the adult population [1]. They may present as a single or multiple nodules. Indications for surgery in multinodular goiters (MNGs) include a suspicion of malignancy, compression symptoms, hyperthyroidism, and cosmetic problems [2]. The incidence of an incidental carcinoma following surgical treatment for MNG varies from 3 to 16% [3, 4]. The decision to perform surgery and which surgical method should be selected is of particular importance in patients with MNG. In this study, we aimed to determine the incidence of an incidental thyroid cancer (ITC) in patients with MNG and to evaluate the primary surgical treatment modality for these patients.

Patients and Methods

This retrospective study included the medical charts and surgical data of a total of 3892 patients who underwent surgery for goiter at our clinic between 2010 and 2015. A total of 581 patients were excluded from the study due to a history of neck irradiation, recurrent goiter, a family history of thyroid cancer, evidence of malignancy, or a suspicion of malignancy during the preoperative fine needle aspiration biopsy (FNAB). Demographic characteristics of the patients, previous medical history, thyroid hormone profiles, thyroid ultrasonography

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(US) findings, FNAB findings, thyroid scintigraphy findings, surgical techniques, early postoperative complications, and histopathological diagnoses were recorded. The patients were divided into two groups including patients with an ITC (ITC group) and those with MNG (MNG group), according to the final histopathological examination of the surgical specimens.

Statistical Analysis

Statistical analysis was performed using the SPSS 18.0 software (SPSS Inc., Chicago, IL, USA). Descriptive data were expressed in mean and standard deviation and percentages for categorical variables. Chi-square test and *T* test were used to compare the parameters between the groups. A *p* value of <0.05 was considered statistically significant.

Results

Of 3311 patients, 2922 (88%) were females and 389 (12%) were males. The mean age was 48.72 ± 11.32 years. All patients underwent thyroid US, T3, T4, and thyroid-stimulating hormone (TSH) at least once previously. A total of 1524 patients (46%) with dominant nodules as evidenced by US underwent FNAB. Among the whole study population, 1790 patients underwent total thyroidectomy (TT) or near total thyroidectomy (NTT), 1066 underwent bilateral subtotal thyroidectomy (BSTT), 354 underwent the Dunhill procedure (DP), and 101 underwent unilateral lobectomy (ULL) due to the presence of unilateral MNG.

Postoperative histopathological examination revealed an ITC (ITC) in 283 patients (8.54%). Of these, 252 were female (252/2922, 8.6%) and 31 were males (31/389, 7.9%). The mean age of the ITC group was 48.67 ± 11.62 years (range, 27 to 79). There was no significant difference in the mean age and sex between the ITC and MNG groups (*p* = 0.579) (Table 1).

According to the postoperative histopathological findings, 201 (201/3311, 6%) patients had a papillary carcinoma, 68 patients (68/3311, 2%) had follicular cancer, 13 patients (13/3311, 0.3%) had medullary cancer, four patients (4/923, 0.4%) had a follicular carcinoma, and one patient (1/3311, 0.03%) had anaplastic cancer.

Table 1 Demographic characteristics of the patients

| Parameters | ITC (<i>n</i> = 283) | MNG (<i>n</i> = 3028) | <i>p</i> value |
|-------------------|-----------------------|------------------------|----------------|
| Age (mean, years) | 48.67 ± 11.62 | 47.29 ± 12.34 | 0.579 |
| Nodule size (mm) | 12 ± 8.9 | 28.3 ± 21.7 | 0.021 |
| Gender (F/M) | 31/252 | 361/2667 | 0.113 |
| Toxicity/Function | 14/269 | 562/2748 | 0.040 |

The mean tumor size was 12 ± 8.9 mm (2–30 mm), indicating significantly lower than the mean nodule size in patients with MNG. According to the thyroid function, 2748 patients (83%) had non-toxic disease, while 562 patients (17%) had toxic disease.

Of the 283 patients with a carcinoma, 269 (269/2748; 10.21%) had non-toxic disease and 14 (14/562; 2.4%) had toxic disease. There was a significant difference in the presence of thyrotoxicosis between the groups (*p* = 0.040) (Table 1). The mean age was 48.69 ± 12.23 years and the mean tumor size was 12 ± 8.7 mm in 201 patients with a papillary carcinoma. A total of 141 patients had also a microcarcinoma. Of these, 124 underwent TT, 43 underwent NTT, 22 underwent DP, and 12 underwent BSTT. Forty-three patients who underwent NTT and all patients who underwent TT required complementary thyroidectomy eventually. In another patient who underwent NTT, complementary thyroidectomy was performed, based on the discretion of the endocrinologist. The remaining 22 patients who underwent the Dunhill procedure required a re-do surgery. Only one patient who underwent complementary thyroidectomy developed postoperative temporary hypocalcemia. There were no other complications. All patients underwent radioactive iodine (RAI) ablation therapy, and subsequent whole body screening revealed no metastasis in these patients. All patients were placed on hormone replacement or suppression therapy. They continued scheduled follow-up visits without any problem (mean 32.1 ± 21.5 months). Histopathological examination of follicular carcinomas (*n* = 68) revealed capsular invasion without any vascular invasion. These patients underwent RAI ablation therapy following the complementary thyroidectomy. The patients are still on replacement therapy and attend to their scheduled visits (mean 23.3 ± 18.8 months).

Discussion

Thyroid nodules are encountered in about 4 to 7% of the overall population, while thyroid cancers occur less frequently. Thyroid cancer accounts for 4 to 5% of all thyroid nodules. Thyroid cancers are responsible for only 0.2% of cancer-related deaths. On the other hand, several studies have reported that the number of well-differentiated thyroid cancers is underestimated, and the disease often remains undiagnosed due to its mild clinical course [5–7]. Correspondingly, 283 patients (8.5%) were diagnosed with ITC in the present study although these patients were initially deemed to have a benign condition.

In a study by Koh et al. [8], malignancy was reported in eight of 107 patients with MNG (7.5%), which was lower than reported in our study [8]. Unlike our study, the mean age was significantly different. In our study, there was no significant difference in the mean age between the MNG and ITC groups

(47.29 years in patients with MNG, 48.69 years in patients with ITC), while the mean age of the patients with ITC was significantly higher in the study by Koh et al. (45.6 years versus 35.2 years) [8]. However, the incidences of the cancer subtypes were similar between the groups.

In a study of 198 patients by Gürleyik et al. [9], the incidence of malignancy was low, similar to the present study. Histopathological examination led to the diagnosis of thyroid cancer in three cases (1.5%). Of these patients, one had papillary, papillary microcancer, and poorly differentiated thyroid cancer [9]. In a similar study conducted by Pelizzo et al., the incidence of ITC was 7.6% in 539 patients (41/539) [10]. This rate is lower than reported in the present study. However, the percentages in male and female patients were similar [8.3% (38/455) versus 8.6% (252/2922)] [(7.9% (31/389) versus 8.4% (9/106)]. In another study including 998 patients, Miccoli et al. [11] reported the largest series of patients with ITC with a ratio of 10.4%. In the present study, the study population was approximately three times larger than that used in the aforementioned study. The incidence of ITC in the present study was 8.54% (283/3311). Similarly, the incidence of ITC was 13.7% in the study Gandolfi et al. [21] and 8.2% in the study by Giles et al. We consider that the selection of different groups of patients might have contributed to the rates that differed from the aforementioned studies. The patients with a single nodule were excluded, while all other patients with MNG were included in the study by Koh et al. [8]. The study by Pelizzo et al. [10] only excluded the patients with a predisposing factor for thyroid cancer. Similarly, only patients with a single thyroid nodule were included in the study by Miccoliet al [11].

In another study including 2306 patients, Kaliszewski et al., among the 2306 MNG patients, ITC was detected in 49 (2.12%) [12]. In another study including 90 patients, Bhuiyan et al., ITC was detected in 11.1%. [13].

The incidence of an incidental carcinoma among patients undergoing thyroidectomy for MNG is higher than anticipated. This finding may prompt the complementary thyroidectomy in selected patients, which has several risks. Hypoparathyroidism is the most common complication following complementary thyroidectomy [14]. The rate of temporary and permanent hypocalcemia was reported to be 3 to 15% and 0 to 3.5% in the literature, following reoperative thyroid surgery, respectively [15, 16]. Recurrent laryngeal nerve (RLN) paralysis is another serious complication. Even specialized centers only performing thyroid surgery report a 1 to 2% rate of permanent RLN paralysis following primary surgery, and a rate up to 2.6 to 4.8% following reoperative thyroid surgery [16]. Giles et al. [17] and Sakorafas et al. [18] recommended the use of TT/NTT to avoid the risk associated with second surgery in patients with suspected malignancy.

Among the patients undergoing surgery at our clinic due to MNG included in the present study, 1790 underwent TT or

NTT, 1066 underwent BSTT, 354 underwent the DP, and 101 underwent ULL due to the presence of unilateral MNG. Of the 283 patients with ITC, 242 underwent TT/NTT, 27 underwent the Dunhill procedure, and 13 underwent BSTT. Based on the current data, we consider that TT is the more appropriate option for patients with MNG due to the risk of recurrence following DP and BSTT and the risk of complications associated with re-do surgery.

The guidelines of the National Comprehensive Cancer Network (NCCN) recommend that complementary thyroidectomy is not required in cases of papillary cancer, if the surgical margin is negative following limited thyroidectomy performed due to MNG, contralateral lesion does not exist, the diameter of the lesion is below 1 cm, and there is no suspected lymph node involvement [18]. Rodrigues et al. [19] also advocated that complementary thyroidectomy is not required in patients with Stage I, well-differentiated incidentally detected papillary carcinoma without lymph node involvement.

Of the 94 patients with papillary carcinoma who did not undergo TT in the present study, 21 underwent complementary thyroidectomy due to an excessive amount of thyroid tissue remaining. The patients who did not undergo complementary thyroidectomy rather NTT and there was no finding during follow-up which suggested a recurrent disease. One patient developed temporary hypocalcemia associated with reoperation. Pezullo et al. [20] evaluated postoperative complications in 35 patients who underwent complementary thyroidectomy. Two patients had temporary hypoparathyroidism, one patient had permanent hypoparathyroidism, three patients had temporary recurrent laryngeal nerve paralysis, and one patient had permanent recurrent laryngeal nerve paralysis. In the present study, seven patients who underwent the Dunhill procedure developed hypocalcemia following complementary thyroidectomy.

Conclusion

In conclusion, the incidence of thyroid cancers in the population is higher than the expected, with 3 to 16% of patients undergoing surgery due to diagnoses other than cancer and suspected malignancy. The frequency of incidental thyroid cancer is too high to be ignored. Thus, TT should be the primary surgical treatment modality to avoid the complications of a complementary thyroidectomy.

Compliance with Ethical Standards

Conflict of Interest The authors declare that there is no conflict of interest.

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