Int J Clin Exp Med 2013;6(10):922-929
www.ijcem.com /ISSN:1940-5901/IJCEM1309011

Original Artice

What do we leave behind after neartotal and subtotal thyroidectomy: just the tissue or the disease?

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Received September 20, 2013; Accepted October 5, 2013; Epub October 25, 2013; Published October 30, 2013

Abstract: Selection of multinodular goiter (MNG) surgery procedure is stilll under discussion. Subtotal thyroidectomy (STT) and neartotal thyroidectomy (NTT) are preferred surgical procedures. However, it is uncertain whether the remnant tissue contains pathological findings or not after these procedures. We aimed to evaluate and comparison the pathologic findings in remnant tissue after NTT and STT. Thyroid tissue samples of 50 patients who underwent TT for MNG disease between January 2010 and August 2011 in our clinic were evaluated. Before the dissection of the thyroid tissue subtotal and neartotal margins were marked in both right and left lobes. After the resection of the specimen, the tissue was excised from the subtotal and neartotal margin marked during the surgery. The pathologic findings of the main tissue, the residual subtotal and neartotal tissues were evaluated and compared. All patients were followed-up 1 year. 43 (86%) females and 7 (14%) males with an average age of 50.5 (23-77) were included in the study. Incidental papillary thyroid cancer was detected in 5 patients (10%). Pathologic findings were present in 31 patients (62%) of subtotal residual tissue and 28 of the patients (56%) of neartotal residual tissue. Papillary microcarcinoma was detected in 3 (9.7%) of subtotal residual tissues and 2 (7.1%) of neartotal residual tissues. There is no significant difference between subtotal and neartotal tissues in terms of existence of pathological findings ($p>0.05$). There is no significant difference between the neartotal and subtotal residual tissues contralateral of dominant nodule ($p>0.05$). 2 of the patients (4%) had temporary hypocalcemia, 1 patient (2%) had seroma and 1 patient (2%) had recurrent laryngeal nerve injury. There are high rates of microscopic pathological findings on residual tissues both after STT and NTT. The neartotal and subtotal residual tissues contralateral to the large nodule also had high levels of pathologic findings.

Keywords: Total thyroidectomy, subtotal thyroidectomy, neartotal thyroidectomy, residual tissue, multinodular goiter

Introduction

Multinodular goiter (MNG) is a relatively common disease of the thyroid gland, and surgery is a treatment option in the presence of indications (compressive symptoms, suspicion of malignancy, hyperthyroidism, cosmetic reasons, etc). There are alternative procedures such as subtotal thyroidectomy (STT), neartotal thyroidectomy (NTT) and total thyroidectomy (TT) in thyroid surgery [1], though the surgical procedure of choice is stilll under discussion [1-6]. STT is chosen for its lower postoperative complication rates and because hormone replacement treatment is not necessary after the procedure. However, the recurrence rate is high after STT, which causes reoperation morbidities. Most of the patients also need thyroxine replacement therapy while undergoing STT [1]. NTT is a preferred option for treatment because of the lower postoperative complication rates [2]. TT has also become a frequently practiced surgical procedured over the last years [7-11]. No remnant thyroid tissue is left in TT, but complication rates can be high if the surgeon is inexperienced [12, 13]. TT can be practiced with low complication rates if the thyroid tissue is dissected closely, the parathyroid

glands are visually identified and protected, the recurrent laryngeal nerve is identified and dissected, and the path of the recurrent nerve is traced and protected.

STT and NTT are preferred procedures because of the low surgical complication rates [2, 14, 15]. There are many clinical studies that compare the complication and recurrence rates resulting from NTT, STT and TT [1, 2, 5, 6]. In this study, we focused on whether the remnant thyroid tissue after STT and NTT had microscopic pathological findings. A study exists in which the histopathologic findings after bilateral subtotal thyroidectomy (BST) in the remnant tissue are analyzed [3]. NTT is also a preferred procedure in the surgical treatment of MNG, but no study exists which analyzes the histopathologic findings of the remnant tissue after NTT. In our study, the relation between the volume of the residual thyroid tissue (NTT and STT) and the pathologic findings were evaluated. The histopathologic findings of the residual thyroid tissue of the same patient after NTT and STT were compared. In addition, we examined the histopathologic findings of the side with the large nodule and the contralateral side of the thyroid gland. Therefore we were able to evaluate if the residual NTT tissue had pathologic findings after the procedure of total thyroidectomy on the dominant side and NTT on contralateral side (Dunhill procedure). Our study will be the first that covers this topic.

Materials and methods

Choosing patients and the chinical follow up procedure

Fifty patients who underwent total thyroidectomy for MNG between January 2010 and August 2011 in our clinic were included in the study. Patients who had not signed the informed consent form, who were diagnosed with thyroid cancer preoperatively, who had unilateral nodular goiter, who received radiation therapy to the neck, or had prior thyroid surgery were excluded from the study. Thyroid ultrasound and thyroid scintigraphy were administered to patients preoperatively. All of the patients underwent TT. The patients were followed for a year. Their preoperative and postoperative blood calcium levels were analyzed. Patients who had corrected blood calcium levels below 8 mg/dl were considered hypocalcemic. Patients who needed calcium and/or vitamin D replacement to maintain normal blood calcium levels after six months were considered to have permanent hypocalcemia. Injury of the recurrent laryngeal nerve up to six months was considered temporary while injury of the recurrent laryngeal nerve after six months was considered permanent.

Surgical technique and histopathologic examination procedure

All the operations were performed by two experienced surgeons. The thyroid gland was reached by Kocher incision. The superior thyroid artery and vein were individually dissected then ligated and cut in the superior pole level to prevent damage to the external branch of the superior laryngeal nerve. The connective tissue in the tracheoesophageal groove was dissected in order to indentify the inferior recurrent nerve. Then the nerve was identified and protected cranially to the cricothyroid junction and caudally to the mediastinum. At this step of the operation saline jet spray was used (saline jet spray cleans the surgical area and spreads the fibers of the connective tissue, leaving nerves and vessels for easier identification; if the nerve is branched, saline spray helps to identify each branch). Later the parathyroid glands were identified. All vessels were ligated close to the thyroid tissue to protect vascularity of the parathyroid glands. Poorly vascularized parathyroid glands were excised and implanted into the SCM muscle. Before the dissection of the thyroid tissue above the trachea, subtotal and neartotal margins (not to include macroscopic nodules) were marked in both right and left lobes with silk sutures. Bilateral total thyroidectomy including the piramidal lobe was completed. After the resection of the specimen, the tissue was excised from the subtotal margin marked during the surgery. The tissues were weighed using a precision scale and about two grams of tissue for each lobe were considered residual tissue for STT. Then the tissue marked with neartotal margin during the operation was separated from the excised subtotal residual tissue. These tissues were also weighed by the precision scale and about one gram tissue for each lobe was considered neartotal tissue. The tissues were fixed using mannitol buffered formolin. The parrafin blocks were cut in 4 μm sections and examined. The sections were stained with hematoxylin-eosin. The histopathologic findings of approximately two grams of tissue on each lobe were counted for the residual tissue examination after STT. The histopathologic

Table 1. Histopathological finding of the neartotal and subtotal residual tissue

	Residual neartotal tissue n=50	Residual subtotal tissue n=50	p
Nopathologic findings	22 (44%)	19 (38%)	
Micronodule	19 (67.9%)	21 (67.7%)	NS
Thyroiditis	7 (25%)	7 (22.6%)	NS
Thyroid cancer	2 (7.1%)	3 (9.7%)	NS

findings of approximately one gram of tissue on each lobe were counted for the residual tissue examination after NTT. The pathologic findings of the main tissue, the residual tissue after STT, and the residual tissue after NTT were evaluated and compared.

Statistical analysis

All data was written in average values (min-max). Statistical analysis was performed using McNemar test with $p<0.05$ considered statistically significant. SPSS 19 for Windows was used.

Results

The results of the postoperative follow-up

Fifty patients, 43 (86%) females and 7 (14%) males with an average age of 50.5 (23-77), were included in the study. Of these, 38 had MNG, 7 had MNG and thyroiditis, and 5 had toxic MNG prior to the operations. The mean preoperative calcium level was 9.35 (8.2-10.4). The mean operation duration was 102.9 (60-170) minutes. Seroma that did not require any surgical treatment developed in one (2%) patient postoperatively and one (2%) patient had temporary recurrent nerve injury. At the end of three months, the tone of the patient's voice returned to normal and the video laryngoscopic examination showed bilateral vocal cord movement. Two of the patients (4%) had temporary hypocalcemia that required calcium and vitamin D replacement. The blood calcium levels of one of these patients returned to normal two weeks after the surgery with tapered treatment while it took three months for the other patient. None of the patients had permanent recurrent nerve injury, or permanent hypocalcemia. There were no intraoperative complications or mortality.

Histopathologic findings

Histopathologic findings of the main tissue: MNG was detected in 38 of the patients (76%); MNG and thyroiditis were detected in 7 patients (14%); and incidental papillary thyroid cancer was detected in 5 patients (10%). Of the patients with incidental thyroid cancer, two had multicentric papillary thyroid microcarcinoma, two had papillary thyroid carcinoma, and one had multicentric papillary carcinoma.

Histopathologic findings of the residual subtotal tissues: Pathologic findings were present in 31 of the patients (62%) regardless of the side (right or left); 21 (67.7%) had micronodules, 7 (22.6%) had lymphocytic thyroiditis, and 3 (9.7%) had papillary thyroid carcinoma. The multicentric microcarcinoma observed in the main specimen of one of these patients was also present in the bilateral residual subtotal tissue. In one patient it was the extansion of the papillary thyroid carcinoma in the main specimen and the other patient had another separate papillary thyroid microcarcinoma focus (**Table 1**).

Histopathologic findings of the residual neartotal tissues: Pathologic findings were present in 28 of the patients (56%) regardless of the side (right or left). Micronodules were detected in 19 (67.9%), lymphocytic thyroiditis was detected in 7 (25%) and papillary microcarcinoma was detected in 2 (7.1%) (One of these patients had multicentric carcinoma in the main specimen and had foci of papillary thyroid microcarcinoma in bilateral neartotal residual tissue while the other had extansion of the papillary thyroid carcinoma in the main specimen) (**Table 1**).

No significant differences were found when the pathologic findings in the residual tissues after neartotal and subtotal thyroidectomy were compared (62% and 56% respectively, p=0.25).

When the right and left tissues were examined separately, no significant differences were detected in pathologic findings between the right and left residual neartotal tissue (p=0.25). Likewise, there were no differences between the right and left residual subtotal tissues (p>0.05).

According to pathology reports the large nodule was located on the right in 24 of the main spec-

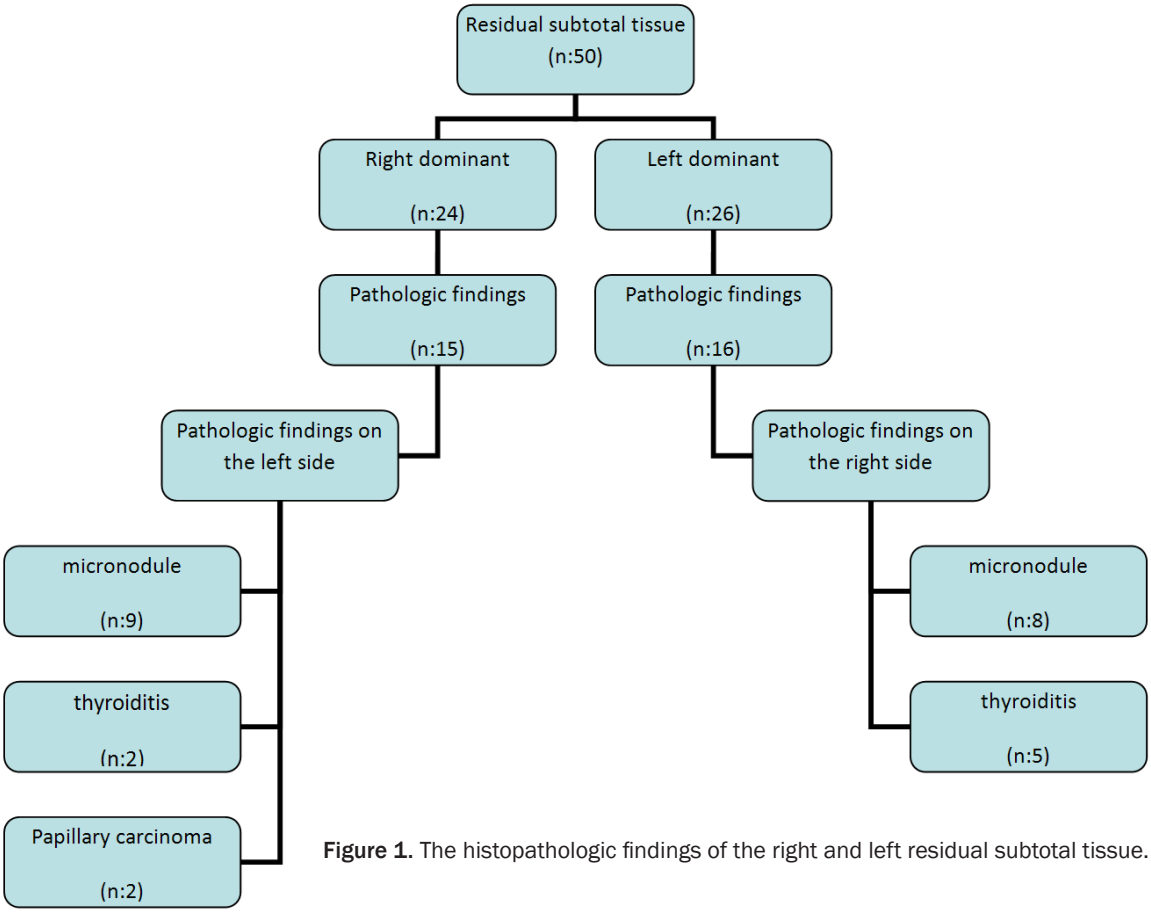

Figure 1. The histopathologic findings of the right and left residual subtotal tissue.

imens (48%) and on the left in 26 of the main specimens (52%).

In the 24 patients who had the large nodule located on the right, 15 (62.7%) had pathologic findings in residual subtotal tissue. Of these, 13 (86.7%) had pathologic findings in the left residual subtotal thyroid tissue: 9 (69.2%) of them were micronodules, 2 (15.4%) were thyroiditis, and 2 (15.4%) were papillary microcarcinoma (**Figure 1**).

In the 26 patients who had the large nodule located on the left, 16 (61.5%) had pathologic findings in residual subtotal tissue. Of these, 13 (81.2%) had pathologic findings in the right residual subtotal thyroid tissue: 8 (61.5%) of them were micronodules and 5 (38.5%) were thyroiditis (**Figure 1**).

In the 13 (54.2%) of the patients who had the large nodule located on the right had pathologic findings in residual neartotal tissue. Of these, 12 (92.3%) had pathologic findings in the left residual neartotal thyroid tissue: 8 (66.6%) of them were micronodules, 2 (16.7%) were thyroiditis and 2 (16.7%) were papillary microcarcinoma (**Figure 2**).

In the 15 (57.7%) of the patients who had the large nodule located on the left had pathologic findings in residual neartotal tissue. Of these, 12 (80%) had pathologic findings in the right residual neartotal thyroid tissue: 7 (58.3%) of them were micronodules and 5 (41.6%) were thyroiditis (**Figure 2**).

When the pathologic findings on the side of the large nodule and on the contralateral side were compared, no differences were detected in the residual neartotal and subtotal tissues (neartotal remnant in right dominancy $p>0.05$, left dominancy $p>0.05$; subtotal remnant in right dominancy $p>0.05$, left dominancy $p>0.05$).

In addition, there were no significant differences in pathologic findings between the residual left subtotal and neartotal thyroid tissues in the patients who had the large nodule located on the right ($p>0.05$), and no significant differenc-

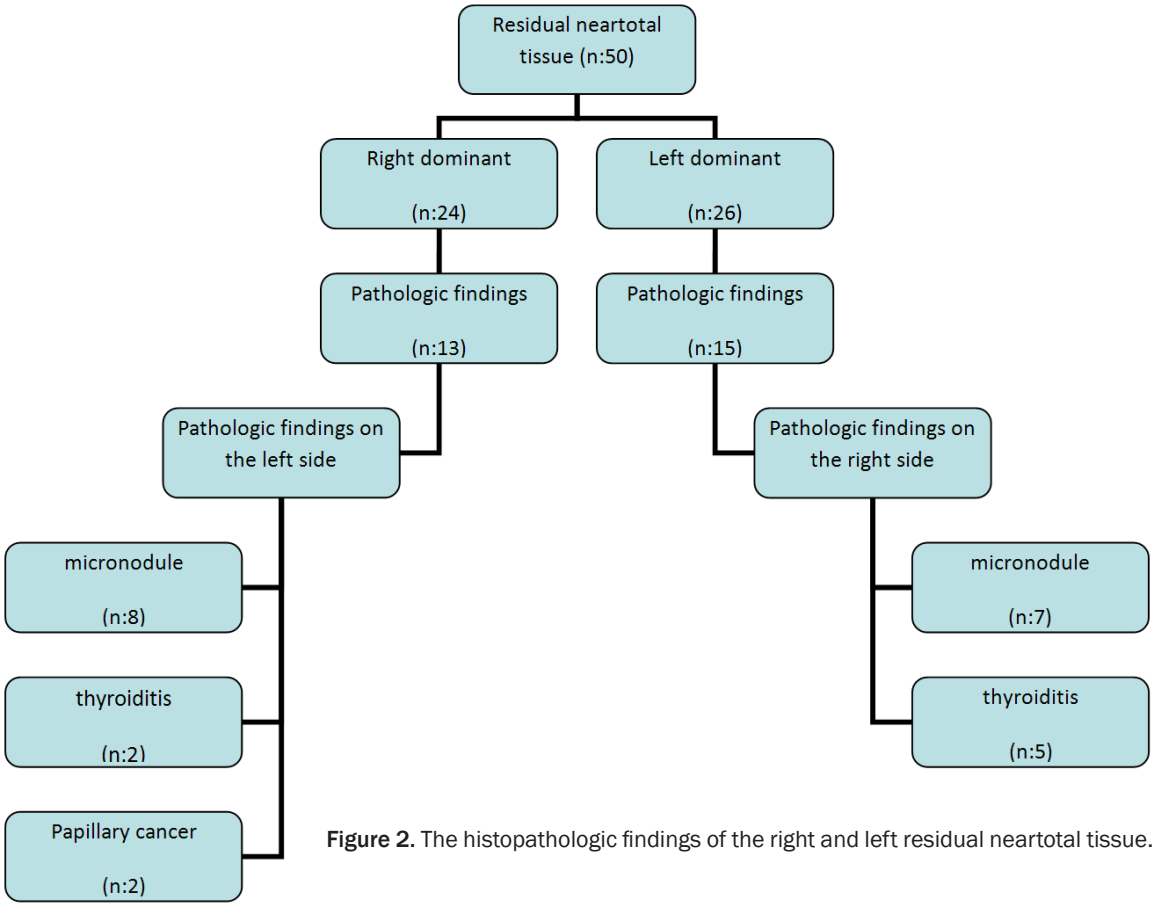

Figure 2. The histopathologic findings of the right and left residual neartotal tissue.

es were detected in pathologic findings between the right residual subtotal and neartotal thyroid tissues in the patients who had the large nodule located on the left ($p>0.05$).

Discussion

The treatment of choice for thyroid diseases is still under discussion. There are several treatment procedures such as STT, NTT and TT [5-15]. But the best choice for treatment is still unclear. Moreover, when STT and NTT procedures are performed, pathologic findings may stilll exist in the remaning tissue. This study sought to answer the question that 'what do we leave behind in a patient with MNG disease if we carried out NTT or STT instead of TT. Just the tissue or the disease?'.

We evaluated whether there is a difference in the histopathologic findings of the residual neartotal and subtotal tissues. Thus we evaluated if there is a correlation between the thyroid tissue volume and pathologic findings. Moreover, we examined the histopathologic findings of the side of the thyroid gland with the large nodule and the contralateral side of the thyroid gland. Thus we were able to evaluate if the residual NTT tissue had pathologic findings after Dunhill procedure. The results of our study showed that more than half of the residual tissue after both NTT and STT had pathologic findings; furthermore 7.1% of the pathologic findings in the neartotal residual tissue and 9.7% of the pathologic findings in the subtotal residual tissue were papillary thyroid carcinoma. The tissue contralateral to the dominant nodule revealed no differences in the neartotal and subtotal residual tissues. More than half of the residual thyroid tissue on the contralateral side of the dominant nodule had pathologic findings.

Subtotal and neartotal thyroidectomy are preferred in the surgical treatment of benign diseases of the thyroid gland because the complication rates are low and the need for hormone replacement therapy is also low, especially after STT. However, the recurrence incidence after these procedures is higher than TT; there-

fore, protection from hormone replacement therapy is highly unlikely [1, 16-19]. According to a study by Özbaş et al., the requirment of hormone replacement therapy after bilateral subtotal thyroidectomy is 100% [1].

There are many studies indicating that the recurrence incidences after NTT and STT are high [1, 4-6, 14, 19, 20]. Some authorities suggest that a 30-year follow-up is needed for actual reccurence rates [17, 18, 21, 22]. Furthermore, in one of the studies, STT recurrence incidence after 30 years is 42% [22]. Whether this is a real reccurence or is the result of the microscopic pathologic findings in the residual tissue is yet unknown. Although there were no macroscopic pathologic findings in 56% of the neartotal residual tissue and 62% (most of them were micronodules) of the subtotal residual tissue in our study, microscopic pathologic findings were discovered.

In the study by Tekin K. et al., micronodules in residual tissue after STT have a Ki-67 proliferation index higher than normal tissue, which may indicate a correlation between high levels of proliferation index of micronodule formation in remnant tissue after subtotal thyroidectomy and recurrence rates [3]. In our study, we determined that 67.9% of the pathologic findings in residual neartotal tissue and 67.7% of the pathologic findings in subtotal residual tissue were micronodules.

NTT is a preferred procedure for the treatment of benign thyroid diseases [2-14]. The reccurence rates after NTT have been reported as 4.7 [5]. Erbil Y. et al. compared the complications after NTT and TT. They reported that hypocalcemia and recurrent laryngeal nerve injury rates were lower after NTT. They suggested that NTT should be preferred for the tratment of benign MNG instead of subtotal or total thyroidectomy. Erbil Y. et al. tried to evaluate the pathologic findings in the remnant tissue using postoperative ultrasonography but they reported that the results were suboptimal due to postoperative edema and scar formation. Relapse rates could not be evaluated in this study [15]. In our study, TT was performed on all of the patients. Seroma that did not require any surgical treatment developed in one (2%) patient postoperatively. One (2%) patient had temporary recurrent laryngeal nerve injury, and two of the patients (4%) had temporary hypocalcemia. None of the patients had permanent recurrent laryngeal nerve injury, or permanent hypocalcemia. Histopathologic examination of the neartotal residual tissue showed various diesases occuring in 56% of cases; two of these cases had papillary thyroid microcarcinoma in neartotal residual tissue.

All our patients had bilateral MNG, so bilateral total thyroidectomy was performed. One study argued that lobectomy is the appropriate treatment in patients diagnosed with unilateral nodular goiter because of the low complication rate, but the recurrence rates of these patients were 11% [24]. Another study reported that unilateral multinodularity was a risk factor for recurrence [25]. In another study, the recurrence rate in patients who had lobectomy for unilateral nodular goiter was 60.6%, although the mean follow up duration was as short as 39.75 ± 21.75 months (5-87). Unilateral multinodularity, the histopathologic characteristic features of the lobectomy specimen and the volume of the thyroid gland were associated with high recurrence rate [20]. One might ask if the patients that were preoperatively diagnosed with unilateral nodular goiter in fact had radiologically undiagnosed micronodules on the contralateral lobe. In a study, 36% of patients diagnosed with solitary nodule preoperatively were reported to have multinodules after surgery [26]. However, more up-to-date studies are needed in this topic. Patients who had unilateral nodular goiter were excluded from our study; therefore this subject was not evaluated.

Sancho et al. compared patients with asymmetric MNG who had total lobectomy on the side with the dominant nodule and contralateral NTT or STT and found that the remnant tissue growth rate and the formation of new nodules in the ultrasonographic follow-up were higher in the STT group [14]. In our study, right and left neartotal and subtotal residual tissues were examined with no significant differences in the pathologic findings when the neartotal tissue was compared to itself and when it was compared to the subtotal tissue. Furthermore, multicentric papillary thyroid cancer was found in one of the patients and papillary thyroid microcarcinoma was present in the bilateral neartotal residual tissue. Thus, total lobectomy to the dominant side and contralateral NTT procedure for patients with benign MNG should also be discussed.

Papillary thyroid cancer is the most common type of thyroid cancer [27]. It is called papillary thyroid microcarcinoma if the nodule is below 10mm [3, 28, 29]. It is mostly diagnosed in patients who have undergone surgery for benign diseases of the thyroid gland [29, 30]. In a study, 71% of the papillary thyroid microcarcinomas were incidentally diagnosed in patients undergoing surgery for benign diseases [31]. Incidental papillary thyroid microcarcinoma rates are reported as 3.1% and 21% respectively in two other studies [32, 33]. In our study, five patients (10%) had incidental papillary thyroid cancer: two were papillary cancer and three were papillary thyroid microcarcinoma. The examination of the residual tissues revealed three (9.7%) papillary thyroid microcarcinoma foci in the subtotal tissue (one was located in the bilateral subtotal residual tissue) and two (7.1%) foci in the neartotal tissue (similarly, one was located in the bilateral neartotal residual tissue). In the study by Jen-Der Lin et al., recurrence and cancer mortality rates in patients with multicentric papillary thyroid microcarcinoma were higher than in patients with unifocal papillary microcarcinoma [28]. Two of the patients included in our study had multicentric papillary thyroid microcarcinoma and one of the patients had microcarcinoma foci in the histopathologic examination of the neartotal and subtotal residual tissue of each side of the gland.

As a result, TT, NTT and STT procedures were histopathologically evaluated in the same patient. Microscopic pathologic findings were present in both neartotal and subtotal residual tissues in more than half of the patients. Moreover, the neartotal and subtotal residual tissues contralateral to the large nodule also had high levels of pathologic findings. The presence of pathologic findings in a tissue may increase the probability of recurrence. Due to high rates of residual pathologic tissue remaining in STT and NTT specimens, it is better to preffer TT for benign thyroid diseases. But more studies to evaluate the correlation of micronodules with recurrence rates are needed.

Disclosure of conflict of interest

None.

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