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Outcomes of total thyroidectomy with vs. without extensive intended dissection of the thyroid embryological remnants single centre experience

El-Sayed Mahmoud Abd-Elwahab[1]✉, Hany Abdelfatah El-hady[2]

Aim: **This study aimed to assess the prevalence of TERs and the value of their dissection during total thyroidectomy in cases with benign multinodular goitre on the surgery outcomes compared to approaches not removing them.** ***Settings and Design:*** **One-hundred consented patients aging 22-60 year (mean 43 ± 10.1 year) were included in this prospective clinical study. It was conducted in the period between July 2011 to December 2014 at Al-Zahraa University Hospital, College of Medicine for Girls, Al-Azha University, Cairo, Egypt.** ***Methods and Material:*** **Patients were divided into two equal groups (50 patients each) to compare between total thyroidectomy with vs. without dissection of TERs for benign multinodular goitre. The study also assessed the type, prevalence and topographic distribution of TERs in the dissection group. Data analysis was carried out using SPSS Version-23 software for percent distribution and significance using Chi-Square Tests. Statistical significance was set at P <0.05.** ***Results:*** **The prevalence of a pyramidal lobe was 54%; ZT was identified in 36 patients (72%), where, 23 patients (46%) were bilateral, 7 patients (14%) located in the left lobe and 6 patients (12%) in located in right lobe. The thyroid rests were found in 17 out of fifty (34%); of them 9 patients (18%) were bilateral, 6 patients (12%) were in the left side and 2 patients (4%) were in the right side. Whereas 4 patients developed recurrence in the control group, no recurrences were observed in the TERs dissection group.** ***Conclusion:*** **Dissection of TERs during total thyroidectomy was associated with higher rate of complications, but it completely avoided the disease recurrence and the burden of reoperation. Complications may be decreased or prevented by expert hands.**

INTRODUCTION

Full knowledge of the anatomical details of the thyroid gland and its embryological and congenital variations is very essential for a safe thyroid surgery with excellent outcomes. Embryologically, the first endocrine gland to develop in the body is thyroid gland; approximately at 24th day of gestation. It originates at the foramen cecum of the tongue and descends to reach the adult position by the 7th week of gestation. Pyramidal lobe (and other remnants of thyroglossal duct), Zuckerkandl's tubercle (ZT) and thyrothymic remnant (thyroid rest) are three thyroid embryological remnants (TERs). All of them play a critical role in the outcomes of thyroidectomy (Figure 1), (Fernando, 2014).

The pyramidal lobe is defined as a thyroid tissue remnant of the thyroglossal tract. It locates to in the pretracheal area between the isthmus and the hyoid bone. If left behind or not completely removed during thyroidectomy, it may cause recurrent goitre (Gurleyik et al., 2015). There is different variation in the prevalence and shape of pyramidal lobe, namely typical lobe, band-like, nodular, and inverted Y. As a part of normal thyroid gland, the anatomical studies reported a prevalence of 15 - 75% for the pyramidal lobe. It commonly arises on the left-hand side with slightly male predominance (Braun et al., 2007).

ZT was firstly described in 1902 as the "processus posterior glandulaethyroidea". Unremoved tubercle may cause persistent or recurrent disease in cases of benign multinodular goiter (Agrawal et al., 2008; Page et al., 2009). Such recurrence may occur in the posterior part of ZT, which may lie behind the oesophagus or in tracheo-esophageal groove (Ruth S et al., 2013). It is formed of embryologic fusion of the lateral process of the fourth pharyngeal pouch and the median thyroid process at the level of the second bronchial arch. Its frequency in adult glands ranges from 60 to 90%. The cause of fusion of lateral process and median process is unknown (James et al., 2014). ZT is an arrow landmark pointing towards the recurrent laryngeal nerve (RLN) during thyroidectomy. It is a condensed thyroid tissue locating in the area of cricothyroid junction that separates between superior and inferior parathyroid glands (Irkorucu, 2016; Serpell, 2010). ZT has four grades, namely grade 0 = unrecognizable tubercle, grade I = only a thickening of the lateral edge, grade II = the tubercle is less than 1 cm, and, grade III = the tubercle is more than 1 cm in diameter (Figure 1), (Gravante et al., 2007). The relations of ZT to the entry of RLN are: A) It indicates the RLN entry or anterior branch, B) It covers RLN entry, and, C) It may locate above or below the entry point. The RLN passes beneath ZT in 91.9%, whereas, the nerve is found lateral in 7.7% of cases

[1]Department of Surgery, Faculty of Medicine for Girls, Al-Azhar University, Egypt; Email: Sayed_hemdana@yahoo.com; [2]Department of Surgery, Faculty of Medicine for Girls, Al-Azhar University, Egypt; Email: hany.elhady@yahoo.com

✉*Corresponding author:*

El-Sayed Mahmoud Abd-Elwahab, Professor, Department of Surgery, Faculty of Medicine for Girls, Al-Azhar University, Egypt; Email: Sayed_hemdana@yahoo.com; Mobile number: 00201001656920

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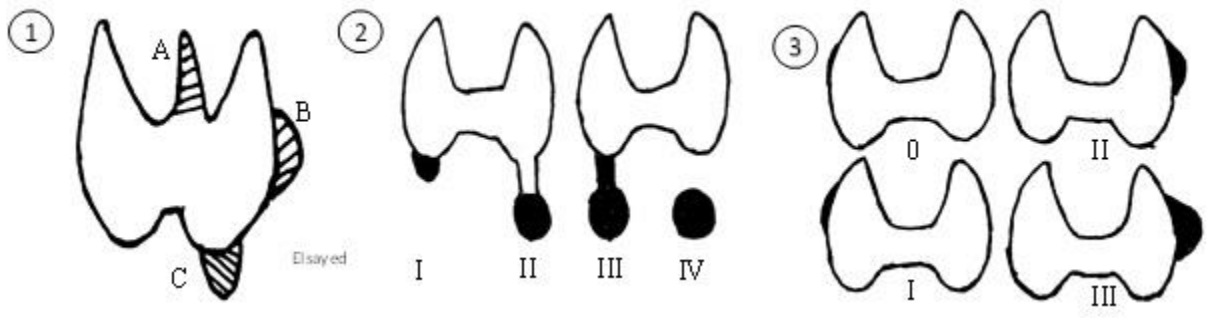

Figure 1 1) The thyroid embryologic remnants sites A) Pyramidal lobe, B) Tubercle of Zuckerkandl, C) Thyrothymic remnants 2) Grades of the thyroid rests. 3) Grades of the tubercle of Zuckerkandl.

(Mayilvaganan et al., 2015). Commonly the nerve runs in a tunnel deep behind the tubercle. Also, the nerve may lie in front when the tubercle is only a Grade-I thickening of the lateral edge of thyroid lobes, or a very small grade II lateral projection (Irkorucu, 2016).

Locating at the lower pole of the thyroid gland, thyroid rest is a small projection of normal thyroid tissue, which presents in the line of the thyrothymic ligament, as an extension of the normal embryologic thyroid descent. It has a frequency of >50% (Sackett et al., 2002). It has four grades in relation to the thyroid gland: 1) Grade I, thyroid rests is a projection of normal thyroid tissue at the inferior pole of the gland in the thyrothymic ligament area, easily differentiated from lower border of the gland, 2) Grade II, thyroid rests is a projection of normal thyroid tissue in the thyrothymic tract and attached to the lower pole by a narrow pedicle of thyroid tissue, 3) Grade III, thyroid rests are similar to grade II but are only attached to the lower pole of thyroid gland by a thin fibrovascular core, and, 4) Grade IV, thyroid rests is completely separated from the lower pole of thyroid gland (Figure 1) (Snook et al., 2007). Radical or aggressive resection during surgery for benign thyroid diseases is needed to avoid recurrence originating from these embryological remnants (Acun et al., 2004).

Moreover, a normal thyroid gland may be present or absent along with uncommon accessory thyroid glands (Braun et al., 2007). The cranial accessory thyroid glands usually present below the hyoid bone on the thyrohyoid membrane or below the thyroid cartilage (along the course of thyroglossal tract). Caudal accessory glands are present between the inferior margin of the thyroid and the aortic arch (along the course of thyrothymic tract). Lateral accessory thyroid glands arise from a developmental failure of fusion of lateral process of the fourth pharyngeal pouch and the median thyroid process in the lateral neck compartment (Paresi Jr & Shah, 2005). In practice, the accessory glands are another cause of recurrent goitre. Indeed, they are not routinely explored during primary total thyroidectomy (Ruth et al., 2013). This is why extra-capsular technique of thyroidectomy and exploration of embryological remnants have a better outcome after total thyroidectomy (Fernando, 2014).

SUBJECTS AND METHODS

This prospective clinical trial enrolled 100 consecutively admitted patients between July 2011 to December 2014, Al-Zahraa University Hospital, College of Medicine for Girls, Al-Azhar University, Cairo, Egypt. The patients aged 22 – 60 years (mean 43 ± 10.1 years); 85 females and 15 males. Patients signed an informed consent and the study was approved by the local Ethical Committee of the hospital. All patients were clinically euthyroid at operation time. These patients were segregated into two groups each for the two approaches of thyroidectomy randomly; unheeding to age, gender, gland size and retrosternal extension of the lesion avoiding selection bias. The total thyroidectomy was done by the same surgeons using the same technique. Patients with recurrent goitre, thyroiditis, previous neck surgery and initial thyroid cancer (diagnosed by fine-needle aspiration cytology; FNAC) were excluded from the study. All patients were prepared by the following investigations: CBC, blood glucose level, liver functions, kidney functions, electrolytes, coagulation profile, free T3, free T4, TSH, serum calcium concentration and vocal cords status was checked by indirect laryngoscopy. Neck ultrasonography, FNAC from suspicious or largest nodule, thoracic inlet X-ray were routinely done, and ECG was done for patients above forty.

Methods

Patients were divided into two groups (50 patients each) to compare between the outcomes of total thyroidectomy with dissection of TERs and total thyroidectomy without extensive dissection of them in patients with benign multinodular goitre (bilateral diseased gland), and to assess the nature and frequency of TERs in the former group. Surgery was done according to the standard procedure that used RLN as a landmark.

Surgical technique of total thyroidectomy with dissection of TERs

A curvilinear skin incision was performed in the lower neck 2 cm above the suprasternal notch. After creating superior and inferior flaps, the strap muscles were divided in the midline and separated from the thyroid gland. Thyroid dissection started on each thyroid lobe by mobilization, medial retraction, ligation and division of the middle thyroid vein. Visualization, dissection, ligation and division of superior thyroid vessels individually with preservation of external branch of superior laryngeal nerve were done.

Exploration of remnants of the lower end of the thyroglossal duct (pyramidal lobe) in the anterior cervical region between thyroid isthmus and the hyoid bone. ZT was explored through dissection of the cricothyroid space by medial retraction of thyroid lobe and lateral retraction of carotid sheath with preservation of superior parathyroid glands. The tubercle was palpated in posterolateral edge of thyroid lobe, to be differentiated from thyroid nodule which is usually firm or hard. The area of thyrothymic ligament was dissected for detection and removal of thyroid rest if present without damage of inferior parathyroid glands which may be located in this ligament (Figure 2). The inferior thyroid pole was mobilized and dissected to identify RLN and inferior

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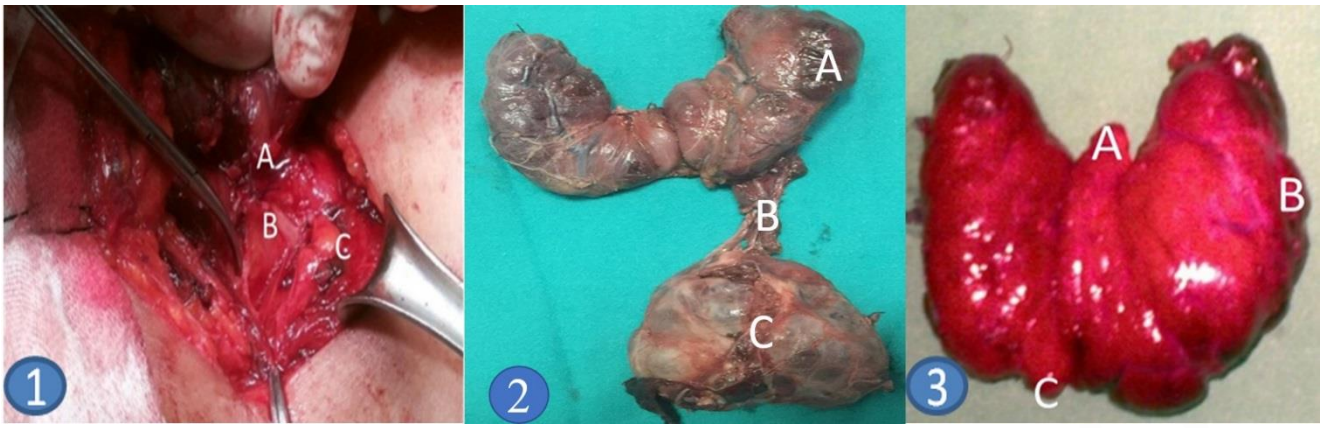

Figure 2 1) Dissected cricothyroid space; A) Left Zuckerkandl's tubercle, B) Entrance of the left recurrent laryngeal nerve (RLN), and, C) Left superior parathyroid. 2) Total thyroidectomy A) Left thyroid lobe B) Fibrovascular core connecting the thyroid to the thyroid rest.C)Left grade III thyroid rest 3) Totally removed thyroid gland with three embryologic thyroid remnants; A) Pyramidal lobe, B) Left grade II Zuckerkandl's tubercle, and, C) Right grade I thyroid rest.

parathyroid glands, and the branches of the inferior thyroid vessels were individually ligated. The thyroid gland was elevated and dissected from the pretracheal fascia and was totally removed (Figure 2).

Operative time (from skin incision to skin closure), type and frequency of TERs, prevalence of parathyroid glands and RLN injury (temporary or permanent) were recorded in each of the study cases. Patients were follow-up for 3 years to detect thyroid recurrence by clinical examination and thyroid ultrasound yearly. Thyroid scan was done only if there is recurrence by clinical examination or ultrasound. The location of the recurrence suggests the recurrence origin (e.g. If the recurrence was seen in the anatomical sites of the TERs it was suggested as the origin of recurrence)

Data analysis was carried out using SPSS Version-23 software for percent distribution and significance using Chi-Square Tests. Statistical significance was set at $P < 0.05$.

RESULTS

A Hundred patients aging 22 - 60 years (mean 43 ± 10.1 year) underwent successful total thyroidectomy; among which 85 were women and 15 were men. Thyroidectomy was either done with (50 patients) or without (50 patients) dissection of TERs to assess the frequency of the latter and to compare the surgical outcomes.

Total thyroidectomy with dissection of TERs revealed a prevalence rate for the pyramidal lobe of 54% (27 out of 50 patients); where 48% of them were to the left of midline and 6% of them were to the right of midline. ZT was identified in 36 patients (72%); where 23 patients (46%) had bilateral, 7 patients (14%) had it in the left lobe and 6 patients (12%) had it in the right lobe. Five patients were grade I, 20 were grade II and 11 were grade III. By dissection of thyro-thymic ligament area, the thyroid rests were found in 17 patients (34%); 10 patients had grade-I, 7 patients had grade-III, 9 patients (18%) of them had bilateral, 6 patients (12%) had one in left side and 2 patients (4%) had one in right side (Table 1).

There were combinations of the presence of the pyramidal lobe with ZT in 20 and with thyroid rest in 4 patients. Also, there were combinations of the presence of ZT with thyroid rest in 7 patients (Table 2).

In patients subjected for total thyroidectomy with dissection of TERs, no thyroid recurrences were detected but complications included temporary RLN palsy in 5 patients (10%), temporary hypoparathyroidism occurred in 8 patients (16%) and wound seroma developed in 4 patients (8%). No permanent RLN palsy occurred. Permanent hypoparathyroidism occurred in 1 patient (2%). Neither wound infection nor mortality was noted. In patients subjected for total thyroidectomy without dissection of TERs, the incidence of thyroid recurrence was 8% (4 out of 50 patients) two years after surgery diagnosed by neck ultrasonography and thyroid scan. The location of recurrence, as well as reoperation for recurrent cases, prove the origin of recurrence were originating from TERs. The recurrence was in the midline just above thyroid cartilage in one patient (2%; a missed pyramidal lobe), in left thyro-thymic area in two patients (4% missed thyroid rests), and, in missed right ZT in one patient (2%). Temporary RLN palsy was recorded in 2 patients (4%), whereas, temporary hypo-parathyroidism occurred in 4 patients (8%). Neither permanent RLN palsy nor permanent hypo-parathyroidism was observed. Wound seroma developed in 3 patients (6%), wound infection occurred in 2 cases (4%) and no mortalities (Table 3). Comparing the types and rate of complications among the two approached thyroidectomy (Table 3), there were non-significant differences except for disease recurrence that had a significantly higher rate in patients without the dissection of TERs ($P = 0.041$). Moreover, there was a significant difference in the operative time between the two approaches favouring thyroidectomy without the dissection of TERs as expected ($P = 0.001$). The operative time was prolonged in TERs dissection group; 110 - 150 vs. 100 - 120 minutes, respectively (Table 3).

DISCUSSION

The most of thyroid surgeons prefer total thyroidectomy for malignant or benign thyroid diseases. The completeness of the removal of thyroid gland and the proper follow-up have a significant effect on the outcomes of the surgical treatment, particularly malignant thyroid diseases. The anatomical features of the thyroid gland create some difficulties in the total removal of the thyroidal tissue, resulting in postoperative tissue remnants (Gurleyik et al., 2015). Such remnants have clinical importance, especially in the development of recurrent thyroid disease. The three embryological sites are the pyramidal lobe, thyroid rests in the thyrothymic tract, and ZT. Their escape may cause recurrence (or persistence) of nodular goitre in these embryological sites (Ruth et al., 2013).

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Table 1 Type and frequency of the embryological thyroid remnants (TERs) among 50 patients subjected to total thyroidectomy with extensive dissection of TERs. Data shown are n (%).

TERs	n (%)	Location and %	
Pyramidal lobe	27 (54%)	To left of midline	48%
		To right of midline	6%
Tubercle of Zuckerkandl	36 (72%)	Bilateral	46%
		In left lobe	14%
		In right lobe	12%
Thyroid rests	18 (36%)	Bilateral	20%
		In Left side	12%
		In right side	4%

Table 2 Topographic distribution of embryological thyroid remnants among 50 patients subjected to total thyroidectomy with extensive dissection of TERs. Data shown are n (%)

TERs	n (%)	Valid %
Pyramidal lobe alone	3 (6)	6.0
Tubercle of Zuckerkandl alone	9 (18)	18.0
Thyroid rests alone	6 (12)	12.0
Pyramidal lobe + Zuckerkandl's tubercle	20 (40)	40.0
Pyramidal lobe + thyroid rest	4 (8)	8.0
Zuckerkandl's tubercle + thyroid rest	7 (14)	14.0
Pyramidal lobe + ZT+ thyroid rest	1(2)	2.0
Total	50 (100)	100.0

Table 3 Types and prevalence of surgical complications and operative time comparing thyroidectomy with (TW) vs. without (TW_{out}) the dissection of embryological thyroid remnants. Data shown are n (%), range (Mean ± SDM) and p values. RLN = recurrent laryngeal nerve.

Groups / Complications	TW	TW_{out}	P value
	n (%)	n (%)	
Thyroid recurrence	0 (0)	4 (8)	0.041
Temporary RLN paralysis	5 (10)	2 (4)	0.240
Temporary hypoparathyroidism	8 (16)	4 (8)	0.218
Permanent hypoparathyroidism	1 (2)	0 (0)	0.315
Seroma	4 (8)	3 (3)	0.695
Wound infection	0 (0)	2 (4)	0.153
Operative Time	110 - 150 min (136.5 ± 9.8)	100 - 120 min (110.0 ± 6.2)	0.001

The pyramidal lobe base is located on the isthmus near the midline, commonly in the left side and, rarely in the right side, and has variable length; longer in females than in males. Because of the variations in the frequency, location and size of the pyramidal lobe, there is an increased risk of incomplete thyroidectomy. Accordingly, during thyroidectomy, the dissection should start from the isthmus and be advanced upward until the hyoid bone to remove the pyramidal lobe completely (Gurleyik et al., 2015). Recurrence in the pyramidal lobe usually appears as nodular midline mass and reoperation is very straightforward, requiring only local excision of the pyramidal tract (Ruth et al., 2013). Reviewing 300 thyroidectomies, Rajaratnam showed that in up to 50% of people, the lower part of thyroglossal duct fails to obliterate and persists as pyramidal lobe (Fernando, 2014). Anatomically, Braun et al, found that the prevalence of a pyramidal lobe is between 15-75% (Braun et al., 2007). In the current study, the frequency of the pyramidal lobe was 54% (27 out of 50 patients), which is lower than that found by Braun et al., Tanriover et al., Ozgur et al. and Zivic et al. who reported frequencies of 55.2%, 57.8%, 65% and 61%, respectively (Acun et al., 2004; Braun et al., 2007; Ozgur et al., 2011; Tanriover et al., 2011; Zivic et al., 2011).

Ogawa et al., found that pyramidal lobe was located on the left-side of the midline in 40.7% of cases and located on the right-side position in 31.2% of cases. A minimally invasive follicular carcinoma arising from the apex of the pyramidal lobe was reported (Ogawa et al., 2009). In our study, the pyramidal lobe was located on the left side of midline in 48% of cases and on the right side of midline in 6% of cases. The important of ZT lies in the fact that enlargement and nodule change inside it may be positioned retro-oesophageal and is not tackled at initial surgery, where the posterior component is left behind leading to posterior persistence or recurrence of disease (Ruth et al., 2013). In our study, ZT was found in 72% of patients, regardless of its grade. This incidence was higher than Mehmood et al. report at 61.90%; 19 patients had Grade-I, 22 patients had grade-II and 11 patients had grade-III (Mehmood et al., 2015). We found that ZT was bilateral in 23 patients (46%), in the left lobe in 7 patients (14%) and in the right lobe in 6 patients (12%). Five patients were grade I, 20 were grade II and 11 were grade III. Emin and Gunay encountered prominent ZT in 53 out of 87 patients (61%) locating to the right lobe, 28 of 73 patients (38%) locating to the left lobes, and bilaterally in 15 out of 60 total thyroidectomy patients (25%) (Gurleyik & Gurleyik, 2012). But Mehanna et al. found ZT on

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the right side in 72.6% of 93 cases and on the left side in 53.9% of 69 cases (Mehanna et al., 2014). 20 - 30% of thyrothymic rests are grade III/IV and may be easily missed at the initial surgery if the thyrothymic ligament is not dissected out. A small thyroid nodule in this location may continue to grow postoperatively causing recurrence after total thyroidectomy (Snook et al., 2007).

In our patients, thyrothymic rests were found in 17 patients (34%) and located bilateral in 18%, in the left side in 12% and in the right side in 4% of them. Ten patients had Grade-I, 7 patients had grade-III. Reportedly, thyroid rests located bilaterally in 30 (57%), on the right side in 16 (30%), and on the left in 7 (13%) of patients, where, 80% of them were grades I – III, and the remaining 20% were grade IV. Most of these rests were small in size; with 88% being <1 cm in diameter (Sackett et al., 2002). In a study done by Sheahan and O'Duffy, the thyrothymic extension was present in 138 out of 414 thyroid lobes (33.3%), where, 57% were bilateral and remaining were divided equally on the two sides. In 5 patients, there was significant nodular enlargement of the thyrothymic rest. The inferior parathyroid gland was closely associated with 8% of thyrothymic extensions (Sheahan & O'duffy, 2016). In the current study, upon dissection of thyro-thymic ligament area, the thyrothymic extension was found in 17 out of fifty patients (34%), where, 9 of them (18%) were bilateral, 6 (12%) were on the left side and 2 (4%) were on the right side. We recommend routine dissection of the thyrothymic ligament near to the inferior pole for removal of all thyroid tissue at the initial operation. The thyroid rest recurrence is usually present with a lower neck swelling.

In this study, dissection of TERs was associated with slightly higher complications than without dissection, but no thyroid recurrence was detected. These complications included temporary RLN palsy in 5 patients (10%), whereas temporary hypoparathyroidism occurred in 8 patients (16%), permanent hypoparathyroidism occurred in 1 patient (2%) and wound seroma developed in 4 patients (8%). However, the incidence of thyroid recurrence was 8% (4 out of 50 patients) in TERs sites, when not dissected. Such recurrence was a missed pyramidal lobe in one patient (2%), was in the left thyrothymic area (missed thyroid rests) in two patients (4%), and, was missed right tubercles of ZT in one patient (2%).

One of the limitations of our study is the short follow up time. Further studies are considered to evaluate the long-term results.

CONCLUSION

Dissection of TERs during total thyroidectomy is risky because of the very close relations with the parathyroid glands and RLN. Injury of parathyroid glands and RLN are commonly at ZT and thyrothymic remnant (thyroid rest). However, no thyroid recurrence after complete removal of TERs. We recommend exploration of TERs sites during total thyroidectomy to avoid reoperation which is riskier than the initial dissection of TERs. However, this procedure must be done by an expert surgeon.

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Article Keywords

Total thyroidectomy, Goitre, Thyroid embryological remnants, Pyramidal lobe, Tubercle of Zuckerkandl, Thyroid rests, Recurrence after thyroidectomy.

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Authors' contribution details

	Contributor 1	Contributor 2
Concepts	√	√
Design	√	√
Definition of intellectual content	√	√
Literature search	√	√
Clinical studies	√	√
Experimental studies	√	√
Data acquisition	√	√
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