Thyroid Tubercle of Zuckerkandl Is More Consistently Present and Larger on the Right: A Prospective Series

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Key Words

Thyroid · Thyroidectomy · Tubercle of Zuckerkandl · Symptoms

Abstract

Objective: The tubercle of Zuckerkandl (TZ) is a lateral projection from the thyroid lobe in the vicinity of the extralaryngeal termination of the recurrent laryngeal nerve (RLN), which is a very useful landmark for identification of the RLN during thyroidectomy. The purpose of the present study was to test our hypothesis that the TZ is more consistently found and is larger on the right than on the left side, and to investigate the frequency of anatomic variations of the TZ. **Study Design:** Prospective cohort study of 156 consecutive patients undergoing primary total thyroidectomy at an academic teaching hospital. Thyroidectomy was performed using a capsular dissection technique, with identification of the RLN only at its entry point into the larynx, using the TZ as a landmark. In vivo recording of size of right and left TZ was performed. The size of the right and left TZ was compared. **Results:** Identification of the TZ was 72.6% right side and 53.9% left side ($p = 0.003$). The mean size of the TZ, when present, was 11.2 mm on the right and 7.5 mm on the left ($p = 0.0002$). In matched-pair analysis, the right TZ was significantly larger than the left TZ ($p < 1 \times 10^{-7}$). The TZ overlay the RLN in nearly all cases; however, there were 2 cases (0.8%) of

a TZ extending medial to the RLN. In 12 cases (4.7%), the TZ appeared as a bilobed structure. **Conclusion:** The right TZ is consistently larger and more often identified than the left.

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Introduction

The thyroid tubercle of Zuckerkandl (TZ) (fig. 1, 2) is an important landmark in thyroid surgery, which was first described by the Viennese anatomist, Emil Zuckerkandl, in 1902 [1]. This structure is usually present as a lateral projection from the lateral thyroid lobe in the vicinity of the extralaryngeal termination of the recurrent laryngeal nerve (RLN). This landmark has been frequently overlooked in surgical textbooks. We have previously reported the TZ to be present in the majority of thyroid lobes, and to be an important landmark for identification of the RLN [2].

In addition to serving as a useful landmark for the RLN, awareness of the TZ is important to ensure complete removal of all thyroid tissue during total thyroidectomy, as failure to remove the entire TZ may be a source of persistent radioiodine uptake in thyroid cancer cases, or even of recurrent thyroid mass in cases of multinodular goiter, as may be seen after subtotal thyroidectomy [3].

Fig. 1. Anatomico-topographical diagram of TZ.

Fig. 2. Total thyroidectomy specimen. Right TZ present. No significant left TZ.

An enlarged TZ has also been suggested to be a cause of local symptoms [4].

In our experience of utilizing the TZ as a landmark during thyroid surgery, it has been our impression that the TZ on the right side is more consistently present, and usually larger, than its counterpart on the left [2]. However, this observation has not been previously investigated. The primary objective of the present study was thus to test our hypothesis that the TZ is more consistently present, and is larger, on the right than on the left side. Our secondary objective was to investigate whether enlargement of the TZ was a significant cause of local symptoms.

Methods

This was a prospective study of 156 consecutive total thyroidectomies performed by a single surgeon (P.S.) between April 2009 and August 2012. The inclusion criteria were all cases of primary total thyroidectomy, with or without central neck dissection. Revision surgical cases were excluded.

Thyroidectomy was performed by a standard approach. After making the neck incision, the straps are separated in the midline, and retracted laterally. The sternothyroid muscle is divided in the upper third bilaterally using a harmonic scalpel. Capsular dissection is undertaken, with ligation of the vessels on the capsule. Identified parathyroid glands are reflected laterally, with preservation of their blood supply. On retraction of the thyroid lobe medially, the TZ, if present, is identified. The TZ is mobilized by dividing vascular and fibrous tissue at its apex (laterally) and along the superior and inferior borders. The TZ is then reflected medially, usually revealing the RLN and Berry's ligament.

All patients underwent laryngoscopy the day following surgery, or at a return clinic appointment within 2 weeks of surgery. None

of the patients received prophylactic calcium and/or vitamin D replacement. Calcium levels were measured at 6 a.m. and 4 p.m. the day following surgery, and at 6 a.m. on the second postoperative day. Symptoms of hypocalcaemia were recorded prospectively. Biochemical hypocalcaemia was considered to be present in any patient with a single calcium level of <2.0 mmol/l. Symptomatic hypocalcaemia was considered to be present in any patient with any symptoms of paraesthesia, numbness, or muscle cramps in the postoperative period.

The presence of the TZ was recorded intraoperatively and its size measured *in vivo* using a ruler. The TZ was considered to be present only when an unequivocal projection was present. The structure of the TZ and relationship with the recurrent laryngeal nerve were also recorded, as were any anatomic variants of the TZ.

The size of the TZ was graded according to the classification proposed by Pelizzo et al. [5]. However, unlike them, we did not consider a mere thickening of the lateral thyroid border to constitute a TZ. Thus, grade 0 (no tubercle) and grade 1 (thickening) were combined in our series. Grade 2 was the presence of a TZ smaller than 1 cm, and grade 3 the presence of a TZ greater than 1 cm.

In some cases, due to extremely friable planes, the presence of invasive tumour, or the presence of enlarged lymph nodes, it was not possible to accurately define and/or measure the TZ. These cases were recorded in our prospective database as 'not assessable'. Cases with either or both TZ recorded as not assessable were excluded from the present analysis.

The average size of the right TZ was established and compared to the average size of the left TZ.

In order to investigate whether the presence of a grade 3 TZ had any correlation with patient age, weight of the thyroid gland, or presence of compressive or swallowing symptoms preoperatively, we divided patients into 3 groups: those with bilateral grade 3 TZ, those with unilateral grade 3 TZ, and those with no grade 3 TZ. The mean size of TZ was also compared between patients with and without local symptoms.

Statistical analysis was performed using Prism 6 (GraphPad software). A Student's *t* test was used to test for significant differ-

Table 1. Comparison of the frequency of TZ and size on right versus left side

	Right side	Left side	p value
Present	93	69	0.003
Grade 0/1 (absent)	35	59	0.003
Grade 2	43	50	0.44
Grade 3	50	19	0.0001
Mean size of TZ when present, mm (range)	11.2 (1–40)	7.5 (2–25)	0.0002
Bilobed	9	3	0.14
TZ behind RLN	1	1	1.0

ences in TZ size between left and right sides. An independent t test was used when only cases with TZ present were included. A dependent t test was used to perform a matched-pair analysis to compare the TZ sizes between left and right in the entire cohort with all cases included, in which case an absent TZ was given a zero value. A Fisher's exact test was used on 2×2 contingency tables. A Wilcoxon ranked-pairs test was used to analyze the likelihood of the right TZ being larger than the left. Comparisons between 3 groups were performed using one-way ANOVA.

Permission to perform the study was obtained from the Cork Clinical Research Ethics Committee.

Results

During the period of the study, 156 total thyroidectomies were performed. In 28 cases, the TZ on one or other side was considered not assessable or its size was otherwise not recorded. These cases were excluded. Thus, the final study cohort consisted of 128 thyroidectomies, where both right and left TZ were documented and measured at the time of surgery.

Indications for surgery were: preoperative cancer diagnosis (19 cases); Thy-3 cytology (33 cases); Graves' disease (18 cases); amiodarone-induced hyperthyroidism (2 cases); goitre with compressive symptoms (21 cases); large size of dominant nodule (18 cases); repeated inadequate cytology (Thy-1) (7 cases); goitre with major retrosternal extension without compressive symptoms (6 cases); visible nodule and patient desire for surgery (3 cases), and as part of surgery for hyperparathyroidism (1 case). 20 patients underwent concomitant central neck dissection (including 7 patients with indeterminate preoperative cytology and intraoperative findings of enlarged central neck nodes). Final histology confirmed 40 cases of carcinoma (32 significant carcinomas, 8 incidental microcarcinomas).

Table 2. Age, weight and frequency of compressive or other symptoms in patients with bilateral grade 3 TZ, unilateral grade 3 TZ, and no grade 3 TZ

	Bilateral grade 3 TZ (n = 11)	One grade 3 TZ (n = 47)	No grade 3 TZ (n = 70)	p value
Mean age, years	52.3	52.1	48.9	0.51
Mean weight, g	55.1	65.0	53.5	0.56
Symptoms, n	2 (18.2%)	7 (14.9%)	14 (20%)	0.77

A TZ was present on the right side in 93 cases (72.6%), and on the left side in 69 cases (53.9%) (table 1). A TZ was significantly more likely to be present on the right than left side ($p = 0.003$). The overall mean size of the TZ (when all 128 cases are included) was 8.1 mm on the right side, and 4.0 mm on the left side. When only cases in which a TZ was present were included, the mean size of the TZ was 11.2 mm on the right side, and 7.5 mm on the left side ($p = 0.0002$) (fig. 1).

The right TZ was larger than the left TZ in 79 cases, smaller in 18 cases, and the same size in 31 cases. The TZ was significantly more likely to be larger on the right than the left ($p < 1 \times 10^{-6}$). Matched-pair analysis demonstrated that the size of the right TZ was significantly larger than that on the left ($p < 1 \times 10^{-6}$).

In the vast majority of cases, the TZ consisted of a unilobular structure, lying lateral to the termination of the RLN. A bilobed TZ was identified in 12 cases (4.7%). In 2 cases (0.8%), the TZ extended medial to the RLN. There was no significant difference in incidence of bilobed or retroneural TZ between left and right sides ($p = 0.14$ and $p = 1.0$, respectively).

Table 2 shows the age, incidence of compressive symptoms, and weight of the thyroid gland in patients with bilateral grade 3 TZ, unilateral grade 3 TZ, and no grade 3 TZ. There was no evidence of a correlation between the presence of an enlarged TZ and any of these variables.

Twenty-three of the 128 patients had compressive or swallowing symptoms preoperatively. The mean weight of the resected thyroid lobe was 98.2 g in those with symptoms, and 50.4 g in those without ($p = 0.0002$). Only 2 of the symptomatic patients had bilateral grade 3 TZ (8.7%), which was almost identical to the proportion of asymptomatic patients with bilateral grade 3 TZ (9/105, 8.6%; $p = 1.0$). There was no significant difference in the mean size of either the right (7.5 vs. 8.3 mm, $p = 0.69$) or left (4.0

vs. 4.0, $p = 0.98$) TZ in patients with and without preoperative compressive symptoms.

The integrity of both RLNs was confirmed intraoperatively in all cases. Postoperative laryngoscopy revealed reduced or absent vocal mobility in 10 cases. Nine (90%) of these had full restitution of vocal mobility within 3 months. One case had still not recovered within 6 months. Thus, the rate of transient vocal cord paresis was 3.5% of RLNs at risk, and 0.4% of permanent vocal cord paralysis.

The incidence of postoperative biochemical hypocalcaemia was 28.1%, and of symptomatic hypocalcaemia, 12.5%.

Discussion

The TZ arises embryologically from the ultimobranchial body of the 4th branchial cleft. During organogenesis, the thyroid descends along the thyroglossal tract from the foramen caecum to the level of the thyroid cartilage, at which stage the right and left lobes develop. Additionally, there is a lateral component which arises from the ultimobranchial body which fuses with the median component at approximately the 5th week of gestation to complete the formation of the thyroid gland [6, 7]. The remnants of the ultimobranchial body, when present, persist as the TZ.

The primary objective of the present study was to test our hypothesis that the right TZ is more consistently present, and larger, than its counterpart on the left. In order to investigate this, we included only cases of total thyroidectomy, to facilitate a matched-pair analysis of the right versus left TZ. Although previous series have reported a larger number of right than left TZ, these studies have included large proportions of cases undergoing thyroid lobectomy alone [2, 5, 6, 8]. The present study includes only cases of total thyroidectomy with comparison of the left and right sides on a matched-pair basis. As such, our study is, to our knowledge, this first to conclusively demonstrate the predominance of the right TZ.

The TZ is a very useful landmark for identification of the RLN, as it is nearly always lateral to the nerve, based on its embryological development. Thus, identification and elevation of the TZ allows for safe identification of the RLN in the vicinity of Berry's ligament. This relationship has facilitated our preferred technique of RLN identification only at its extralaryngeal termination, in the vicinity of Berry's ligament. In the past, it was the usual practice of most surgeons to identify the RLN low in the tracheo-oesophageal groove early during the course of

thyroidectomy. This technique allowed for safe early identification of the RLN; however, it obliges the surgeon to extensively follow the RLN along its cervical course, which may increase the risk of compromising blood supply to the parathyroid glands. This is obviated by identifying the nerve only at its termination, around Berry's ligament. However, the nerve can be difficult to find in this location, and may be confused with terminal branches of the inferior thyroid artery. In this scenario, we have found the TZ to be very useful in aiding TLN identification, as the nerve is nearly always just medial, and readily apparent once the TZ is freed and reflected medially [2].

Utilizing the TZ as a landmark for the recurrent laryngeal nerve, we encountered an incidence of transient vocal paresis of 3.5%, and of permanent vocal paralysis, 0.4%. These figures compare favourably to published rates of transient (3.3–10.9%) and permanent (0–2%) vocal palsy after thyroidectomy [9–11].

The published incidence of post-thyroidectomy hypocalcaemia is highly variable and dependent to a large degree on the definition of hypocalcaemia used; whether or not patients are placed on prophylactic calcium; and type of surgeries included (total versus subtotal or other less-than-total thyroidectomy operations, and inclusion or not of cases with central neck dissection). Among series using inclusion criteria and definitions of hypocalcaemia similar to ours, published rates of biochemical hypocalcaemia range from 21 to 50% [12–16]. Our 28.1% incidence of biochemical hypocalcaemia also compares favourably with these series.

Rarely, the RLN can be found superficial to the TZ, placing it at increased risk of injury during surgery. In our series, this was found in 0.8% of cases. Some authors have reported the RLN to be lateral to the TZ in 6–7% of cases [6, 17]. However, Hisham and Lukman's [17] series included reoperative cases, which were also found to be significantly more likely to be associated with the finding of a RLN lateral to the TZ, while Gauger et al. [6] stated that in patients operated on by before and after their published series, the incidence of RLN lateral to the TZ appeared much lower. In our experience, the presence of TZ medial to the RLN in primary thyroidectomy is rare, and, in such cases, is probably due to nodular enlargement of thyroid tissue in close proximity to the RLN medial to the nerve, and, as such, may not represent a 'true' TZ.

In 12 cases (4.7%), we noted a bilobed TZ. A similar incidence was also noted by Gil-Carcedo Sanudo et al. [8] (5.8%). There is no embryological basis which would underlie the development of a bilobular TZ. Thus we feel

that this finding is also most likely due to nodular change in the TZ.

An enlarged TZ has been reported to be a source of local symptoms for the patient and/or recurrence. Hisham et al. [4] performed a small prospective study of patients who underwent total thyroidectomy for pressure symptoms. In those with grade 3 tubercles, over a third had small goitres <100 g, and 1 patient had a gland weighing only 21 g, leading them to conclude that an enlarged TZ may be the cause of pressure symptoms. We did not find any conclusive correlation between the presence of grade 3 TZ and local symptoms, although this does not exclude the possibility that an enlarged TZ in some selected cases may cause tracheal and/or oesophageal compression and local symptoms.

Conclusion

The TZ is an important landmark in thyroid surgery. The surgeon should be aware that it is more consistently found, and usually larger, on the right side than on the left side. Anatomic variations of the TZ may arise due to nodular change within TZ tissue. We did not find any conclusive evidence of an association between TZ size and presence of local symptoms.

Disclosure Statement

None of the authors have any conflicts of interest to declare.

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