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The shape of the thyroid influences the surgical anatomy of the external branch of the superior laryngeal nerve in the treatment of thyroid carcinoma

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Research Article

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Abstract

Background

Patients with a Cernea type 2b external branch of the superior laryngeal nerve (EBSLN) have the highest risk of EBSLN injury during thyroidectomy. Therefore, evaluating the probability of the Cernea type 2 anatomical variant preoperatively is beneficial to avoid EBSLN injury. In this study, we aimed to assess the effect of gland shape on the relationship of the EBSLN to the superior pole of the thyroid considering the Cernea classification.

Methods

A retrospective descriptive study of 154 patients (89 unilateral lobectomy and 65 bilateral total thyroidectomy) with 219 neck sides was conducted. The EBSLN was meticulously visualized and functionally identified during dissection of the thyroid upper pole and categorized according to the Cernea classification. The relative upper distance (RUD) and the ratio of the thyroid length to the relative upper distance (TL/RUD) were used to describe the shape of the thyroid lobes. Factors influencing the surgical anatomy of the EBSLN, described by the Cernea classification, and the factors influencing the presence of a type 2b EBSLN were evaluated.

Results

Out of the 219 sides, the EBSLN was identified in 211, and the nerve identification rate was 96.35%. Among the 211 EBSLNs identified, 20 (9.478%) were type 1, 87 (41.23%) were type 2A, and 104 (49.29%) were type 2B. The mean RUD of resected thyroid lobes was 24.75 ± 2.05 mm (range 21–29), 25.99 ± 2.01 (range 20–31) and 27.88 ± 2.04 mm (range 21–35) in types 1, 2a and 2b, respectively. The comparison between the three groups was statistically significant ($p < 0.001$). The neck length/thyroid length (NL/TL) and TL/RUD also showed statistically significant changes in the Cernea classification. In multinomial logistic regression analysis, RUD was the only independent factor associated with the Cernea type 2b nerve course.

Conclusion

The shape of the thyroid lobe described by the RUD and TL/RUD can influence the relative localization of the EBSLN and the degree of Cernea classification. A longer RUD increased the likelihood of a type 2b EBSLN, which is at highest risk during thyroidectomy.

Introduction

In thyroid surgery, the external branch of the superior laryngeal nerve (EBSLN) is an important anatomical structure that provides the motor innervations to the cricothyroid muscle (CTM), which acts to elongate and thin the true vocal folds during phonation, contributing to the production of high pitch sounds [1, 2]. Nerve-muscle unit dysfunction due to EBSLN injury can result in vocal fatigue, weak voice and deterioration in high pitch phonation, and these detrimental voice changes may negatively impact patient quality of life, especially in professional voice users [3, 4]. The reported incidence of EBSLN injury is up to 58% [5, 6].

For the purpose of identification and protection, several classifications of the EBSLN relative to anatomical landmarks have been proposed [7, 8, 9, 10]. The most generally accepted is the Cernea classification, which describes the position of the nerve relative to the upper pole of the thyroid and the superior thyroid artery (STA) [7].

Due to their low-lying course, type 2b nerves are considered to be at highest risk of iatrogenic injury during dissection of the upper thyroid poles [11, 12]. Although there are several articles showing the incidence of the different types of EBSLN [13], few studies have focused on the factors influencing the classification. In some studies, the relationship between gland volume or weight and EBSLN type has been investigated [14, 15]. However, in clinical practise, during thyroid surgery, most patients with papillary thyroid cancer (PTC) have normal-sized glands.

In the present study, we expect to measure the parameters of the thyroid that describe the shape of the lobe, which influences the anatomical positional relationship between the EBSLN and the superior pole of the thyroid.

Methods

A retrospective descriptive study was conducted in our department between January of 2022 and June of 2022. Patients who underwent total thyroidectomy or unilateral lobectomy were assessed for eligibility for recruitment to the study, and patients with previous neck surgery or neck irradiation history were excluded. This study was performed according to the Declaration of Helsinki and approved by the ethics committee of Harbin Medical University cancer hospital (No. JJQN2023-07). Written informed consent was obtained from all patients.

All patients underwent open thyroidectomy under general anaesthesia by the same surgical team. The EBSLN was visually identified in the sternothyroid–laryngeal triangle using the insertion of the sternothyroid muscle onto the oblique line of the thyroid cartilage as a landmark [16]. The nerve was confirmed with a nerve stimulator, and contraction of the CTM under electrostimulation of 1 mA represented the functional integrity of the EBSLN during the operation.

If the nerve was not clearly visualized, the nerve tract on the constrictor muscle was indirectly stimulated to create and observe the physiological response of the CTM. After identification, the exposed nerve was

followed downstream until it entered into the inferior constrictor or cricothyroid muscle at the nerve entry point (NEP) and traced upstream until it crossed over the STA.

After proper exposure of the EBSLN, it was categorized according to the classification system proposed by Cernea [7] as follows: a type 1 nerve passes more than 1 cm above the superior thyroid pole, type 2a nerve crosses less than 1 cm from the superior pole, and a type 2b nerve crosses at or below the superior pole.

Each thyroid lobe and corresponding EBSLN were considered a single, independent unit. Clinical factors, such as age, sex, tumour site and size, presence of malignancy, and thyroiditis, were recorded. Other parameters measured using preoperative ultrasound, enhanced CT and intraoperative measurement included the following: 1) neck length (NL), which was measured between the tip of the mastoid bone and the upper edge of the sternoclavicular joint with the neck in hyperextension; 2) length of the thyroid lobe (TL), which was the distance between the upper and lower edge of the thyroid lobe; 3) relative upper distance (RUD), which was the distance between the upper edge of the lobe and the upper edge of the isthmus; 4) thyroid lobe volume, which was determined by using the formula: (length x width x depth) x 0.479 (standard WHO correction) = cm^3 (cc) [17,18]. We further calculated the ratios of NL/TL and TL/RUD. The effects of these data were evaluated concerning the distribution of Cernea classification, and we also evaluated the factors influencing the presence of a type 2b EBSLN using logistic regression analysis.

Continuous variables were described using the means ± the standard deviations, and categorical variables were described using sample size (percentage). The Kruskal–Wallis rank test was used to compare continuous variables with abnormal distributions among the three groups. The chi-square test was used for the distribution among three groups of categorical variables. Multivariate analysis was performed by multivariate logistic regression. A P value < 0.05 was considered statistically significant. The data were analysed with SPSS 22.0 statistical software (SPSS Inc., Chicago, IL, USA).

Results

In the present study, a total of 154 patients were recruited: 119 were female, and 35 were male. Their mean age was 46.43±9.435 years (range 20-71). Eighty-nine patients underwent unilateral thyroid lobectomy, while 65 underwent bilateral total thyroidectomy, resulting in 219 lobectomies. The general distribution of the patients is given in Table 1.

For all 219 sides, the EBSLN was identified in 211, and the nerve identification rate was 96.35%. Among the 211 EBSLNs identified, 20 (9.478%) were type 1, 87 (41.23%) were type 2A, and 104 (49.29%) were type 2B, as per the Cernea classification (as shown in Table 2).

The differences in age, sex, lobe sides, and the presence of thyroiditis or cancer were not significant between the Cernea types. There was also no significant difference between EBSLN Cernea types concerning neck length, thyroid length and lobe volume.

Based on the cut off volume of 50 cc [17], a thyroid lobe with a volume of >50 cc was defined as a large goitre. In our study, the prevalence of large goitres was 1 (5%), 3 (3.45%), and 5 (4.8%) in types 1, 2a and 2b, respectively. There was also no significant difference between the three types.

The NL/TL ratios were 3.29±0.28, 3.13±0.31, and 3.03±0.32 in types 1, 2a and 2b, respectively. The comparison between the three groups was statistically significant ($p < 0.001$).

The mean RUD of resected thyroid lobes was 24.75±2.05 mm (range 21-29), 25.99±2.01 (range 20-31) and 27.88±2.04 mm (range 21-35) in types 1, 2a and 2b, respectively. The comparison between the three groups was statistically significant ($p < 0.001$).

The TL/RUD also showed a statistically significant change between Cernea classifications, and the mean ratio of TL/RUD was 2.00±0.11, 1.99±0.28, and 1.90±0.27 in types 1, 2a and 2b, respectively. ($p < 0.001$).

In multinomial logistic regression analysis, RUD was the only independent factor associated with the Cernea type 2b nerve course. (Table 3).

Discussion

The EBSLN descends posterior to the sternothyroid muscle towards the cricothyroid muscles, along with the STA [19]. Because of its close proximity to the resection area and multiple variations, the EBSLN is at potential risk of injury during thyroidectomy [20]. Preservation of the anatomical and functional integrity of the EBSLN is important for postoperative voice quality [21].

Therefore, various modes of classification have been described in relation to the surrounding anatomic structures. Cernea [7], Friedman [8], and Selvan [9] describe the nerve's course in relation to the STA and the upper pole and the relationship with the inferior pharyngeal constrictor and the cricoid cartilage, respectively. Recently, Wu's classification based on the relationship of its lowest point with the superior thyroid pole was proposed [10]. Among these, the Cernea classification is still the most widely accepted since it is based on the potential nerve injury risk during surgery.

Because it travels medially through the superior pole vessels below the upper pole of the thyroid, which is the inevitable area for surgery, the type 2b EBSLN has the highest injury risk, even with the use of nerve monitoring [22,23]. Precise knowledge of the different variations in the EBSLN course is essential for its preservation [24].

Previous studies have shown a significant relationship between Cernea type 2b and large goitres or toxic glands [14,15,16,25,26]. It is thought that the increase in the thyroid volume extends cranially in the thyroid superior pole, drawing the goitre closer to the EBSLN [25].

However, the majority of patients in the thyroid surgical department suffer from thyroid cancer with relatively normal gland size and normal thyroid function. In this study, we expected that through the study of these nonenlarged goitres, we could identify the factors that affect the classification of EBSLN

and reduce the risk of EBSLN injury during thyroidectomy. We assumed that the position of the EBSLN is relatively constant for a patient, and the gland growing cranially will change the anatomical positional relationship between the EBSLN, the STA and the superior pole of the thyroid, increasing the proportion of type 2b EBSLNs. This might be caused by the variations in thyroid shape.

The thyroid gland consists primarily of the two lobes with the isthmus interconnecting them, which appears on the boundary between the first and second pharyngeal sacs and gradually descends to the neck and obtains its adult shape and location during the development process [27]. The shape of the thyroid has many variations, not only in regard to the morphology of the pyramidal lobe but also in the relative position of the glandular lobe in proximity to the isthmus. (As shown in Fig. 1).

Even for two thyroid lobes with the same length, volume and weight, the shape and position of the lobe will be different due to the different distances between the upper pole and the upper edge of the isthmus, which we define as the RUD.

In the present study, the EBSLN was successfully identified in 96.35% of 219 thyroid lobectomies in this series. Among the 211 EBSLNs identified, 19 (9%) were Cernea type 1, 88 (41.7%) were Cernea type 2a, and 104 (49.3%) were type 2b. These results are similar to those of previous studies [16,19] but also inconsistent with some studies [7,28 29]. In addition to ethnicity reasons, we believe that this may be different under the conditions of the surgeon pulling the upper pole during surgery, which may change the relative position between the anatomical structures in the upper polar region, and the classification of the EBSLN [30].

Cernea reported that the nerve crosses relatively higher in relation to the upper thyroid pole in Caucasians (5.0%) than in other races (41.0%) [31]. It is generally believed that Caucasians have relatively long necks.

According to our results, there was no significant difference between the Cernea types concerning age, sex, side, thyroiditis, thyroid cancer, neck length, and thyroid length, and no significant relationship was found for Cernea type 2b, similar to previous studies. In contrast to previous studies, there was no significant difference between the Cernea types concerning lobe volume. When we labelled the lobe with a volume greater than 50 cc as a large goitre, there was also no significant difference between the Cernea types in regard to large goitres. We suggest that this might be because most of the patients included in the study were thyroid cancer patients with small tumour diameters and normal gland sizes, and the proportion of grossly enlarged glands was small. In addition, in our study, some patients with large goitres had substernal goitres, and the excessive drop of the lobe made the upper pole far away from the EBSLN instead of growing cranially and getting closer to the EBSLN.

Similar to a previous study [10], the NL/TL ratio between the Cernea types was statistically significant, which may partially explain why the proportion of typing varies greatly in studies of different countries [13,19] since ethnic groups will change the anatomical parameters of the neck.

In the present study, we defined the distance from the upper pole to the upper edge of the isthmus as the relative upper distance. We used the value of RUD and the ratio of TL/RUD to describe the shape of the thyroid lobe and found that the type of EBSLN was closely related to the shape of the glands. Both the RUD and the TL/RUD showed statistically significant changes in Cernea classification. In logistic regression analysis, RUD was the only independent factor associated with the Cernea type 2b nerve course, and all the remaining independent variables were not related to type 2b EBSLN.

These results confirmed our hypothesis that it is not only the larger gland volume or longer thyroid length that will affect the EBSLN typing. Even for thyroids of the same length with the same neck length, different gland shapes caused by various reasons can affect nerve typing, including but not limited to 1) gland enlargement and growth cranially; 2) formation of tumours in the upper region of the lobe or extra thyroid invasion changing the anatomical position of the upper pole; and 3) variation during thyroid development leading to different gland shapes. The larger relative upper length reflects the relative position of the upper pole that is closer to the cranial side, as well as the EBSLN, and increases the probability of type 2b EBSLNs.

It is worth mentioning that the RUD can be measured accurately in preoperative evaluations using ultrasound, contrast-enhanced CT, and palpation. It might be useful to reduce surgical complications by evaluating and predicting the possibility of a type 2b EBSLN preoperatively. Different from mature techniques to identify the recurrent laryngeal nerve, there is no clear consensus or standard technique for the identification of the EBSLN, and there are three strategies for the preservation of the EBSLN during surgery: dissection and visualization, identification via nerve stimulation, or EBSLN avoidance [31]. Because visualization of the EBSLN is not always easy to perform, some surgeons tend to avoid rather than routinely expose and identify the EBSLN. However, for patients with a high probability of type 2b, great care, as well as intraoperative EBSLN identification, by visual or neural monitoring is critical to protect the nerve.

We acknowledge this study's limitations. First, we measured the relative upper distance as defined by the distance between the upper pole and the upper edge of the isthmus; however, there are also variations in the location of the isthmus. Limited by the retrospective nature, we did not analyse the absolute position of the upper pole, but rather referred to the skeletal structures of the larynx, such as the cricoid cartilage. Second, we only confirmed the EBSLN visually and functionally during the operation, but no postoperative voice assessment or laryngoscopy was performed. Third, in this study, our exposure rate did not reach 100%, and we speculated that unexposed nerves were more likely to be type 1 EBSLNs; such an imperfect exposure rate may lead to typing deviation. Finally, the influence of other gland parameters on classification, such as upper volume or upper weight, also needs to be further improved.

Conclusion

Identification and protection of the EBSLN during thyroidectomy is important to achieve complication-free surgery. The shape of the thyroid lobe described by the RUD and RUD/TL can influence the

relationship of the EBSLN with the superior pole and vessels. A higher RUD value and RUD/TL ratio increased the likelihood of a type 2b EBSLN, which is at the highest risk for injury. Detailed preoperative evaluation can provide information to minimize the potential for iatrogenic intraoperative injury. This information should therefore be taken into consideration in preoperative planning. For such patients, surgeons should pay more attention to sufficiently expose, identify and protect the nerves during surgery to avoid iatrogenic injury.

Abbreviations

CTM

cricothyroid muscle

EBSLN

external branch of the superior laryngeal nerve

NEP

nerve entry point

NL

neck length

PTC

papillary thyroid cancer

RUD

relative upper distance

STA

superior thyroid artery

TL

length of the thyroid lobe

Declarations

Ethics approval and consent to participate

This study was performed according to the Declaration of Helsinki and approved by the ethics committee of Harbin Medical University cancer hospital (No. JJQN2023-07). Written informed consent was obtained from all patients.

Consent for publication

Written informed consent for publication of clinical data and images was obtained from all patients.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing Interests

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Author Contributions

Zhaoming Ding-Designed the study, writing and submission; Mengshi Chen- Literature review, data collection; Chunlei- Administrative support and design. All authors contributed to the article and approved the submitted version.

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Tables

Tables 1 to 3 are available in the Supplementary Files section.

Figures

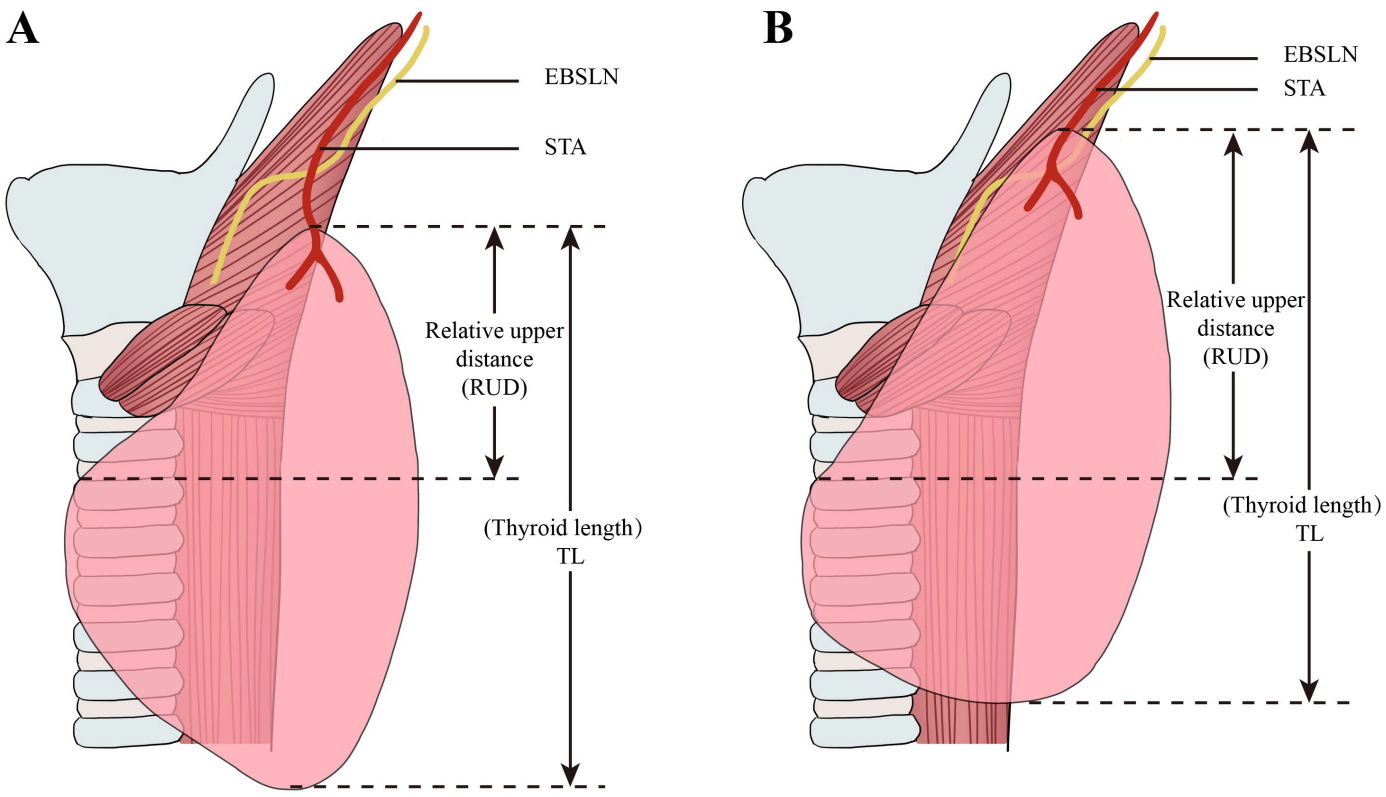


Figure 1

The influence of gland shape on the relative anatomical position of the upper polar region. In two thyroid lobes with the same length, the thyroid lobe with a shorter RUD has its upper pole away from the EBSLN, making it safer to perform a thyroidectomy (A), while the thyroid lobe with a longer RUD has the upper pole closer to EBSLN, and carries a higher risk of injury during surgery.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Table1.Characteristicsoftheenrolledpatientsn154.xlsx
- Table2.FactorsinfluencingthenervecourseofEBSLNaspertheCerneaclassification..xlsx
- Table3.Evaluationofthefactorsinfluencingtype2bEBSLNbymultinomiallogisticregressionanalysis.xlsx