Routine exposure of recurrent laryngeal nerve in thyroid surgery can prevent nerve injury

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Abstract
To determine the value of dissecting the recurrent laryngeal nerve during thyroid surgery with respect to preventing recurrent laryngeal nerve injury, we retrospectively analyzed clinical data from 5,344 patients undergoing thyroidectomy. Among these cases, 548 underwent dissection of the recurrent laryngeal nerve, while 4,796 did not. There were 12 cases of recurrent laryngeal nerve injury following recurrent laryngeal nerve dissection (injury rate of 2.2%) and 512 cases of recurrent laryngeal nerve injury in those not undergoing nerve dissection (injury rate of 10.7%). This difference remained statistically significant between the two groups in terms of type of thyroid disease, type of surgery, and number of surgeries. Among the 548 cases undergoing recurrent laryngeal nerve dissection, 128 developed anatomical variations of the recurrent laryngeal nerve (incidence rate of 23.4%), but no recurrent laryngeal nerve injury was found. In addition, the incidence of recurrent laryngeal nerve injury was significantly lower in patients with the inferior parathyroid gland and middle thyroid veins used as landmarks for locating the recurrent laryngeal nerve compared with those with the entry of the recurrent laryngeal nerve into the larynx as a landmark. These findings indicate that anatomical variations of the recurrent laryngeal nerve are common, and that dissecting the recurrent laryngeal nerve during thyroid surgery is an effective means of preventing nerve injury.

Key Words
neural regeneration; peripheral nerve injury; thyroid diseases; nerve injury; thyroidectomy; recurrent laryngeal nerve; dissection; nerve anatomy; variations; inferior parathyroid gland; middle thyroid vein; grants-supported paper; neuroregeneration

Research Highlights
(1) This retrospective clinical controlled study demonstrated that dissecting the recurrent laryngeal nerve during thyroid surgery is clinically significant for preventing nerve injury.
(2) Dissecting the recurrent laryngeal nerve during thyroid surgery can effectively prevent nerve injury in the presence of anatomical variations.
(3) The inferior parathyroid gland is an optimal anatomical landmark for locating the recurrent laryngeal nerve during thyroid surgery.
(4) The middle thyroid vein is also an important anatomical landmark of dissecting the recurrent laryngeal nerve.
INTRODUCTION

Recurrent laryngeal nerve injury is the most common serious complication of thyroid surgery. Unilateral injury may cause hoarseness of the voice and dysphonia, affecting the quality of patient’s life. Bilateral injuries can cause dyspnea and even suffocation. Therefore, preventing recurrent laryngeal nerve injury is an important goal in thyroid surgery. To reduce the recurrent laryngeal nerve injury rate during thyroid surgery, intraoperative neuromonitoring of the recurrent laryngeal nerve is the best measure[1-2]. However, at present, most low-level Chinese hospitals have no systems for recurrent laryngeal nerve monitoring. Therefore, some surgeons routinely dissect the recurrent laryngeal nerve during thyroid surgery[3-7]. However, it remains controversial as to whether dissecting the recurrent laryngeal nerve is beneficial, and it may even increase the risk of the recurrent laryngeal nerve injury because of improper operation[8-9]. To determine the value of dissecting the recurrent laryngeal nerve during thyroid surgery, clinical data of 5 344 cases undergoing thyroidectomy in Xinhua Hospital, Shanghai Jiao Tong University School of Medicine, China from January 2005 to January 2011 were analyzed. The difference in the incidence rate of recurrent laryngeal nerve injury between two groups was assessed.

RESULTS

Quantitative analysis of participants
There were 5 564 patients undergoing thyroidectomy in Xinhua Hospital, Shanghai Jiao Tong University School of Medicine, China from January 2005 to January 2011, and 5 344 patients in accordance with inclusion criteria were recruited in our retrospective clinical control study. Among these cases, 548 underwent dissection of the recurrent laryngeal nerve (dissection group), and 4 796 did not (undissection group). All 5 344 cases were involved in the final analysis.

Baseline data of patients undergoing thyroidectomy
There were no statistical differences in gender or age between the dissection (n = 548) and undissection (n = 4 796) groups (P > 0.05; Table 1).

Influence of recurrent laryngeal nerve dissection on the incidence of recurrent laryngeal nerve injury
In the dissection group, 12 patients (2.2%) had sustained recurrent laryngeal nerve injury. Of these, 10 occurred immediately after surgery (1.8%), and two occurred during the 3 weeks following surgery (0.4%). The undissection group contained 512 patients (10.7%) who had sustained injury to the recurrent laryngeal nerve. Of these, 430 occurred immediately after surgery (9.0%), and 82 occurred during the 3 weeks following surgery (1.7%). The difference in the total rate of recurrent laryngeal nerve injury between two groups was statistically significant (P < 0.01).

Table 1 Baseline data of subjects

| Item                                | Dissection group (n = 548) | Undissection group (n = 4 796) | X² (v = 1) | P   |
|-------------------------------------|---------------------------|-------------------------------|-----------|-----|
| Gender (male/female, n)             | 136/412                   | 1 282/3 514                   | 0.923     | > 0.05 |
| Age (year)                          | 45(3–86)                  | 51(5–84)                      | 1.316     | > 0.05 |
| Thyroid disease [n (%)]             |                           |                               | 7.358     | > 0.05 |
| Thyroid adenomas                    | 106(19.3)                 | 1 276(26.6)                   |           |     |
| Thyroid cancer                      | 164(29.9)                 | 1 046(21.8)                   |           |     |
| Nodular goiter                      | 203(37.0)                 | 1 670(34.8)                   |           |     |
| Hashimoto’s thyroiditis             | 25(4.6)                   | 29(0.6)                       |           |     |
| Thyroid neoplasm behind sternum     | 50(9.1)                   | 776(16.2)                     |           |     |
| Type of surgery [n/total%]          |                           |                               | 4.299     | > 0.05 |
| Near-total thyroidectomy            | 358(65.3)                 | 4 574(95.4)                   |           |     |
| Radical thyroidectomy               | 130(23.7)                 | 156(3.3)                      |           |     |
| Number of surgeries [n/total%]      |                           |                               | 2.251     | > 0.05 |
| First operation                     | 423(77.2)                 | 3 423(71.4)                   |           |     |
| Reoperation or repeated operation   | 125(22.8)                 | 1 373(28.6)                   |           |     |

There were no significant differences in gender, age, type of thyroid disease, type of surgery, and number of surgeries between two groups using chi-square analysis (P > 0.05), indicating that these two groups were comparable.

Influence of type of thyroid disease, type of surgery, and number of surgeries on incidence of recurrent laryngeal nerve injury
Next, we performed a stratified analysis on the type of thyroid disease, type of surgery, and number of surgeries between the two groups (Table 2). The recurrent laryngeal nerve injury rates in the dissection group were significantly lower than in the undissection group (P < 0.01). These differences remained significant even when each case was compared with those involving the same type of thyroid disease (not including Hashimoto’s thyroiditis or thyroid neoplasm behind sternum), the same type of surgery, and the same number of surgeries
In both groups, the recurrent laryngeal nerve injury rate of patients undergoing radical thyroidectomy was significantly higher than that of patients undergoing near-total thyroidectomy or total thyroidectomy \((P < 0.01)\), and the recurrent laryngeal nerve injury rate among patients undergoing reoperation or repeated operation was also significantly higher than that of patients undergoing their first operation \((P < 0.01)\). In the undissection group, the recurrent laryngeal nerve injury rate among patients with thyroid cancer was significantly higher than that among patients with benign diseases of the thyroid, and the recurrent laryngeal nerve injury rate among patients undergoing total thyroidectomy was significantly higher than that of patients undergoing near-total thyroidectomy \((P < 0.01)\).

### Table 2: Differences in the recurrent laryngeal nerve injury rates among patients undergoing thyroidectomy with or without dissection of the recurrent laryngeal nerve according to type of thyroid disease, type of surgery, and number of surgeries

| Item                              | Dissection group \((n = 548)\) | Undissection group \((n = 4796)\) | \(\chi^2\) \((v = 1)\) | \(P\)  |
|-----------------------------------|-------------------------------|----------------------------------|---------------------|------|
| **Type of thyroid disease**       |                               |                                  |                     |      |
| Thyroid adenomas                  | 0.10(6)                       | 7.1(1,276)                       | 7.997               | < 0.01 |
| Thyroid cancer                    | 4.9(164)                      | 19.7(1,046)                      | 21.377              | < 0.01 |
| Nodular goiter                    | 1.0(203)                      | 8.1(1,670)                       | 13.589              | < 0.01 |
| Hashimoto’s                      | 0.25(5)                       | 0(28)                           | –                   | –    |
| Thyroiditis                       |                               |                                  |                     |      |
| Thyroid neoplasm                  | 4.0(50)                       | 10.3(776)                       | –                   | –    |
| **Type of surgery**               |                               |                                  |                     |      |
| Near total thyroidectomy          | 1.7(358)                      | 9.7(4,574)                      | 25.649              | < 0.01 |
| Total thyroidectomy               | 1.5(130)                      | 26.9(156)                       | 35.100              | < 0.01 |
| Radical thyroidectomy             | 6.7(60)                       | 42.4(66)                        | 21.209              | < 0.01 |
| **Number of surgeries**           |                               |                                  |                     |      |
| Once                              | 0.9(423)                      | 6.9(3,423)                      | 22.907              | < 0.01 |
| Twice and repeated operations     | 6.4(125)                      | 20.0(1,373)                     | 13.889              | < 0.01 |
| Total rate of recurrent laryngeal nerve injury | 2.2(548)                     | 10.7(4,796)                     | 40.043              | < 0.01 |

The number inside the bracket represents the percentage of the number of patients with nerve injury out of the total patients with that type of disease, while the number inside the bracket represents the number of patients with that type of disease.

### Method of dissecting the recurrent laryngeal nerve and its influence on recurrent laryngeal nerve injury

Among the 548 cases in the dissection group, seven of the 442 cases (1.6%) with the inferior parathyroid gland as a landmark for locating recurrent laryngeal nerves showed recurrent laryngeal nerve injury; two of the 79 cases (2.5%) with the middle thyroid vein as a landmark were injured; and three of the 27 cases (11.1%) with the recurrent laryngeal nerve into the larynx as the landmark showed recurrent laryngeal nerve injury. The injury rate was significantly higher when the laryngeal entrance of the recurrent laryngeal nerve was used as a landmark compared with the other two locations \((P < 0.01)\).

### Anatomical variations of the recurrent laryngeal nerve during recurrent laryngeal nerve dissection

Anatomical variations were found in 128 cases in the dissection group. Of these, there were 43 cases with outer positions, which did not run upper along the tracheoesophageal ditch until passing the inferior thyroid artery; 56 cases with front positions of the recurrent laryngeal nerves, which ran upper very close to the envelope posterior thyroid; 29 cases with furcal recurrent laryngeal nerves, which were divided into two branches before entering the larynx; and no cases of non-recurrent laryngeal nerve.

### Discussion

Injury to the recurrent laryngeal nerve may cause hoarseness of the voice, difficulty breathing, and even suffocation. Because of the extrusion and infiltration of tumors, the traction and adhesion of postoperative scar tissues, and natural anatomical variability, the course of the recurrent laryngeal nerve differs. This is one of the main reasons why recurrent laryngeal nerve injury is the most common complication of thyroid surgery, and has made the prevention of intraoperative recurrent laryngeal nerve injury a concern among thyroid surgeons. To decrease the chances of recurrent laryngeal nerve injury, Mättig and colleagues suggested routine exposure of the recurrent laryngeal nerve in thyroid surgery. However, this technique remains controversial. Surgeons opposing the exposure of the recurrent laryngeal nerve claim that dissecting the recurrent laryngeal nerve increases the risk of recurrent laryngeal nerve injury, and advocate protection of the running area of the recurrent laryngeal nerve. For example, Procacciante et al. considered that it was inevitable to increase the chance of bleeding during recurrent laryngeal nerve dissection, and thus the procedure of dissecting, especially hemostatic operation, increased the risk of recurrent laryngeal nerve injury. However, other surgeons consider that dissecting the recurrent laryngeal nerve is the best method of protection because of many anatomical variations of the recurrent laryngeal nerve. The outcome of the present study showed that the total...
recurrent laryngeal nerve injury rate in the dissection group (2.2%) was significantly lower than that in the undissection group (10.7%). Furthermore, these differences remained significant even when each case was compared with those with the same type of thyroid disease (not including Hashimoto’s thyroiditis or thyroid neoplasm behind sternum), the same type of surgery, and the same number of surgeries. The recurrent laryngeal nerve injury rate among patients undergoing total thyroidectomy (26.9%) was significantly higher than that among patients undergoing near-total thyroidectomy (9.7%) in the undissection group. In the dissection group, however, the injury rates were similar. Among 548 cases of the dissection group in the present study, there were 128 cases with anatomical variations of the recurrent laryngeal nerve (23.4% occurrence rate). Nearly 25% of cases had anatomical variations of the recurrent laryngeal nerve. Of these, however, no recurrent laryngeal nerve injury was found, suggesting that dissecting the recurrent laryngeal nerve during thyroid surgery is an effective means of preventing nerve injury. Although there are many anatomical variations of the recurrent laryngeal nerve in the area affected by thyroid surgery, the recurrent laryngeal nerve has its own form and a regular position. Fully understanding the anatomical characteristics of the recurrent laryngeal nerve may help surgeons dissect the recurrent laryngeal nerve in a safe, fast, and correct way.

The inferior thyroid artery and the entry of the recurrent laryngeal nerve into the larynx are generally considered the key sites to look for the recurrent laryngeal nerve[18-21]. However, according to our experience, the inferior thyroid artery is an insufficient landmark. First, it is not easy to find the recurrent laryngeal nerve at the inferior thyroid artery as the topographical relationship between the inferior thyroid artery and the recurrent laryngeal nerve is not consistent across patients. Second, the process of dissecting the inferior thyroid artery can easily cause bleeding and increase the chance of injury to the recurrent laryngeal nerve. Although the entry of the recurrent laryngeal nerve into the larynx involves a constant position, it is close to the Berry ligament. Because the thyroid gland is closely attached to the surface of the laryngeal cartilage, dissecting the recurrent laryngeal nerve is very difficult and can easily cause thyroid bleeding, which can lead to an unclear operative field, making injury to the recurrent laryngeal nerve even more likely. Furthermore, considering the prevailing preference for aesthetically pleasing popular small incisions, the limited operating space makes exposing the recurrent laryngeal nerve even more difficult. However, using the inferior parathyroid gland as an anatomic landmark makes finding the recurrent laryngeal nerve simple and practical. First, the inferior parathyroid gland is easy to identify. Second, the recurrent laryngeal nerve is usually located deep inside the parathyroid. Furthermore, there are usually few blood vessels in this field, which decreases the amount and likelihood of bleeding.

In our study, seven of the 442 cases (1.6%) with location of the recurrent laryngeal nerve in the inferior parathyroid gland showed recurrent laryngeal nerve injury. The inferior parathyroid gland is one of the most useful anatomical landmarks for locating the recurrent laryngeal nerve; among the 79 cases with the middle thyroid vein as the landmark for locating recurrent laryngeal nerve, two (2.5%) were injured. Importantly, no recurrent laryngeal nerve injury was found in the 43 cases with outer-positions of the recurrent laryngeal nerve, as we used the middle thyroid vein as the landmark for its location. Therefore, the middle thyroid vein is a practical anatomical landmark to expose the recurrent laryngeal nerve when there are anatomical variations, especially for occurrence of outer-position recurrent laryngeal nerves. We found that three of the 27 cases (11.1%) with the recurrent laryngeal nerve located using the entry of the recurrent laryngeal nerve into the larynx showed recurrent laryngeal nerve injury. The injury rate for the larynx was much higher than that for the other two landmarks. Thus, these data suggest that the inferior parathyroid gland and the middle thyroid vein may be practical anatomic landmarks with high clinical value for location of the recurrent laryngeal nerve in thyroid surgery.

Although routine anatomy of the recurrent laryngeal nerve in thyroid surgery is an effective way to prevent nerve injury, recurrent laryngeal nerve injury can still occur (2.2%) in the dissection group. According to clinical data collected in this study, recurrent laryngeal nerve injury in the dissection group occurred mainly in patients undergoing reoperation and in patients undergoing radical thyroidectomy. It is likely that these procedures caused the nerve to vary greatly in its placement, usually due to traction from postoperative scar tissue, the difficulty of separating the recurrent laryngeal nerve from the scar tissue, and infiltration by cancer cells. Neuromonitoring of the recurrent laryngeal nerve may help surgeons minimize the rate of injury to this nerve during complex surgeries, as intraoperative neuromonitoring can improve the recognition rate of the recurrent laryngeal nerve, speed up confirmation of the
recurrent laryngeal nerve during surgery, and reduce the injury rate\cite{22-29}.

SUBJECTS AND METHODS

Design
A retrospective clinical control study.

Time and setting
The experiments were conducted at the Department of Otolaryngology & Head and Neck Surgery, Ear Institute, Xinhua Hospital, Shanghai Jiao Tong University School of Medicine, China from April 2011 to March 2012.

Subjects
A total of 5 344 patients undergoing thyroidectomy were recruited from the Department of Otolaryngology & Head and Neck Surgery, Ear Institute, Xinhua Hospital, Shanghai Jiao Tong University School of Medicine, China from January 2005 to January 2011. All of the patients underwent surgery under general anesthesia. The cases with dysarthria, mental disease, or lymph node dissection were excluded. Included cases were divided into groups according to whether their intraoperative anatomical recurrent laryngeal nerve had been exposed. Dissection of the recurrent laryngeal nerve during thyroid surgery is surgeon dependent, but is unrelated to the properties of the thyroid mass or clinical factors such as whether the patients were undergoing a first or subsequent operation.

Formal research inquiry methods and processes were conducted according to the ethical concepts of the Declaration of Helsinki.

Methods
Recurrent laryngeal nerve anatomic landmarks and methods
We used three of the main landmarks and methods of locating the recurrent laryngeal nerve in thyroid surgery, as follows:

(1) The inferior parathyroid gland: First, we located the parathyroid close to the inferior of the thyroid and separated the nerve slightly deep inside the parathyroid to find the recurrent laryngeal nerve running longitudinally from the lower to upper of human body. The inferior parathyroid gland, which was approximately the size of a soybean (6 mm), was easy to recognize, and was similar in appearance to adipose tissue, although less transparent. The recurrent laryngeal nerve was usually located deep inside the parathyroid and was rarely more than 0.2 cm from the parathyroid. Separating the recurrent laryngeal nerve from its superficial to deep locations through the gap between the thyroid and parathyroid rarely caused bleeding as there were usually no blood vessels connecting them. This was a simple and practical method for locating the recurrent laryngeal nerve. Within the inferior parathyroid group, the recurrent laryngeal nerves of most patients were smooth (Figure 1).

(2) Middle thyroid vein: The recurrent laryngeal nerve may also be found using the middle thyroid vein for an anatomic landmark when it is not found easily using the inferior parathyroid gland. The recurrent laryngeal nerve was located in the deep face of the middle thyroid vein,
and the recurrent laryngeal nerve and the middle thyroid vein are cross-shaped. The recurrent laryngeal nerve was usually found after ligation of the middle thyroid vein (Figure 2).

Figure 2  Recurrent laryngeal nerve with the middle thyroid vein as a landmark.
(A) Recurrent laryngeal nerve has not yet been exposed.
(B) Middle thyroid vein has been processed, and the recurrent laryngeal nerve is partially exposed.
(C) Thyroid section of the recurrent laryngeal nerve has been completely exposed.
V: Middle thyroid vein; T: tumor; M: strap muscles; N: recurrent laryngeal nerve.

(3) Entry of the recurrent laryngeal nerve into the larynx: The recurrent laryngeal nerve can also be found at the point at which it enters the larynx (Figure 3). After location of the recurrent laryngeal nerve along its course, we performed nerve dissection. The thyroid section of the recurrent laryngeal nerve was dissected if the operation was limited to the thyroid area. We dissected the recurrent laryngeal nerve through the supraclavicular margin if the operation required clearance of the central lymph node.

Figure 3  Recurrent laryngeal nerve with the entry of the recurrent laryngeal nerve into the larynx.
(A) Entry of the recurrent laryngeal nerve into the larynx is shown.
(B) Entry of the recurrent laryngeal nerve into the larynx is further exposed.
N: Recurrent laryngeal nerve (N in B was the entry of the recurrent laryngeal nerve into the larynx); T: tumor; M: strap muscles; P: superior parathyroid gland.

**Process of thyroid surgery**
Under general anesthesia, the patient was placed in the operation bed in a recumbent position. After routine disinfection and drape, a transverse incision of 3.5 cm was made along the dermatoglyph in the lower anterior area of the neck. The flap was turned, the thyroid was exposed, and the upper pole of the thyroid gland was severed. Next, we located the recurrent laryngeal nerve using anatomic landmarks such as the inferior parathyroid gland to protect it. Tissues were frozen for pathology after the removal of the diseased thyroid on one side. If the pathological results were malignant, resection of the thyroid gland on the other side and partition of cervical lymph node dissections were necessary. If patients had lymph node metastases in the lateral neck region, functional cervical lymph node dissections were performed.

**Diagnostic criteria of recurrent laryngeal nerve injury**
When vocal cord mobility was normal before surgery, recurrent laryngeal nerve injury was defined as postoperative hoarse voice or vocal cord movement.
disorder assessed through indirect laryngoscopy (FENTEX HI-CAM/CCD; Sony, Tokyo, Japan). Vocal cord movement disorders that resolved within 6 months of surgery were considered temporary recurrent laryngeal nerve injuries, and those that displayed continued weak mobility were considered to be permanent recurrent laryngeal nerve injuries.\(^{[30]}\)

**Statistical analysis**

Comparison of the recurrent laryngeal nerve injury rates between the two groups was performed using chi-square analysis. A value of \(P < 0.01\) was considered statistically significant.

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