

ORIGINAL ARTICLE

Clinical analysis of total endoscopic thyroidectomy via breast areola approach in early differentiated thyroid cancer

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Summary

Purpose: The purpose of this study was to explore the efficacy and safety of total endoscopic thyroidectomy (TET) via breast areola approach in the treatment of early differentiated thyroid cancer.

Methods: The clinical data of 134 patients with early differentiated thyroid cancer were retrospectively analyzed. The patients underwent different treatments, including TET via breast areola approach in endoscope group (n=67), and conventional small incision open surgery in control group (n=67). The surgery-related indexes, complications, postoperative incision recovery, visual analogue scale (VAS) pain score, postoperative patients' satisfaction, tumor recurrence and survival conditions were compared between the two groups.

Results: Compared with control group, the endoscope group showed significantly longer operation time, smaller intraop-

erative bleeding, less postoperative drainage, shorter duration of postoperative catheter indwelling and shorter postoperative length of stay. Meanwhile, in the endoscope group, the postoperative VAS pain score was markedly lower than that in control group, and the postoperative patients' satisfaction was higher than that in control group. The neurological severity score (NSS) had statistically significant differences between the two groups at 3 months and 6 months after operation. Moreover, no tumor recurrence and metastasis were found during the follow-up period.

Conclusions: TET via breast areola approach is safe and effective in the treatment of early differentiated thyroid cancer, and it can achieve a better cosmetic effect and high satisfaction of patients, which is worthy of clinical application.

Key words: thyroid cancer, total thyroidectomy, endoscope, efficacy

Introduction

As a common malignant tumor of the thyroid gland, thyroid cancer accounts for about 1% of systemic malignant tumors [1]. In China, more than 90% of thyroid cancers are papillary carcinoma, with low malignancy and good prognosis [2,3]. Since Ikeda et al and Ohgami et al reported the first case of endoscopic thyroid surgery via non-cervical approach in 2000, the endoscopic thyroid surgeries

via different approaches have been widely developed and applied in China and foreign countries [4-7]. Based on the excellent cosmetic effect, the indications for endoscopic treatment have been extended from the early benign lesions to the low-risk differentiated thyroid cancer.

Endoscopic thyroidectomy has definite clinical efficacy, with little impact on the neck appearance,

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and it is more acceptable for patients, which, therefore, has gradually replaced the traditional open surgery as the preferred treatment for thyroid cancer [8,9]. In order to explore the application value of total endoscopic thyroidectomy (TET) via breast areola approach, the clinical data of 134 patients with early differentiated thyroid cancer treated in our hospital were retrospectively analyzed, and the clinical efficacy and safety were compared between TET via breast areola approach and conventional small incision open surgery in the treatment of early differentiated thyroid cancer, hoping to provide a basis for developing clinical treatment strategies for such patients.

Methods

General data

The clinical data of 134 patients with early differentiated thyroid cancer treated in our hospital were collected. There were 37 males and 97 females aged 30.3-68.8 years old with an average of (45.1±9.7) years old, including 45 cases of papillary thyroid carcinoma, 75 cases of papillary thyroid microcarcinoma, and 14 cases of follicular thyroid carcinoma. All patients underwent subtotal thyroidectomy or total thyroidectomy + central lymph node dissection, and divided into endoscope group (TET via breast areola approach, n=67) and control group (conventional small incision open surgery, n=67) according to the operation methods. In terms of the methods of thyroid surgery, there were 37 cases of unilateral and isthmus resection of the thyroid gland, and 30 cases of bilateral thyroidectomy in endoscope group, 34 cases of unilateral and isthmus resection of the thyroid gland, and 33 cases of bilateral thyroidectomy in control group. Inclusion criteria: 1) patients definitely diagnosed with thyroid tumors with a diameter of <2 cm via imaging examination, 2) those without cervical lymph node metastasis (cN₀) according to preoperative imaging examination, and 3) those without distant me-

tastasis. Exclusion criteria: 1) patients with a history of surgery or radiotherapy on the neck, 2) those complicated with hyperthyroidism, 3) those complicated with thyroiditis, or 4) those complicated with other severe organ dysfunction or contraindications to surgery. The general clinical data had no statistically significant differences between the two groups of patients (p>0.05), and they were comparable at the baseline (Table 1). This study adhered to the *Declaration of Helsinki* and was approved by the Ethics Committee of our institution, and all patients enrolled signed the informed consent.

Operation methods

Endoscope group: The patients received related examinations, and underwent total endoscopic unilateral or bilateral thyroidectomy via breast areola approach + central lymph node dissection under general anesthesia. In a supine position, a 10 mm-long incision was made at the midpoint of the line of two breasts (slightly towards the unaffected side), from which 100 mL of inflation fluid (1:20000 adrenaline saline) was injected. The muscles were bluntly separated to construct the subcutaneous tunnel. Then a 10 mm Trocar was punctured through the incision, a 10 mm 30° endoscope was placed, and CO₂ was injected at a pressure of 6-8 mmHg. Next, a 5 mm-long incision was made at the superior border of the left and right areolas, respectively, and the Trocar and operation instruments were placed. The subcutaneous loose tissues were separated with an ultrasound knife, and the thyroid gland was dissociated and exposed. The recurrent laryngeal nerves and the parathyroid gland were exposed and protected, and the inferior thyroid arteries and veins were cut off. Next, the superior pole of thyroid was dissociated to expose the superior thyroid arteries and superior laryngeal nerves, the superior thyroid vessels were treated with the ultrasound knife, and the isthmus was cut off. The lymphatic and adipose tissues in the central region were scavenged. After the specimens were harvested, the incision was washed and bleeding was stopped, followed by placement of drainage tube. Finally, the chest incision was sutured and bandaged with chest strap to reduce exudation.

Table 1. Baseline demographic and clinical characteristics of the studied patients

Indicators	Endoscope group (n=67) n (%)	Control group (n=67) n (%)	p
Age, years	44.34±9.82	45.56±8.91	0.453
Gender (Male/Female)	21/46	16/51	0.440
BMI (kg/m ²)	23.43±2.34	23.87±1.59	0.205
Tumor diameter (cm)	1.5±0.6	1.7±0.5	0.083
Surgical method			0.729
Unilateral and isthmus of thyroid gland	37 (69.5)	34 (65.6)	
Bilateral	30 (30.5)	33 (34.4)	
Pathological type			0.664
Papillary thyroid carcinoma	21 (31.3)	24 (35.8)	
Micro-lesion papillary thyroid carcinoma	40 (59.7)	35 (52.2)	
Follicular thyroid carcinoma	6 (9.0)	8 (12.0)	

BMI: body mass index.

Control group: The patients underwent unilateral or bilateral thyroidectomy + central lymph node dissection. In the supine position, a 2.0-2.5 mm-long incision was made in the skin fold at 2 cm above the sternal notch. The skin, subcutaneous tissues were separated layer by layer, and the flaps were dissociated. Later, the capsule of thyroid gland was separated to fully expose the thyroid gland, and a 5 mm 30° endoscope was placed. Under the guidance of endoscope, the isthmus of thyroid gland was cut open with the ultrasound knife, and the vessels were cut off. Then the superior pole of thyroid was dissociated, the superior thyroid arteries were clamped and cut off using the ultrasound knife, and the superior laryngeal nerves were protected. Thereafter, the recurrent laryngeal nerves were exposed and protected, and the inferior thyroid arteries were clamped and cut off with the ultrasound knife. Subsequently, the lymphatic and adipose tissues in the central region were scavenged, and the parathyroid gland was protected. If total thyroidectomy was needed, the contralateral thyroid gland was treated in the same way. Finally, the drainage tube was placed, and the incision was sutured intradermally layer by layer.

Observation indexes

The operation time, amount of intraoperative bleeding, number of dissected lymph nodes, duration and amount of postoperative drainage, postoperative length of stay, and postoperative complications (mainly including hemorrhage, laryngeal edema, recurrent laryngeal nerve injury, tracheal compression, subcutaneous effusion and subcutaneous emphysema) were observed and recorded in both groups. The postoperative incision recovery was observed, and the postoperative patients' satisfaction score and neurological severity score (NSS) about the cosmetic effect were recorded. The scores range from 0 point (unsatisfactory) to 10 points (satisfactory), and the higher the score is, the better the satisfaction will be [4]. The postoperative pain of patients was evaluated using the visual analogue scale (VAS) score.

Postoperative treatment and follow-up: At 1 d after operation, the blood calcium concentration, five-item thyroid functions, parathyroid function and thyroglobulin antibody were routinely detected. Cervical B-mode ultrasound was adopted in imaging examination. According to the levels of blood calcium and parathyroid hormone, calcium and vitamin D were supplemented intravenously or orally. The thyroid function and thyroid ultrasound were reviewed at 1 month after operation and then once every 3 months, based on which the dose of levothyroxine sodium tablets was adjusted. The patients

were followed up till August 2019, and the tumor recurrence and patients' survival condition were recorded.

Statistics

SPSS 22.0 software (IBM, Armonk, NY, USA) was used for statistical analysis. Measurement data were expressed as mean \pm standard deviation, and t-test was performed for the intergroup comparison. Enumeration data were expressed as rate (%), and χ^2 test was performed for the intergroup comparison. $P < 0.05$ suggested statistically significant difference.

Results

Comparison of surgery-related indexes between the two groups

The operation time was significantly longer in endoscope group than that in control group [(115.2 \pm 21.3) min vs. (95.6 \pm 17.4) min], and the difference was statistically significant ($p < 0.001$). In endoscope group, the amount of intraoperative bleeding was remarkably smaller [(28.2 \pm 6.9) mL vs. (34.3 \pm 7.9) mL, $p < 0.001$], the amount of postoperative drainage was obviously smaller [(53.8 \pm 24.1) mL vs. (91.6 \pm 29.3) mL, $p < 0.001$], the duration of postoperative catheter indwelling was notably shorter [(2.5 \pm 0.5) d vs. (3.6 \pm 0.7) d, $p < 0.001$], the postoperative length of stay was evidently shorter than those in control group [(5.7 \pm 2.3) d vs. (8.1 \pm 3.5) d, $p < 0.001$]. However, there was no statistically significant difference in the number of dissected lymph nodes between the two groups [(5.4 \pm 1.6) vs. (5.1 \pm 1.3), $p = 0.236$] (Table 2).

Incidence of postoperative complications in both groups

The operation was successful in both groups. After operation, the level of serum thyroxine was kept within the normal range, the level of thyroid-stimulating hormone was normal or declined slightly, and the thyroglobulin antibody was negative. In cervical ultrasound examination, no residual glands and residual lesions on the affected side, no recurrent or new lesions in residual glands, no recurrent lesions at the puncture site and tunnel, and no enlargement of

Table 2. Comparison of indicators related to surgery

Indicators	Endoscope group (n=67)	Control group (n=67)	p
Operation time (min)	115.2 \pm 21.3	95.6 \pm 17.4	0.001
Blood loss (ml)	28.2 \pm 6.9	34.3 \pm 7.9	0.001
Postoperative drainage volume (ml)	53.8 \pm 24.1	91.6 \pm 29.3	0.001
Postoperative intubation time (day)	2.5 \pm 0.5	3.6 \pm 0.7	0.001
In-hospital time (day)	5.7 \pm 2.3	8.1 \pm 3.5	0.001
Number of lymph nodes dissection	5.4 \pm 1.6	5.1 \pm 1.3	0.236

cervical lymph nodes were found. In endoscope group, there were 2 cases of temporary recurrent laryngeal nerve injury, 8 cases of transient hypocalcemia, 3 cases of subcutaneous emphysema, 2 cases of subcutaneous effusion, 1 case of hemorrhage and 1 case of incision infection after operation, and the total incidence rate of complications was 34.3% (23/67). In control group, there were 2 cases of temporary recurrent laryngeal nerve injury, 13 cases of transient hypocalcemia, 1 case of subcutaneous emphysema, 2 cases of subcutaneous effusion, 3 cases of hemorrhage and 3 cases of incision infection after operation, and the total incidence rate of complications was 43.3% (29/67). It could be seen that the incidence rate of postoperative complications had no statistically significant difference between the two groups ($p=0.153$). After calcium supplementation for 6 months, the level of blood calcium returned to normal, and it was confirmed via laryngoscope that the vocal cord mobility also became normal at 1 month after operation (Table 3).

Comparison of postoperative patients' satisfaction, VAS score and NSS

In endoscope group, the postoperative VAS pain score was markedly lower ($p<0.001$), and the postoperative patients' satisfaction was higher

than those in control group, in which there were significantly more patients with 7-10 points than control group, showing a statistically significant difference ($p<0.001$). The NSS exhibited statistically significant differences between the two groups at 3 months and 6 months after operation [(8.3±1.4) points vs. (4.8±1.2) points, (7.2±1.1) points vs. (3.7±0.9) points, $p<0.001$] (Table 4). Besides, the formation rate of incision scar was 4.5% (3/67) and 19.4% (13/67), respectively, in endoscope group and control group, and the difference was statistically significant ($p=0.008$).

Follow-up results of patients' survival

The median follow-up time was (36.4±6.3) months and (34.8±5.9) months, respectively, in the two groups as of August 2019. During the follow-up period, 1 case was lost to follow-up in endoscope group, with a follow-up rate of 98.5% (66/67), while 2 cases were lost to follow-up in control group, with a follow-up rate of 97.0% (65/67), and no tumor recurrence and metastasis were found. There was 1 death of myocardial infarction and 1 death of cerebral infarction in endoscope group, while 1 death of rupture of aortic dissection and 1 death from traffic accident in control group. No thyroid tumor-related deaths occurred in either group.

Table 3. Comparison of adverse reactions between the two groups of patients

Indicators	Endoscope group (n=67) n (%)	Control group (n=67) n (%)	p
Hemorrhage	1 (1.5)	3 (4.5)	0.310
Incision infection	1 (1.5)	3 (4.5)	0.310
Laryngeal edema	2 (3.0)	4 (6.0)	0.404
Recurrent laryngeal nerve injury	2 (3.0)	2 (3.0)	1.000
Transient hypocalcemia	8 (11.9)	13 (19.4)	0.235
Tracheal compression	2 (3.0)	1 (1.5)	0.559
Subcutaneous effusion	2 (3.0)	2 (3.0)	1.000
Subcutaneous emphysema	3 (4.5)	1 (1.5)	0.310
Chest discomfort	2 (3.0)	0 (0)	0.496

Table 4. Comparison of posttreatment VAS score, Satisfaction score and NSS score between the two groups of patients

Indicators	Endoscope group (n=67)	Control group (n=67)	p
VAS score	2.7±0.9	4.1±1.0	0.001
Satisfaction score, n (%)			0.001
0-2	5 (7.5)	15 (22.4)	
3-6	23 (34.3)	40 (59.7)	
7-10	39 (58.2)	12 (17.9)	
NSS score			
3 months posttreatment	8.3±1.4	4.8±1.2	0.001
6 months posttreatment	7.2±1.1	3.7±0.9	0.001

VAS: visual analogue scale; NSS: numerical score system.

Discussion

Differentiated thyroid cancer is the most common type of thyroid cancer. Endoscopic surgery is preferred by female patients with high requirements for aesthetics, while traditional open thyroid surgery will lead to obvious surgical scars on the neck, affecting aesthetics [10-12]. Studies have demonstrated that patients are more satisfied with the cosmetic effect of endoscopic surgery compared with traditional open thyroid surgery [13,14]. In 1997, Gottlieb reported the first case of primary hyperparathyroidism treated with endoscopic parathyroidectomy, which laid a good foundation for endoscopic thyroid surgery [15]. After application and development for nearly 20 years, endoscopic thyroid surgery has become increasingly mature [16].

Currently, the thoracic endoscopic approach is the most widely used in China, based on which the breast areola approach has been developed [17,18]. In TET via breast areola approach, the incision is made at the junction of areola edge and skin, which is highly concealed with little tension and low proneness to scar hypertrophy, thus further improving the cosmetic effect.

At present, the treatment of differentiated thyroid cancer with endoscopic thyroid surgery is still controversial, and whether the endoscope can reach the region of central lymph node dissection in traditional open surgery, such as some lymph nodes behind the sternum (region VII) and right recurrent laryngeal nerves, is the main focus of attention [19,20]. Central and lateral lymph node dissection via anterior thoracic approach is difficult due to the obscuration of the sternal manubrium and clavicular head, with a certain blind area. Therefore, it is necessary to accurately evaluate the condition of cervical lymph nodes before surgery and select appropriate patients for surgery, so as to avoid incomplete dissection. With the increase of skills and experience of surgeons, and improvement of surgical instruments, the indications have been extended. At present, endoscopic thyroid surgery is mainly used in the surgical treatment of low-risk thyroid microcarcinoma. In this study, the patients with a maximum tumor diameter of 2 cm, cN₀ and no distant metastasis were selected as the subjects of study. In Korea, Hong et al studied 57 patients undergoing endoscopic percutaneous transvenous mitral commissurotomy via thoracic approach, and found that both operation time and length of stay in endoscope group are longer than those in open surgery group, but the number of central lymph nodes dissected and the incidence rate of postoperative

complications are similar between the two groups [21]. Moreover, according to a report, 84 patients with papillary thyroid microcarcinoma are treated with surgery via anterior thoracic approach and preventive central lymph node dissection [6.5 (2-14) on average], in which metastasis occurs in 44 cases (44/84, 52.4%). In this study, the operation time in endoscope group was longer than that in control group, and such a result may be related to the time spent on separating subcutaneous tissues to create the operation space. Besides, endoscope group had obviously smaller amount of intraoperative bleeding, smaller amount of postoperative drainage, shorter duration of drainage, shorter length of stay than control group ($p < 0.05$). However, there was no significant difference in the number of dissected lymph nodes between the two groups ($p > 0.05$).

In this study, the incidence rate of common postoperative complications (temporary recurrent laryngeal nerve injury and temporary hypocalcemia) was similar between endoscope group and control group ($p > 0.05$). The prethoracic flaps need dissociating when the operation space is created, so prethoracic discomfort is also one of the common complications of endoscopy. Jiang et al argued that postoperative pain and discomfort are related to the layer of surgical separation, rather than its range. Postoperative pain is not worsened in the case of separation at the correct layer [22]. In this study, prethoracic discomfort occurred in 2 patients in endoscope group after operation, which was remarkably relieved and disappeared after 3-6 months.

After endoscopic thyroidectomy, the trauma is small, the patients recover quickly, and no scar tissues are formed on the neck. In this study, it was found that the postoperative patients' satisfaction in endoscope group was higher than that in control group, in which there were significantly more patients with 7-10 points than control group, consistent with previous research reports [23,24]. The above findings demonstrate that endoscopic thyroidectomy greatly improves the postoperative cosmetic effect, and reduces the psychological burden of patients, thereby significantly raising the patients' postoperative quality of life.

However, there are deficiencies in this study, such as the limited sample size, shorter follow-up time, and incomprehensive follow-up contents. Therefore, the rigorous, highly-reliable, large-sample prospective clinical research is still needed for the objective evaluation of the efficacy of TET via breast areola approach on early differentiated thyroid cancer.

Conclusions

TET via breast areola approach is safe and effective in the treatment of early differentiated thyroid cancer, and it can achieve a better cos-

metic effect and high satisfaction of patients, which is worthy of clinical application.

Conflict of interests

The authors declare no conflict of interests.

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