Original Article

Effects of laparoscopic and traditional open surgery on the levels of IL-6, TNF-α, and Gal-3 in patients with thyroid cancer

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Background: Traditional open surgery and laparoscopic surgery are common treatments for thyroid cancer patients, this paper aims to explore their effects on the levels of interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), and galectin-3 (Gal-3) in patients with thyroid cancer.

Methods: The clinical data of patients with thyroid cancer who received surgery in our hospital from September 2017 to February 2020 were collected. In total, 106 cases that met the inclusion and exclusion criteria were included. The patients were then allocated into two groups according to the surgery received, including a study group (56 cases treated with endoscopy) and a basic group (50 cases treated with traditional open surgery). Rehabilitation indicators and inflammatory cytokines were compared between the two groups.

Results: There was no significant difference in the number of intraoperative lymph node dissections (P>0.05), postoperative complication rate (16.08% *vs.* 20.00%, P>0.05), and 6-month rate of recurrence or metastasis (P>0.05) between the two groups. Compared to the basic group, the operation time of the study group was longer, while the amount of intraoperative blood loss, 24 h drainage of the catheter and the length of hospital stay were significantly lower in the study group (P<0.05). The pain scores of the study group at 24 and 48 h after surgery were significantly lower than those of the basic group (P<0.05). The levels of IL-6, TNF-α, Gal-3, and other inflammatory factors in the two groups increased on the first day postoperatively, however the levels of these factors in the study group were lower than those in the basic group (P<0.05). Finally, the postoperative cosmetic satisfaction rate of the study group (94.64%) was higher than that of the basic group (86.00%), and the difference was statistically significant (P<0.05).

Conclusions: The use of laparoscopic treatment can reduce the amount of intraoperative blood loss in patients with thyroid cancer, effectively reduce the degree of postoperative pain, and inhibit postoperative inflammation in the patient to a certain extent. Moreover, laparoscopic treatment can increase postoperative cosmetic satisfaction, reduce the occurrence of postoperative complications and recurrence rate, and improve the patient's prognosis.

Keywords: Laparoscopic surgery; traditional open surgery; thyroid cancer; interleukin-6 (IL-6); tumor necrosis factor-α (TNF-α); galectin-3 (Gal-3)

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Introduction

The thyroid gland is mainly composed of follicular epithelial cells and para-follicular epithelial cells, the uncontrolled growth of which may lead to the occurrence of thyroid cancer. Thyroid cancer is a common type of malignant tumor in the head and neck. The main clinical manifestations of thyroid cancer include a lump in the neck with swelling and pain, difficulty when swallowing and breathing, and frequent coughing, etc. (1). According to different cell origins, thyroid cancer can be divided into differentiated thyroid cancer (DTC), thyroid-like cancer, undifferentiated cancer, and other rare types, among which DTC is the most common type, accounting for more than 90% (2). This cancer is common in women; the incidence of thyroid cancer in women in China is approximately three times that of men.

Surgical resection is the main treatment for most thyroid cancers. Traditional open surgery and laparoscopic surgery are common treatments for thyroid cancer patients; both are widely used in clinical settings and both have their advantages, making the choice of surgical method controversial (3,4). Galectin-3 (Gal-3) was characterized as a sensitive indicator for both differentiated and undifferentiated thyroid cancers (5), which could possibly improve the management of patients by reducing unnecessary thyroid surgery. This study explores the effects of laparoscopic and traditional open surgery on the levels of interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), and Gal-3 in patients with thyroid cancer and aims to provide a reference for clinical treatment. We present the following article in accordance with the STROBE reporting checklist (available at http://dx.doi.org/10.21037/gs-21-60).

Methods

General information

The clinical data of patients with thyroid cancer who required surgery and were admitted to our hospital from September 2017 to February 2020 were collected. The inclusion criteria were as follows: (I) all patients that met the diagnostic criteria of the "Guidelines for the Diagnosis and Treatment of Thyroid Cancer (2015 Edition)" (6) and were confirmed by preoperative biopsy; (II) the tumor diameter did not exceed 3 cm; (III) patients with no history of surgery or trauma in a relevant organ; (IV) the tumor was single and there was no cervical lymph node metastasis; and (V) the information was complete, and the patient voluntarily signed the informed consent. The exclusion criteria were as follows: (I) patients with serious diseases in vital organs; (II) patients who were intolerant to surgery and anesthesia; (III) patients with other malignant tumors and systemic infectious diseases; (IV) patients with abnormal coagulation function; and (V) patients with abnormal mental state or poor coordination.

In total, this study included 106 patients who met the inclusion and exclusion criteria. The patients were allocated into two groups according to the surgery received: a study group (56 cases, receiving laparoscopic thyroidectomy) and a basic group (50 cases, receiving open surgery). In the study group, there were 16 males and 40 females, aged between 22 and 43 years, with an average of 30.28±3.16 years. The patients in this group had tumors with a diameter ranging from 1 to 3 cm (average diameter, 1.25±0.97 cm). Based on the pathological types, there were 38 cases with papillary thyroid carcinoma and 18 cases with thyroid follicular carcinoma, and according to the affected side, 30 cases were on the left side and 26 cases were on the right side.

Patients in the basic group were aged between 23 and 42 years, with an average age of 30.56±3.27 years, and a tumor diameter ranging from 1 to 3 cm (average diameter, 1.16±1.02 cm). According to the pathological type, patients in the basic group were divided into papillary thyroid carcinoma (35 cases) and thyroid follicular carcinoma (15 cases), and according to the affected side, 27 cases were on the left side and 23 cases were on the right side. There were no significant differences between the two groups in terms of clinical data such as gender, age, tumor diameter, pathological type, etc. ($P>0.05$).

All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the ethics committee of Sichuan Provincial People's Hospital. Written informed consent was obtained from the patients.

Surgery

Both groups of patients completed preoperative examinations, including lung computed tomography (CT), neck radiography, electrocardiogram, laryngoscopy, thyroid function test, as well as routine blood and biochemical tests, and were fully prepared for the operation.

Traditional open surgery treatment was used for patients in the basic group (7). Specifically, the patient lay in the supine position with the shoulders raised to hyperextend

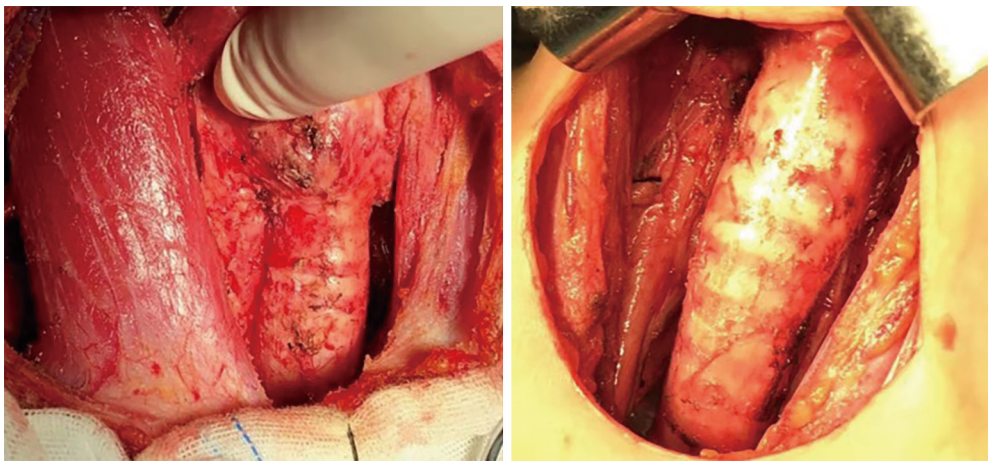

Figure 1 Pictures showing open surgery for thyroid cancer.

the neck. Tracheal intubation was performed for general anesthesia, and the surgical site was then routinely disinfected and draped. A 6-cm arc-shaped incision was then made at the position approximately 3 cm to the suprasternal fossa, and the muscle tissue covering the thyroid lobe was then separated layer by layer, so that the thyroid lobe was fully exposed. Partial or total resection of the affected side of the thyroid gland was performed, the central lymph nodes were cleaned, and a drainage tube was then placed in the wound. The incision was subsequently sutured, and the operation was completed (*Figure 1*).

Laparoscopic thyroidectomy was used for patients in the study group (8). The patient lay in the supine position with the shoulders raised to hyperextend the neck, and the neck was completely exposed to the field of vision. Tracheal intubation was then performed for general anesthesia, and the surgical site was routinely disinfected and draped. Surgical path: breast milk path. Diluted epinephrine was injected into the superficial fascia of the anterior sternum to prevent bleeding. A 10-mm incision was made to the patient's anterior midline of the flat nipple, and the trocar and cavity lens were subsequently inserted. The incision served as the observation point, and carbon dioxide (CO_2) was filled to maintain the operating space. Next, 10 and 7 mm arc incisions were made 5 mm to the upper edge of the areola on both sides, reaching the deep superficial fascia layer. These two incisions served as operating points, and the trocar and cavity lens were placed for surgery. An ultrasonic knife was used to penetrate the deep superficial fascia, and to incise the subcutaneous loose connective tissue to expose the suprasternal fossa and the inner edge of the sternocleidomastoid muscle, and continued to the level of the lower edge of the thyroid cartilage. Subsequently, the ultrasonic knife was then used to separate the anterior neck muscle layer from the neck white line to the affected location and to cut the envelope covering the outer layer of the thyroid. Once the recurrent laryngeal nerve and parathyroid glands were exposed, they were taken care of, and the thyroidectomy was then applied to the affected side. The lymph nodes in the central area were swept and the surgical site was continuously washed with distilled water. After the sternocleidomastoid muscle was thoroughly cleaned, a drainage tube was placed on the upper edge of the areola, and the wound was sutured layer by layer (*Figure 2*).

Observation indicators

Surgery-related indicators

The operation time, intraoperative blood loss, 24 h drainage of the catheter, number of lymph node dissections, and length of hospital stay were recorded by the responsible nurse.

Pain score at different periods after the operation

The main complaint level of pain was used for the grading of pain (9). Specifically, 0–3 points signified that the patient felt pain but could tolerate it, and the pain did not interfere with normal life or sleep; 4–7 points meant that the patient had obvious pain that was unbearable, required medication for pain relief, and sleep was disturbed; 8–10 points denoted that the patient had severe pain and required medication for analgesia, the pain seriously interfered with sleep, and

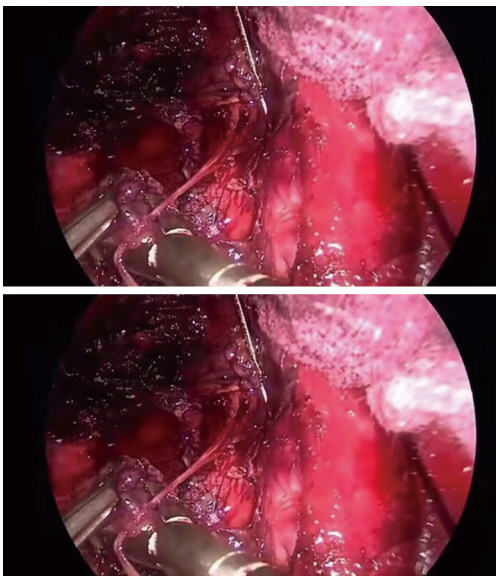

Figure 2 Pictures of the treatment of thyroid cancer with laparoscopic thyroidectomy.

passive posture may appear. Using this scoring system, the patients were evaluated at 24, 48, and 96 h after surgery.

Inflammatory factors

The levels of IL-6 (JL14113), TNF-α (JL10208), and Gal-3 (JL18302), and other inflammatory indicators were measured 96 h before and 36 h after surgery. For all of these measurements, the double antibody sandwich enzyme-linked immunosorbent assay (ELISA) method was used. All kits were provided by Shanghai Jianglai Biotechnology Co., Ltd. (Shanghai, China), and the relevant operations were carried out in strict accordance with the manufacturer's instructions.

Postoperative complications and recurrence

Postoperative complications, including difficulty drinking water, choking, hoarseness, numbness of the limbs, and temporary hypocalcemia, were determined after the operation. Total incidence = sum of all complications/total number of cases × 100%. After discharge from the hospital, all patients were followed up regularly for 6 months. CT was used to check for recurrence, and the recurrence rate was calculated accordingly.

Cosmetic satisfaction

Cosmetic satisfaction, including satisfaction, general satisfaction, and dissatisfaction (10), was also determined. Specifically, satisfaction meant that the incision healed with a small scar, and the incision had no depression or bulge. General satisfaction signified that the patient's incision healed well, the scar was small, and the incision had slight depression or bulge. Dissatisfaction denoted that the patient's incision had not healed well, the scar was large, and the incision had obvious depressions and bulges. Total satisfaction = (number of satisfactory cases + number of general satisfaction cases)/total number of cases ×100%. The patients' evaluation of satisfaction with the operation were collected at the third month of follow-up after discharge.

Statistical analysis

The data in this study were analyzed by SPSS 22.0 software (IBM, US). Count data were expressed as n (%), and the F/*t*-test was used. Measurement data were expressed by the mean ± standard deviation ($\bar{x}\pm s$), and the chi-squared (χ^2) test was used for the comparison of the measurement data. Differences were considered statistically significant when $P<0.05$.

Results

Comparison of the surgical indicators between the two groups

There was no significant difference in the number of lymph node dissections between the two groups ($P>0.05$). The operation time of the study group was longer than that of the basic group, while the amount of blood loss, 24 h drainage of the catheter, and the length of hospital stay were significantly lower in the study group compared to the basic group, and the difference was statistically significant ($P<0.05$, *Table 1*).

Comparison of the pain scores between the two groups at different periods postoperatively

There were no differences in the pain scores between the two groups at 96 h postoperatively ($P>0.05$). However, with time, the pain scores of the two groups gradually decreased, and the pain scores of the study group at 24 and 48 h after surgery were significantly lower than those of the basic group, ($P<0.05$, *Table 2*).

Table 1 Comparison of various surgical indicators between the two groups ($\bar{x}\pm s$)

Indicators	Study group	Basic group	t	P
Cases	56	50	–	–
Operation time (min)	82.69±14.26	63.48±15.58	6.628	0
Blood loss (mL)	48.36±11.06	87.56±12.37	17.226	0
24 h drainage of the catheter (mL)	97.39±29.68	116.59±32.25	3.192	0.002
Number of lymph node dissections	3.31±0.52	3.25±0.67	0.518	0.606
Hospital stay (d)	5.25±0.64	7.82±0.58	21.567	0

Table 2 Comparison of pain scores ($\bar{x}\pm s$, points) between the two groups at different periods after surgery

Groups	Cases	24 h postoperatively	48 h postoperatively	96 h postoperatively	F	P
Study group	56	5.23±1.10	4.02±1.25	3.20±0.73	53.01	0.000
Basic group	50	6.87±1.56	5.42±1.32	3.05±0.61	137.36	0.000
t	–	6.185	5.606	1.140	–	–
P	–	0.000	0.000	0.257	–	–

Table 3 Comparison of serum inflammatory factor levels between the two groups ($\bar{x}\pm s$)

Indicators	Study group	Basic group	t	P
Cases	56	50	–	–
IL-6 (pg/mL)				
Preoperatively	21.38±5.46	20.96±5.32	0.4	0.69
1 d postoperatively	25.67±3.24[a]	29.42±4.82[a]	4.745	0
TNF-α (ng/mL)				
Preoperatively	4.25±1.21	4.32±1.22	0.296	0.768
1 d postoperatively	15.58±3.96[a]	24.66±2.26[a]	14.267	0
Gal-3 (ng/mL)				
Preoperatively	5.56±1.01	5.31±0.98	1.29	0.2
1 d postoperatively	3.64±0.58[a]	4.58±0.88[a]	6.558	0

[a], P<0.05 versus preoperatively.

Comparison of serum inflammatory factor levels between the two groups

There were no significant differences in the levels of IL-6, TNF-α, Gal-3, and other inflammatory factors between the two groups preoperatively (P>0.05). However, 1 day after the operation, the levels of inflammatory factors including IL-6, TNF-α, Gal-3, etc. were increased compared with their preoperative levels. The increased levels of the above indicators were significantly lower in the study group compared to those in the basic group (P<0.05, *Table 3*).

Comparison of postoperative complications and recurrence between the two groups

As shown in *Table 4*, the incidence of postoperative complications in the study group (16.08%) and the basic group (20.00%) was not statistically different (P>0.05). Furthermore, there was no recurrence or metastasis in

Table 4 Comparison of postoperative complications between the two groups [n (%)]

Indicators	Study group	Basic group	χ^2	P
Cases	56	50	–	–
Limb numbness	1 (1.79)	3 (6.00)	0.542	0.462
Coughing during drinking	1 (1.79)	0 (0.00)		
Hoarse voice	2 (3.57)	1 (2.00)		
Hypocalcemia	5 (8.93)	6 (12.00)		
Total incidence (%)	16.08	20		

Table 5 Comparison of postoperative cosmetic satisfaction rate between the two groups [n (%)]

Indicators	Study group	Basic group	χ^2	P
Cases	56	50	–	–
Satisfaction	25 (44.64)	17 (34.00)	4.711	0.03
General satisfaction	28 (50.00)	26 (52.00)		
Dissatisfaction	3 (5.36)	7 (14.00)		
Satisfaction rate (%)	94.64	86		

the two groups of patients during the 6 months follow-up period after discharge.

Comparison of postoperative cosmetic satisfaction rates between the two groups

As shown in *Table 5*, the postoperative cosmetic satisfaction rate of the study group (94.64%) was higher than that of the basic group (86.00%), and the difference was statistically significant (P<0.05).

Discussion

Thyroid cancer is a malignant tumor. An enlarged thyroid or nodules are common symptoms, and manifest as hard nodules of the thyroid, which can move up and down when swallowing. Radiation exposure, viral infection, or family inheritance can all be the triggers for DTC, especially for people with a history of radioactive exposure, and the risk of disease is significantly increased (11). DTC accounts for more than 90% of thyroid cancers. DTC has a relatively low malignancy, and thus its treatment efficacy is more significant; however, cancer cells can often metastasize to the neck, which can aggravate the condition and lead to poor prognostic survival (12). Thyroid cancer resection combined with lymph node dissection can effectively inhibit the development of the patient's disease by removing the tumor tissue, and thereby prolong the patient's disease-free survival.

Laparoscopic surgery and traditional open surgery are widely used in the treatment of thyroid cancer (13,14). However, some studies have found that open thyroidectomy may cause damage to the tissues and nerves around the thyroid. If the recurrent laryngeal nerve is injured, the patient will have persistent hoarseness and difficulty when eating, in addition to other complications, and their long-term recurrence and tumor progression rates remain high (15). It has been found that total laparoscopic thyroidectomy can reduce surgical wounds and improve the cosmetic appearance of the wound following an incision. The results of this study showed that the postoperative cosmetic satisfaction rate (94.64%) of the study group was higher than that of the basic group (86.00%), and the difference was statistically significant (P<0.05), which is consistent with other reports.

Furthermore, the trauma caused by full laparoscopic surgery is small, the anatomical position of nerves and other tissues can be clearly observed during laparoscopic surgery, and the protection of the recurrent laryngeal nerve can also be improved under the pressure of gas (16). Studies have demonstrated that laparoscopic thyroidectomy has a higher rate of complete resection of local thyroid gland tissue, and the dissection of the lymph node area is also relatively complete. The results of this study showed that the amount of intraoperative blood loss, pain at 24 and 48 h postoperatively, and the length of hospital stay were significantly lower in the study group compared to the basic group; however, the overall operation time was longer (P<0.05). These findings suggest that the small wounds of the laparoscopic surgery can effectively reduce the risk of bleeding from the wound, thereby reducing the degree of postoperative pain in patients. However, due to the difficulty of laparoscopic surgery, the operation time will inevitably be longer. This requires that the surgeon practice the operation under the laparoscopy to improve proficiency in order to shorten the operation time and reduce the risk.

Since surgery will cause unavoidable trauma to the patient's body, the inflammatory reaction that occurs at the wound site will cause transient high expression levels of inflammatory factors, such as TNF-α, Gal-3, and IL-6, which are effective indicators to assess the degree of the postoperative inflammatory response in patients (17). IL-6

is a pleiotropic cytokine with a wide range of functions. It participates in the immune response, acute-phase response, and hematopoietic function, and also plays an important role in acute inflammation, such as internal and external trauma, surgery, infection, etc. In these cases, it can be rapidly generated, and thus serves as an indicator for early inflammation in the body (18). TNF-α is a multidirectional pro-inflammatory factor, which participates in the occurrence of the local inflammatory reaction, and is also often used as an index to clinically detect the degree of the inflammatory response in the body (19). Gal-3 can promote angiogenesis, tumor occurrence, and metastasis, and is also a powerful pro-inflammatory factor (20). In this study, by measuring the levels of TNF-α, Gal-3, and IL-6 in patients with thyroid cancer before and after surgery, we observed that the two groups of patients showed an increase in the above-mentioned inflammatory factors on the first day after surgery. This suggests that the patients had an acute postoperative inflammatory response, however the degree of postoperative inflammatory factor increase in the study group was significantly lower than that of the basic group, indicating that laparoscopic surgery can effectively reduce the patient's postoperative inflammatory response. A small number of patients in both groups had postoperative complications, but they were able to relieve themselves or improved following treatment. The absence of recurrence during the 6-month postoperative follow-up period indicates the high safety of laparoscopic surgery (21).

In summary, laparoscopic surgery generates smaller wounds, high cosmetic satisfaction, and can reduce intraoperative blood loss and postoperative pain in patients with thyroid cancer. It can also improve postoperative recovery and shorten hospitalization time. With its high safety, laparoscopic surgery can also effectively suppress the degree of postoperative inflammation in patients.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at http://dx.doi.org/10.21037/gs-21-60

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/gs-21-60). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the ethics committee of Sichuan Provincial People's Hospital. Written informed consent was obtained from the patients.

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