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Original Article

Total versus subtotal thyroidectomy for differentiated thyroid carcinoma and their influence on related indexes

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Abstract: Objective: To evaluate the clinical efficacy of total thyroidectomy (TT) versus subtotal thyroidectomy (ST) in the treatment of differentiated thyroid carcinoma (DTC) and their influence on related indexes. Methods: A total of 120 patients with DTC in Jiangsu Taizhou People's Hospital were enrolled for prospective study. They were randomly allocated into an observation group (n=60) and a control group (n=60). Patients in the observation group were treated with TT, while those in the control group were treated with ST. Related indexes were recorded during and after surgery, and evaluations of clinical efficacy, levels of tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6), neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR), as well as 3-year recurrence and postoperative complications were carried out. Results: Observation group showed shorter surgical duration and less intraoperative blood loss than control group (P<0.05). The total effective rate in observation group was higher than that in control group (91.38% vs 77.97%) (P<0.05). Levels of TNF-α, IL-6, NLR and PLR in the two groups improved significantly after surgery (P<0.05), and the observation group was significantly lower than the control group (all P<0.05). There was no significant difference in 1-year recurrence between the two groups, but the 2-year and 3-year recurrence in observation group were lower than those in control group (P<0.05). The incidence of complications in observation group was higher than that in control group, with no statistical difference (P>0.05). Conclusions: TT is effective in the treatment of DTC, which reduces the levels of inflammatory factors and postoperative recurrence, however, increases the incidence of postoperative complications. Therefore, surgical modality should be carefully selected according to the patient's condition.

Keywords: Total thyroidectomy, differentiated thyroid carcinoma, clinical efficacy, inflammatory factors, prognosis

Introduction

Thyroid carcinoma (TC) is a prevalent malignant tumor in clinic and accounts for 1% of all malignancies, with a higher incidence in women. It is histologically subdivided into differentiated thyroid carcinoma (DTC) and undifferentiated thyroid carcinoma (UTC), of which the proportion of DTC exceeds 90% [1-3]. Owing to the weak metastasis and low malignancy of TC, patients generally have a good prognosis after active treatment [4]. At present, surgery is the preferred option for the treatment of DTC that prolongs the survival of patients [5, 6] and achieves a 10-year survival rate of 70% [7]. However, the recurrence rate after surgery ranges from 1.4% to 35%, showing the instability [8]. Total thyroidectomy (TT) and subtotal thyroidectomy (ST) are two main surgical treatments for DTC, but their selection is still controversial [9-11]. On the one hand, TT has a larger operation range and more thorough resection of lesions and peripheral metastases than ST, thereby resulting in a lower postoperative recurrence, however, a higher incidence of peripheral nerve injury [12]. On the other hand, ST is associated with fewer complications and higher quality of life, and there is no statistical difference in postoperative recurrence compared with TT [13]. This study is designed to explore the clinical efficacy of ST and TT and their impact on related indexes.

Materials and methods

General data

A total of 120 patients with DTC, aged 20-74 years and averagely aged 41.4±8.7 years, who were admitted to the General Surgery Depart-

ment of Jiangsu Taizhou People's Hospital from May 2014 to May 2017, were enrolled for prospective study. They were allocated into an observation group and a control group with 60 cases each. Patients averagely aged 41.4±9.6 years in observation group were treated with TT, whereas those averagely aged 41.3±7.8 years in control group received ST. All patients were followed up for a long time after surgery and signed the informed consent. The study was approved by the Ethics Committee of Jiangsu Taizhou People's Hospital.

Inclusion and exclusion criteria

Inclusion criteria: (1) Following guidelines for patients with thyroid nodules and differentiated thyroid cancer (2012 Chinese edition) [14]; (2) Aged 18-75 years old. Exclusion criteria: (1) Patients with surgery intolerance; (2) Patients with severe heart, liver and kidney diseases; (3) Patients with declined quality of life induced by mental disorders or cerebrovascular diseases; (4) Patients with severe coagulation disorder; (5) Patients lost to follow-up or not suitable for surgery.

Surgical procedure

(1) Observation group: After general anesthesia, patients were placed in a supine position. A 7 cm curved incision was made two fingers above the sternal notch. The skin flap was separated from the anterior cervical muscles to fully expose the thyroid. Suspensory ligament of the thyroid was severed. The upper, middle and lower blood vessels were ligated. Afterwards, the dorsal side of the thyroid was fully exposed. Without damaging the recurrent laryngeal nerve, the glandular lobe, isthmus and contralateral glandular lobe on the affected side were resected, then lymph nodes were removed from the lesion area. Next, debridement and drainage tube placement were performed and the wounds were sutured layer by layer.

(2) Control group: Operations of anesthesia, body position, incision position, and tissue separation were the same as those in the observation group. Most of anterior thyroid glands and isthmus were removed, and dorsal glands and capsule tissues were preserved. Afterwards, the lymph nodes were removed from the lesion area. Next, debridement and drainage tube placement were performed and the wounds were sutured layer by layer.

Requirements are as follows to ensure the quality of surgery: (1) All surgeries were performed by experienced surgeons; (2) Same suture material and drainage tube were used for the same surgery; (3) Both groups adopted the same treatment and nursing plan before and after surgery; (4) Intraoperative bleeding was controlled timely, incisions were routinely treated after surgery to prevent infection, and thyroid hormone replacement therapy was performed; (5) Both groups shared the same follow-up plan.

Patients included in this study were followed up in outpatient clinic for one month after surgery, and those in stable condition were followed up every three months. Relevant indexes were reexamined and the recurrence of patients was monitored. The follow-up ended in May, 2020.

Outcome measures

Main outcome measures: (1) Surgical duration: From skin incision to skin closure. (2) Intraoperative blood loss: From the beginning of surgery to the end of surgical suture. (3) Postoperative hospital stay: From hospitalization after surgery to discharge. (4) Drainage tube removal time: From drainage tube placement to its removal. (5) Evaluation of efficacy: Classified as markedly effective, effective, and ineffective following Guidelines for Prevention and Treatment of Thyroid Diseases. Manifestations of TC: Pain in the mass, tracheal compression, dysphagia, Horner's syndrome. Markedly effective: Complete disappearance of symptoms after surgery; Effective: Significant improvement of symptoms after surgery; Ineffective: No improvement of symptoms after surgery. Total effective rate = (markedly effective cases + effective cases)/total number of cases * 100%. (6) Determinations of inflammatory factors: 5 mL of fasting venous blood was collected at admission and at 8:00 a.m. 7 days after surgery, then stored in sterile tubes containing ethylenediamine tetraacetic acid (EDTA). Serum separated by centrifuge was added with 40 μL phosphate buffer containing protease inhibitor (Tongwei Biotechnology Co., Ltd., Shanghai, China), and the serum tumor necrosis factor (TNF)-α, interleukin (IL)-6, were deter-

Table 1. Comparison of general data and baseline data

Item	Observation group (n=58)	Control group (n=59)	χ^2/t	P
Age (year)	41.4±9.6	41.3±7.8	0.062	0.951
Gender (male/female)	20/38	24/35		
Types of cancer				
Papillary thyroid carcinoma (case)	55	57	0.227	0.634
Follicular thyroid carcinoma (case)	3	2		
Tumor size (cm)	4.79±1.59	4.68±1.47	0.389	0.698
Body mass index (kg/m^2)	22.58±2.48	22.69±2.75	0.227	0.821
Comorbidity				
Hypertension (case)	12	13	0.031	0.859
Type 2 diabetes (case)	14	12	0.244	0.621
Hyperlipidemia (case)	10	9	0.085	0.771
Obesity (case)	11	11	0.002	0.956
Average follow-up months (month)	41.2±7.5	40.2±8.3	0.683	0.496

Table 2. Comparison of intraoperative and postoperative related indexes

Item	Observation group (n=58)	Control group (n=59)	t	P
Hospital stay (d)	6.5±1.3	6.4±1.2	0.432	0.666
Surgical duration (min)	71.69±12.78	108.39±20.39	11.641	<0.001
Intraoperative blood loss (mL)	51.38±10.89	88.54±15.34	15.092	<0.001
Drainage tube removal time (d)	3.9±1.2	3.7±1.3	0.864	0.389

mined by enzyme-linked immunosorbent assay (ELISA). Routine blood test was performed by the Beckman Coulter LH 750 (ABC, USA). NLR = neutrophil/lymphocyte ratio and PLR = platelet/lymphocyte ratio.

Secondary outcome measures: (1) Postoperative recurrence: All patients were followed up for a long time, and thyroid color Doppler ultrasound and CT were carried put at the 1st, 2nd and 3rd year and the recurrence time and cases were recorded. (2) Postoperative complications: Incidence of parathyroid injury, hypocalcemia, hoarseness and recurrent laryngeal nerve injury was monitored.

Statistical methods

SPSS 22.0 statistical software was employed for data processing. Continuous variables were expressed by mean ± standard deviation ($\bar{x}$ ± sd). Data with normal distribution and homogeneity of variance were analyzed by t test (denoted by t). Intra-group comparisons were conducted with paired samples t test, and inter-group comparisons were conducted with independent samples t test. Pearson chi-square test was performed on the counting data (denoted as chi-square). A value of $P<0.05$ was considered to be statistically significant.

Results

Comparison of general data and baseline data

Of the 120 patients, 58 cases in observation group (2 lost to follow up) and 59 cases (1 lost to follow up) in control group were finally included in the study. There was no statistical difference in age, sex, cancer type, tumor size, body mass index, comorbidity, and average follow-up months between the two groups (P> 0.05), as shown in **Table 1**.

Comparison of intraoperative and postoperative indexes

There was no significant difference in hospital stay and drainage tube removal time between the two groups, but the surgical duration and intaoperative blood loss in observation group were lower than those in control group (P< 0.001), as shown in **Table 2**.

Comparison of curative efficacy

The total effective rate in observation group was significantly higher than that in control

Table 3. Comparison of curative efficacy

Item	Cure	Effective	Invalid	Total effective rate (%)
Observation group (n=58)	41 (70.69)	12 (20.69)	5 (8.62)	91.38
Control group (n=59)	29 (49.15)	17 (28.81)	13 (22.03)	77.97
χ^2		6.467		4.042
P		0.039		0.044

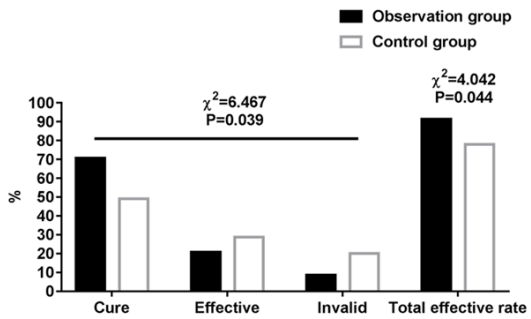

Figure 1. Comparison of curative efficacy.

group (91.38% vs 77.97%) (P<0.05), as shown in **Table 3** and **Figure 1**.

Comparison of inflammatory factors

There was no significant difference in TNF-α, IL-6, NLR and PLR between the two groups before surgery (P>0.05), but the levels improved significantly after surgery (P<0.05), and the observation group was remarkably lower than the control group (P<0.01), as shown in **Table 4**.

Comparison of 3-year recurrence

There was no significant difference in 1-year recurrence between the two groups, but the 2-year and 3-year recurrence in observation group were lower than those in control group (P<0.05), as shown in **Table 5**.

Comparison of postoperative complications

The incidence of complications in observation group was higher than that in the control group, however, with no statistical difference (P>0.05), as shown in **Table 6**.

Discussion

Surgical treatments are effective in improving the survival of patients with DTC [15]. As common surgical modalities, TT and ST have their own advantages and disadvantages. This present study shows that TT is superior to ST in terms of surgical duration and intraoperative blood loss, which may be related to the total resection of thyroid in TT and separation and retention of dorsal glands in ST.

Further study on the clinical efficacy turned out that the total effective rate in TT group was higher than that in ST group. There is a previous study reveals that the total effective rate of TT is 93.33%, higher than 68.89% of ST, which is consistent with our results [16]. However, another study comes to a conclusion diametrically opposed to ours (76.0% vs 98.0%) [13].

Inflammation plays an important role in DTC and autoimmune thyroiditis. In inflammatory microenvironment, it works together with diseased cells to accelerate the progression of diseases and adversely affect the prognosis [17, 18]. TNF-α regulates cell migration during inflammation and promotes tumor cell production, as well as simulates tumour angiogenesis. TNF-α exerts anti-infection effects and regulates inflammatory response in tissue repair at low concentration. When the concentration increases, the body's immunity is destroyed, leading to activated neutrophils, enhanced phagocytosis of leukocytes, large secretion of inflammatory factors, and increased vascular permeability [19]. IL-6 is one of the inflammatory factors that regulates immunity and promotes proliferation of epithelial cells and fibroblasts, thereby accelerating tumour progression. And there is evidence that IL-6 increases in patients with DTC due to disordered autoimmune and the imbalance of T and B cells [20]. NLR and PLR are markers of immune activity in human body and are closely related to the disease severity and prognosis of cancer patients [21, 22]. Decreased lymphocytes and increased neutrophils make the NLR rise [23]. Platelets secrete vascular endothelial growth factors to induce the proliferation and migration of endothelial cells, and to increase the permeability of tissues and cells, so as to promote the proliferation and migration of tumor cells in vivo. Moreover, they can release and activate various factors and stimulate the differentiation and proliferation of tumour cells

Table 4. Comparison of inflammatory factors

Item	TNF-α (pg/mL)	IL-6 (pg/mL)	NLR	PIR
Before surgery				
Observation group (n=58)	971.46±202.48	182.34±30.78	2.05±0.42	123.87±13.68
Control group (n=59)	972.58±203.67	180.26±31.24	2.03±0.45	125.69±14.27
t	0.030	0.363	0.248	0.704
P	0.976	0.718	0.804	0.483
After surgery				
Observation group (n=58)	507.14±103.68#	78.01±15.90#	1.47±0.36#	112.39±10.69#
Control group (n=59)	631.47±124.25#	102.66±20.14#	1.69±0.39#	118.54±11.21#
t	5.872	7.341	3.169	3.036
P	<0.001	<0.001	0.002	0.003

Note: Compared with before treatment in the same group, #P<0.05. NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; TNF-α: tumor necrosis factor-α; IL-6: interleukin-6.

Table 5. Comparison of 3-year recurrence

Item	1-year recurrence	2-year recurrence	3-year recurrence
Observation group (n=58)	0 (0.00)	1 (1.72)	2 (3.45)
Control group (n=59)	2 (3.39)	8 (13.56)	10 (16.95)
χ^2	2.000	5.770	5.729
P	0.157	0.016	0.016

Table 6. Comparison of postoperative complications

Postoperative complications	Observation group (n=58)	Control group (n=59)	χ^2	P
Parathyroid injury	1 (1.72%)	0 (0.00%)	1.206	0.311
Hypocalcemia	3 (5.17%)	1 (1.69%)	1.701	0.301
Hoarse voice	3 (5.17%)	2 (3.39%)	0.227	0.634
Recurrent laryngeal nerve injury	2 (3.45%)	0 (0.00%)	2.070	0.150
Total number of cases	9 (15.52%)	3 (5.08%)	3.458	0.063

[24]. In this present study, TNF-α, IL-6, NLR and PLR in observation group decreased significantly after surgery, suggesting that TT can more thoroughly remove lesions and reduce serum inflammatory factors, as well as inhibit tumor differentiation and facilitate the postoperative recovery of immune function.

Postoperative recurrence is common in TC. Complete resection of lesions and potential metastases by TT effectively reduces the recurrence and avoids secondary surgery [25]. Since 60% of patients with DTC have lesions on both sides, it is believed that ST is unable to completely removeall lesions and is prone to postoperative recurrence. In addition, tissue adhesion after recurrence is not conducive to the implementation of secondary surgery, resulting in postoperative adverse reactions [26]. TT is superior to ST in reducing the incidence of local recurrence and distant metastasis of tumors and increasing the long-term survival of patients with TC [27, 28]. After a 3-years follow-up, it was found that the 2-year and 3-year recurrence of TT were lower than that of ST, indicating that TT is effective in decreasing postoperative recurrence, which is consistent with the above results.

In terms of postoperative complications, TT, a crippling procedure [29], may induce complete loss of thyroid function and parathyroid and recurrent laryngeal nerve injuries [30, 31]. Disorders of calcium and phosphorus metabolism are likely to occur after parathyroid injury, and recurrent laryngeal nerve injury causes hoarseness. The incidence of complications after TT is higher than that after ST, contrary to our findings (with no statistical difference), which may be related to the small sample size enrolled [32].

To sum up, TT is effective in the treatment of DTC, which reduces the levels of inflammatory factors and postoperative recurrence, however, increases the incidence of postoperative

complications. Therefore, surgical modality should be carefully selected according to the patient's condition.

Disclosure of conflict of interest

None.

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