JBUON 2019; 24(2): 813-818
ISSN: 1107-0625, online ISSN: 2241-6293 • www.jbuon.com
E-mail: editorial_office@jbuon.com

ORIGINAL ARTICLE

Analysis of risk factors for postoperative recurrence of thyroid cancer

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Summary

Purpose: *The study was designed to analyze the risk factors related to postoperative recurrence of thyroid cancer to reduce the recurrence rate.*

Methods: *A total of 250 patients with thyroid cancer after operation were collected and divided into non-recurrent group (n=220) and recurrent group (n=30) according to whether the cancer recurred after operation or not. The postoperative recurrence rate of thyroid cancer was analyzed. The general condition, tumor characteristics, surgical approach, conditions of postoperative I^{131} treatment and pathological type of the two groups of patients were compared. The correlations of the postoperative recurrence of thyroid cancer with clinical risk factors were analyzed by means of Logistic regression analysis.*

Results: *The recurrence rate of thyroid cancer after operation was 12%, and the cumulative recurrence rates at 1, 2 and 3 years after operation were 3.20%, 6.00% and 10.40%, respectively. The recurrence rate in males was higher than that in females ($p<0.05$). The larger tumor diameter, the lower rate of lymph node metastasis and the lower level of tissue differentiation would eventually lead to the higher recurrence rate ($p<0.01$). Tumor diameter, lymph node metastasis and pathological type were correlated with the postoperative recurrence of thyroid cancer ($p<0.05$).*

Conclusion: *Gender, tumor diameter, lymph node metastasis and pathological type are risk factors for recurrence after thyroidectomy.*

Key words: *postoperative recurrence, risk factors, thyroid cancer*

Introduction

Thyroid cancer is a common malignant tumor of the head and neck, whose incidence rate is increasing gradually in recent years [1]. It is mainly treated by operations, but the surgical treatments can hardly dissect the cancer tissues and cervical lymph nodes thoroughly due to the complex anatomic structure of the thyroid gland, thus leading to easy recurrence after operation [2, 3]. According to epidemiologic investigations, the postoperative recurrence rate of thyroid cancer is up to 23-30%, indicating that the recurrence risk of the disease cannot be underestimated [4]. Therefore, analyzing the risk factors for the postoperative recurrence of thyroid cancer is conducive to the early screening of patients with high recurrence risk of thyroid cancer after operation, and the risk factors need intervention and treatment as early as possible, so as to improve the cure rate of thyroid cancer.

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Received: 27/08/2018; Accepted: 24/09/2018

Methods

Participants included

A total of 250 patients with thyroid cancer confirmed by pathology, who received radical thyroidectomy in Department of Otorhinolaryngology, Head and Neck Surgery of the First Affiliated Hospital of Xiamen University from June 1, 2012 to December 31, 2017, were selected. Inclusion criteria: 1) patients aged ≥18 years old, 2) patients undergoing operations for thyroid cancer, including total thyroidectomy, subtotal thyroidectomy and ipsilateral lobe plus isthmus resection, who were definitely diagnosed by pathology, 3) patients not complicated with cardiac, hepatic and renal dysfunctions, 4) patients without other malignant tumors, and 5) patients who had complete clinical data and cooperated in follow-up. All the patients were divided into non-recurrent group (n=220) and recurrent group (n=30) according to whether the cancer recurred after operation or not. There were 35 males and 185 females in the non-recurrent group, with an average age of (45.42±8.56) years old. The recurrent group included 12 males and 18 females with an average age of (44.21±7.92) years old. Patients in both groups signed the informed consent, which was approved by the Ethics Committee of the hospital.

Research methods

The information of the patients undergoing radical thyroidectomy was retrospectively collected and sorted from the case management system of the hospital, including name, gender, age, body mass index (BMI), educational level, tumor size, lymph node metastasis, distant metastasis, tumor stage, surgical approach, lymph node dissection, postoperative I^{131} treatment, pathological type and other possible factors influencing the recurrence of thyroid cancer.

Follow-up

The patients were followed up mainly through outpatient department and telephone and reexamined once every month in the first year after operation, and then followed up and reexamined once every 3 months to obtain the recurrence conditions and recurrence-free survival of the patients. The time of surgical treatments for the patients was regarded as the starting point of observation, and the recurrence of thyroid cancer in the patients was regarded as the end-point event. The cutoff date for observation was December 31, 2017. The patients who did not have recurrent thyroid cancer during follow-up were divided into the non-recurrent group, while those who had recurrent thyroid cancer after operation were enrolled into the recurrent group. As for the patients with recurrence, the recurrence-free survival referred to the duration from the starting point of observation to the end-point event. For the patients without recurrence, the recurrence-free survival referred to the duration from the starting point of observation to the cutoff date of observation.

Statistics

SPSS 20.0 software (IBM, Armonk, NY, USA) was adopted for statistical analysis, and chi-square test was performed for comparisons of risk factors between the two groups. The recurrence rate was analyzed by means of Kaplan-Meier, and the survival curve for recurrence was plotted. Logistic regression analysis was applied to analyze the correlations of the postoperative recurrence of thyroid cancer with the clinical risk factors. P<0.05 suggested that the difference was statistically significant.

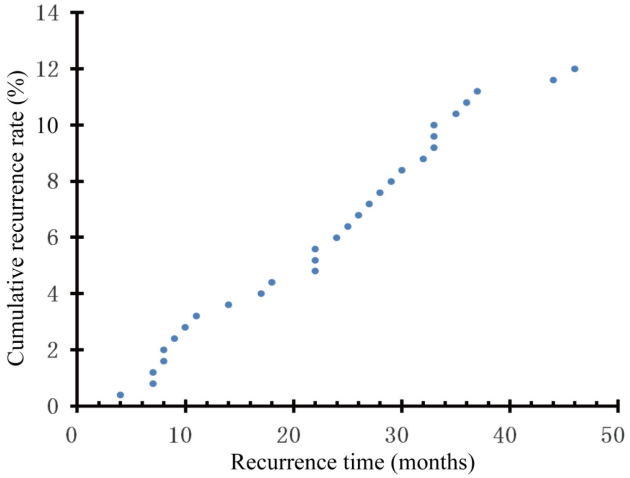

Figure 1. Kaplan-Meier survival curve for recurrence in patients with thyroid cancer.

Results

Postoperative survival analysis

The follow-up time was 1-54 months from the date of operation accomplished to December 31, 2017, and the median follow-up time was 36 months. During follow-up, there were 30 cases of postoperative recurrence of thyroid cancer, with a recurrence rate of 12.00%. The cumulative recurrence rates of thyroid cancer at 1, 2 and 3 years after operation were 3.20%, 6.00% and 10.40%, respectively. The survival curve for recurrence is shown in Figure 1.

Comparisons of general data

There was a difference in the recurrence rate of thyroid cancer in terms of gender between the two groups (p<0.01), of which males had a higher recurrence rate than females (Table 1).

Comparisons of tumor characteristics

There recurrence rate of thyroid cancer had differences in the comparisons of tumor size and existence of lymph node metastasis between the two groups (p<0.01). A larger tumor diameter indicated a higher recurrence rate, and the recurrence

rate was also higher in the case of complication of lymph node metastasis (Table 2).

Comparison of surgical approaches

There was no difference in the recurrence rate of thyroid cancer in the aspect of surgical approaches between the two groups (p>0.05) (Table 3).

Comparison of postoperative I^{131} treatment

There was no difference in the recurrence rate of thyroid cancer regardless of whether I^{131} treatment was conducted after operation or not between the two groups (p>0.05) (Table 4).

Comparison of pathological type

There were differences in the recurrence rate of thyroid cancer in terms of pathological types between the two groups (p<0.01), of which undifferentiated carcinoma had the highest recurrence rate (Table 5).

Multivariate correlation analysis for postoperative recurrence

According to the analysis results in Tables 1-5, a total of 4 risk factors with statistical significance were included in the multivariate logistic regression analysis. Such risk factors as tumor diameter,

Table 1. Comparisons of general clinical data between the two groups of patients

Data	*n*	*Non-recurrent group n=220, n (%)*	*Recurrent group n=30, n (%)*	*Recurrence rate (%)*	x^2	*p*
Gender					10.037	0.002
Male	47	35 (74.47)	12 (25.53)	25.53		
Female	203	185 (91.13)	18 (8.87)	8.87		
Age (years)					0.000	0.987
<45	108	95 (87.96)	13 (12.04)	12.04		
≥45	147	125 (85.03)	17 (11.57)	11.56		
BMI ($kg \times m^{-2}$)					0.009	0.996
≤24	90	79 (87.78)	11 (12.22)	12.22		
24-28	127	112 (88.19)	15 (11.81)	11.81		
≤28	33	29 (87.88)	4 (12.12)	12.12		
Educational level					0.150	0.985
Elementary school and below	65	57 (87.69)	8 (12.31)	12.31		
High school	119	105 (88.24)	14 (11.76)	11.76		
College	37	33 (89.19)	4 (10.81)	10.81		
Undergraduate and above	29	25 (86.21)	4 (13.79)	13.79		

Table 2. Comparisons of tumor characteristics between the two groups of patients

Characteristics	*n*	*Non-recurrent group n=220, n (%)*	*Recurrent group n=30, n (%)*	*Recurrence rate (%)*	x^2	*p*
Tumor diameter (cm)					22.187	0.000
≤1	27	25 (92.59)	2 (7.41)	7.41		
1-4	199	181 (90.95)	18 (9.05)	9.05		
≥4	24	14 (58.33)	10 (41.67)	41.67		
Lymph node metastasis					47.924	0.000
Yes	49	29 (59.18)	20 (40.82)	40.82		
No	201	191 (95.02)	10 (4.98)	4.98		
Distant metastasis					0.011	0.915
Yes	40	35 (87.50)	5 (12.50)	12.50		
No	210	185 (88.10)	25 (11.90)	11.90		
Tumor stage					0.145	0.986
Stage I	52	45 (86.54)	7 (13.46)	13.46		
Stage II	67	59 (88.06)	8 (11.94)	11.94		
Stage III	88	78 (88.64)	10 (11.36)	11.36		
Stage IV	43	38 (88.37)	5 (11.63)	11.63		

lymph node metastasis and pathological type were correlated with the postoperative recurrence of thyroid cancer (p<0.05) (Table 6).

Discussion

As a common kind of endocrine malignant tumor, thyroid cancer accounts for 1-3% of the malignant tumors. Epidemiologic investigations have revealed that the incidence rate of thyroid cancer increased by nearly 3 times from 4.9/100,000 in 1975 to 14.3/100,000 in 2009 in the USA, which is rising year by year along with the improvement of living standards [5]. The thyroid tissues contain abundant blood vessels and lymphatic vessels, through which tumors are prone to metastasize. In spite of the generally good prognosis of thyroid cancer after operation, some patients still have recurrence and metastasis after operation, and the postoperative recurrence is the leading cause of the patient's death [6]. The study of Lote et al. [7] indicated that the recurrence rate of lymph node metastasis within 10 years after operation for thyroid cancer is as high as 15-25%, while in this study, the recurrence rate after operation for thyroid cancer was 12.00%. The high recurrence rate after thyroidectomy may be related to the preoperative examinations such as computed tomography (CT), magnetic resonance imaging (MRI) and radionuclide scan of the thyroid gland, which are unable to completely detect the cancer lesion scope and distinguish the conditions of lymph node metastasis, so the lesion cannot be cleaned thoroughly. Therefore, long-term standardized follow-up of patients with thyroid cancer after operation can discover the recurrence and metastasis to facilitate early

Table 3. Comparison of surgical approaches between the two groups of patients

Surgical approach	*n*	*Non-recurrent group n=220, n (%)*	*Recurrent group n=30, n (%)*	*Recurrence rate (%)*	x^2	*p*
Total thyroidectomy	143	127 (88.81)	16 (11.19)	11.19		
Subtotal thyroidectomy	68	63 (92.65)	5 (7.35)	7.35		
Ipsilateral lobe plus isthmus resection	39	31 (79.49)	8 (20.51)	20.51	4.241	0.120
Cervical lymph node dissection					0.141	0.708
Yes	74	66 (89.19)	8 (10.81)	10.81		
No	176	154 (87.50)	22 (12.50)	12.50		

Table 4. Comparison of postoperative I^{131} treatment between the two groups of patients

Postoperaive I^{131} treatment	*n*	*Non-recurrent group n=220, n (%)*	*Recurrent group n=30, n (%)*	*Recurrence rate (%)*	x^2	*p*
Yes	45	40 (88.89)	5 (11.11)	11.11		
No	205	180 (87.80)	25 (12.20)	12.20	0.041	0.839

Table 5. Comparison of pathological type between the two groups of patients

Factor	*n*	*Non-recurrent group n=220, n (%)*	*Recurrent group n=30, n (%)*	*Recurrence rate (%)*	x^2	*p*
Papillary carcinoma	164	153 (93.29)	11 (6.71)	6.71		
Follicular carcinoma	34	26 (76.47)	8 (23.53)	23.53		
Medullary carcinoma	33	32 (96.97)	1 (3.03)	3.03		
Undifferentiated carcinoma	19	9 (47.37)	10 (52.63)	52.63	40.849	0.000

Table 6. Multivariate logistic regression analysis of postoperative recurrence of thyroid cancer

Risk factors	*β*	*Standard error*	*Wald/x^2*	*OR*	*p*
Gender	0.701	0.498	1.207	2.324	0.412
Tumor diameter	1.279	0.617	4.398	3.679	0.042
Lymph node metastasis	-2.472	0.456	17.279	0.089	0.000
Pathological type	1.032	0.545	5.792	3.256	0.040

treatment. Meanwhile, according to the follow-up results, the risk factors related to recurrence and metastasis can also be summarized and analyzed, and early intervention and treatment can be provided, thereby improving the treatment effects of operation for thyroid cancer.

In this research, the retrospective case-control analysis results showed that the postoperative recurrence rate of thyroid cancer in men was higher than that in women, while multivariate Logistic regression analysis indicated that it was not associated with gender differences. These results are in line with the findings of Lin [8], Cunningham [9], Kruijff [10], et al., illustrating that male patients are more vulnerable to the postoperative recurrence of thyroid cancer, and the high recurrence rate is possibly correlated with the effects of estrogen, which regulates the proliferation of thyroid cells and affects the invasiveness and prognosis of thyroid cancer by binding to estrogen receptor α (ERα) and ERβ [11-13]. Therefore, more active treatments should be performed for male patients. In addition, both analysis of variance and multivariate logistic analysis in this research discovered that the postoperative recurrence of thyroid cancer had close correlations with tumor diameter, lymph node metastasis and pathological type of tumor, which is consistent with the findings of a majority of scholars [14-18]. When the tumor diameter is <1 cm, the infiltration of cancer cells is inhibited, so metastasis and recurrence are not easy to occur. As the tumor keeps growing with a larger diameter, the incidence rate of central cancer lesion becomes higher, and the risk of capsule infiltration and lymph node metastasis is also elevated, so it is even harder to completely remove the lesion by means of operations, ultimately resulting in higher postoperative recurrence rate of thyroid cancer [18,19]. The patients with lymph node metastasis have a higher postoperative recurrence rate than those without lymph node metastasis. Yang et al. [20] believe that the existence of lymph node metastasis implies the increased number of occult lesions of thyroid cancer, so the postoperative recurrence rate of the disease is higher. As a result, it is suggested that preventive neck dissection be performed for the patients with lymph node metastasis. The undifferentiated carcinoma tissues have a low grade of differentiation, but their malignancy is higher than that of other types of tumor, thus increasing the difficulty of surgical treatments and the incidence rate of postoperative recurrence. Hence more attention should be paid to the postoperative treatment and follow-up of undifferentiated carcinoma.

The postoperative recurrence of thyroid cancer is the primary cause of death from the disease. Moreover, reoperations after its recurrence can cause serious injuries to the patient's physical and mental health. Therefore, accurate preoperative assessment of thyroid cancer should be conducted, the treatment protocols should be optimized, and close follow-up and active treatment should be adopted for high-risk patients who are male and are accompanied by large tumor diameter and lymph node metastasis, hoping to reduce the postoperative recurrence rate of thyroid cancer. Furthermore, other factors in this research were not correlated with the postoperative recurrence of thyroid cancer, which may be related to the limited number of patients enrolled. Hence, the sample size will be increased in further investigations, and multicenter studies will be conducted.

Conclusions

As shown in the present report, gender, tumor diameter, lymph node metastasis and pathological type are risk factors for recurrence after thyroidectomy.

Conflict of interests

The authors declare no conflict of interests.

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