



An Analysis of Clinical and Pathological Characteristics of 14431 Cases of Thyroid Carcinoma

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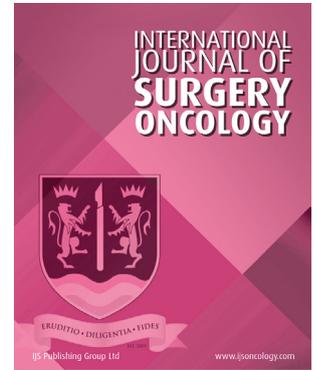
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ABSTRACT

Objective: To retrospectively analyze the clinicopathological characteristics of thyroid cancer patients with respect to age, gender, benign lesions, and lymph node metastasis and to explore the clinicopathological features of multifocal and unifocal papillary thyroid carcinoma with cervical lymph node metastasis.

Methods: The clinicopathological data of 14,431 patients with thyroid cancer who underwent surgical treatment for the first time in the Department of Head and Neck Oncology of our hospital from January 2011 to December 2015 were collected, analyzed, and compared in terms of age, gender, pathological type, benign lesions, and lymph node metastasis.

Results: Among 14431 cases, there were 3259 males and 11172 females, with a male-to-female ratio of 1:3.43. Patients aged 30–59 years accounted for 82.15%. The number of thyroid cancer cases showed an increasing trend year by year ($P < 0.001$), and papillary carcinoma was the most common (98.47%). Among 14,210 patients with papillary thyroid carcinoma, 4736 cases were in the multi-focus group and 9474 cases were in the single-focus group. Comparison of the pathological characteristics between the two groups showed that the multi-focus group had a higher probability of lymph node metastasis ($P < 0.001$). A single-focus combination of papillary thyroid carcinoma with benign lesions was more common ($P < 0.001$), and the difference was statistically significant. Among the cases of multifocal papillary thyroid carcinoma, there were 2812 cases in the multifocal papillary thyroid carcinoma group, and 1924 cases in the unilateral and/or isthmus group. The analysis showed that there were more males, younger patients, more patients with benign lesions, and a higher incidence of unilateral microcarcinoma in the unilateral and/or isthmus multifocal thyroid carcinoma group ($P = 0.017$). $p < 0.001$, $p < 0.001$, and $p < 0.001$, respectively). There were more patients with cervical lymph node metastasis in the bilateral multifocus group ($p = 0.016$), and the difference was statistically significant.



CASE CONTROL STUDY



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Conclusion: Multiple lesions are one of the clinical features of papillary thyroid carcinoma, which are more prone to cervical lymph node metastasis and more aggressive than single lesions.

BACKGROUND

Thyroid carcinoma (TC) is one of the most common cancers in head and neck cancer worldwide, affecting people in both developing and developed countries, with an incidence of 600,000 new cases diagnosed annually [1–3]. Since the 21st century, the incidence of TC has increased every year, owing to the development of the economy, improvement of medicine, changes in diet structure, ecological environment, and other factors, which have made TC become the fastest growing malignant tumor [4, 5]. Multiple studies have shown that isthmus PTC is more aggressive and is associated with poor prognosis, and its characteristics include multifocal, capsule invasion, extrathyroid extension and lymph node metastasis [6]. Early identification of patients with advanced or high-risk PTC who require more aggressive evaluation may help reduce morbidity and increase life expectancy. In this study, 14431 cases of TC patients diagnosed with TC, the clinical and pathological characteristics were analyzed to provide information for clinical diagnosis and treatment.

MATERIALS AND METHODS[7]

PATIENTS' CHARACTERISTICS

We retrospectively analyzed the data of 14431 patients who underwent thyroidectomy between January 2011 and December 2015 from Tianjin Medical University Cancer Institute and Hospital. The exclusion criteria were as follows: 1) non-diagnostic or incomplete data, 2) recurrent cancer, and 3) metastatic thyroid cancer. The final subject population was composed of 3259 men and 11172 women (male to female ratio of 1:3.43), with a mean age of 45.83 ± 10.83 years (range: 6–85 years). Among the 14431 patients, papillary carcinoma accounted for 98.47% (14210 cases), follicular carcinoma accounted for 0.25% (36 cases), medullary carcinoma accounted for 0.73% (106 cases), poorly differentiated carcinoma accounted for 0.14% (21 cases), squamous cell carcinoma accounted for 0.11% (16 cases), malignant lymphoma accounted for 0.17% (25 cases), others accounted for 0.12% (17 cases).

ETHICAL APPROVAL

Name of body giving ethical approval: Medical Ethics Committee of Airport Hospital, Tianjin Cancer Hospital; Approval number: LWK-2022-0003.

STATISTICAL ANALYSIS

The clinical and pathological characteristics were compared annually. For data analysis, we used SPSS20.0 for Microsoft Windows Software. Chi-square test or Chi-square trend test was used for comparison of count data, and ($x \pm s$) was used for measurement data. T-test or non-parametric test was used for comparison between groups. All statistical results were considered statistically significant with $p < 0.05$.

RESULTS

The pathological features of the patients are summarized in Table 1. 14431 patients fulfilled the inclusion criteria, including 14210 (98.47%) papillary carcinoma cases, 36 (0.25%) follicular carcinoma cases, 106 (0.73%) medullary carcinoma cases, 21 (0.14%) undifferentiated carcinoma cases, 16 (0.11%) squamous carcinoma cases, 25 (0.17%) malignant lymphomas cases, and 17 (0.12%) other cases. From 2011 to 2015, the number of surgical cases of TC increased annually ($Z = 37.183$, $P < 0.000$), the incidence and constituent ratio of papillary carcinoma showed an increased trend ($Z = 41.239$, $P < 0.000$). In contrast, the incidence of medullary cancer declined ($Z = 11.667$, $P = 0.001$) and that of follicular cancer was relatively stable ($P = 0.075$).

The distributions of age and sex are shown in Table 2. The mean age was 45.83 ± 10.83 years (range: 6–85 years), and the sex ratio (Male:Female) was 1:3.43. Patients were divided into seven groups according to age, among which the 30–59 year-old group had the highest incidence of aging, accounting for 82.15%. There were also significant differences in the sex ratio among different groups (non-parametric test, $P < 0.001$).

LYMPH NODE METASTASIS

Among the 14210 patients with papillary thyroid carcinoma, 12792 patients had definite lymph node metastasis, among which 5514 patients had pathological definite lymph node metastasis, accounting for 38.8% of papillary thyroid carcinoma. The lymph node metastasis rate of patients under 20 years old was the highest, and the lymph node metastasis rate of papillary thyroid carcinoma decreased with age ($P < 0.001$). In addition, we found that age, gender, tumor size, lesion distribution,

PATHOLOGICAL TYPES	YEAR					TOTAL
	2011	2012	2013	2014	2015	
Papillary carcinoma(%)	1268(97.09)	1824(97.70)	3171(98.42)	3288(98.59)	4659(99.11)	14210(98.47)
Follicular carcinoma(%)	3(0.23)	10(0.54)	7(0.22)	9(0.27)	7(0.15)	36(0.25)
Medullary carcinoma(%)	18(1.38)	18(0.96)	23(0.71)	25(0.75)	22(0.47)	106(0.73)
Undifferentiated carcinoma(%)	4(0.31)	0(0)	7(0.22)	8(0.24)	2(0.04)	21(0.15)
Squamous cell carcinoma (%)	4(0.31)	3(0.16)	4(0.12)	1(0.03)	4(0.09)	16(0.11)
Malignant lymphoma (%)	7(0.54)	7(0.37)	3(0.09)	4(0.12)	5(0.11)	25(0.17)
Other (%)	6(0.46)	5(0.27)	7(0.22)	0(0)	2(0.43)	17(0.12)
Total	1306	1867	3222	3335	4701	14431

Table 1 Histological case types and proportion of thyroid cancer patients in total thyroid cancer from 2011 to 2015.

AGE (YEARS)	MALE		FEMAL		TOTAL		SEX RATIO
	CASES	COMPOSITION RATIO	CASES	COMPOSITION RATIO	CASES	COMPOSITION RATIO	
<20	28	0.86	36	0.32	64	0.44	1:1.28
20-29	266	8.16	743	6.65	1009	6.99	1:2.79
30-39	680	20.87	2181	19.52	2861	19.82	1:3.21
40-49	1122	34.43	3981	35.63	5103	35.36	1:3.55
50-59	824	25.28	3082	27.58	3906	27.07	1:3.74
60-69	285	8.75	1001	8.96	1286	8.91	1:3.51
≥70	54	1.66	148	1.32	202	1.40	1:2.74
Total	3259	100	11172	100	14431	100	1:3.43

Table 2 Incidence and composition ratio of thyroid cancer in different genders in different age groups.

concurrent Hashimoto's thyroiditis, and nodular goiter were the influencing factors of lymph node metastasis. Multivariate logistic regression revealed that male sex, tumor size(>1 cm), and bilateral lobe of thyroid were independent risk factors for lymph node metastasis of papillary thyroid carcinoma ($P < 0.001$), while age was a protective factor for lymph node metastasis of papillary thyroid carcinoma. The older the age, the lower the lymph node metastasis rate ($P < 0.001$) (Table 3).

CONCURRENT WITH BENIGN CASES

Among the 14210 patients with papillary thyroid carcinoma, 4736 patients in the multi-lesion group and 9474 patients in the single-lesion group (Table 4). It was found to have a higher probability of lymph node metastasis in the multi-lesion group ($2 = 416.819$, $P < 0.001$) by comparing the pathological characteristics of the two groups (Table 5). There were more cases of single lesion combination with benign lesions in papillary thyroid carcinoma ($2 = 416.819$, $P < 0.001$), and the difference was statistically significant ($P < 0.001$) (Table 6).

In the multifocal cases of papillary thyroid carcinoma, the bilateral multifocal group was compared with the unilateral and/or isthmus multifocal group (Table 6). In the multifocal cases of papillary thyroid carcinoma, 2812 cases were bilateral and 1924 cases were unilateral and/or isthmus. The analysis and comparison showed that the unilateral and/or isthmus multi-lesion group had more males, younger age, more benign lesions, and higher incidence of unilateral microcarcinoma ($P = 0.017$, $P < 0.001$, $P < 0.001$, $P < 0.001$), and the differences were statistically significant. There were more patients with cervical lymph node metastasis in bilateral multi-lesion group ($2 = 5.802$, $P = 0.016$).

DISCUSSION

Thyroid cancer(TC) is the most common endocrine tumor among head and neck malignant tumors [8]. Studies have shown that since 2004, thyroid cancer patients in the United States have been increasing at an annual rate of 6.6% for females and 5.5% for males, becoming the fastest growing malignant tumor in the United

GROUP	THE LYMPH NODE METASTASIS			
	CASE	COMPOSITION RATIO%	χ^2	P
age				
≤45	3040	44.18	126.103	0.000
>45	2474	33.76		
gender				
male	1502	52.78	139.587	0.000
female	4012	40.34		
Tumor size				
≤1	2247	33.62	513.777	0.000
>1	3267	53.49		
Cancer distribution				
Unilateral or combined isthmus	4210	41.14	70.692	0.000
On both sides	1304	50.94		
concurrent with Hashimoto's thyroiditis				
Yes	292	37.34	11.287	0.001
no	5222	43.48		
concurrent with nodular goiter				
Yes	1176	40.55	9.969	0.002
no	4338	43.85		

Table 3 The lymph node metastasis of papillary thyroid carcinoma in different groups.

BENIGN DISEASE	YEARS					TOTAL
	2011	2012	2013	2014	2015	
Hashimoto thyroiditis	65	54	185	208	309	821
Nodular goiter	420	509	813	789	763	3294
Thyroid adenoma	38	107	154	118	315	732
Lymphocytic thyroiditis	10	30	13	8	9	70
Subacute thyroiditis	1	3	5	3	6	18
Benign lesions(>1)	20	22	17	20	29	108
Other thyroid nodules	1	2	0	1	3	7
Total	555	727	1187	1147	1434	5050

Table 4 Papillary carcinoma with benign disease at different time periods.

FACTOR	SINGLE LESION GROUP N = 9474	MULTIFOCAL GROUP N = 4736	χ^2	P
gender				
Male	2127	1037	0.552	0.457
Female	7347	3698		
age				
≤45	4616	2265	1.019	0.313
>45	4858	2471		
With benign lesions				
Yes	3916 (40.18%)	1134 (23.94%)	416.819	0.000
No	5558	3602		
Cervical lymph node metastasis				
Yes	3382 (39.91%)	2132 (49.42%)	105.859	0.000
No	5096	2182		

Table 5 Comparison of papillary thyroid carcinoma with multiple lesions and with single lesion.

FACTOR	BILATERAL MULTIFOCAL GROUP N = 2812	UNILATERAL LOBE N = 1924	χ^2	P
gender				
Male	584 (20.77%)	454 (23.60%)	5.672	0.017
Female	2228	1470		
age				
≤45	1384 (49.22%)	1046 (54.37%)	12.120	0.000
>45	1428	878		
With benign lesions				
Yes	311 (11.06%)	823 (42.78%)	630.993	0.000
No	2501	1101		
Cervical lymph node metastasis				
Yes	1305 (50.94%)	827 (47.20%)	5.802	0.016
No	1257	925		
Simple small				
Yes	1271 (45.20%)	1153 (59.93%)	99.175	0.000
No	1541	771		

Table 6 Comparison of unilateral and bilateral multifocal thyroid papillary carcinoma.

States [9, 10]. In a study on the incidence of head and neck cancer inpatients in China from 1993 to 2011, it was found that thyroid cancer increased at an average annual rate of 25.3%, which was the tumor with the fastest increase in incidence. This study analyzed the clinicopathological data of 11431 patients with thyroid cancer who underwent surgical resection for the first time in Tianjin Medical University Cancer Institute and Hospital in the past 5 years. It showed that the number of patients undergoing surgical treatment showed an increasing trend year by year ($P < 0.001$), and papillary cancer showed an increasing trend similar to the overall trend ($P < 0.001$). The incidence of other pathological types was relatively stable or decreased. At the same time, we found that the incidence of follicular carcinoma and Tianjin Medical University Cancer Institute and Hospital were much lower than the data frequently cited in many literatures [11]. This may be due to the significant increase in the incidence of papillary thyroid cancer in the past 20 years, resulting in a decrease in the proportion of follicular cancer and medullary cancer in the overall thyroid cancer. In addition, we also found that the incidence of medullary carcinoma was higher than that of follicular carcinoma ($P < 0.05$), which was different from the results of most studies [12, 13], which may be related to RET proto-oncogene mutation caused by severe environmental pollution and ionizing radiation, or due to regional differences. The specific mechanism needs to be further studied.

Papillary thyroid cancer is the most common pathology of TC, and multicentricity is one of its clinical

features [14, 15]. We found that 33.33% of patients were multifocal with bilateral lobe, which is nearly 1.5 times that of unilateral lobe involvement, which was similar to domestic and foreign reports [16, 17]. Multifocal patients were more likely to have cervical lymph node metastasis, especially those with bilateral lobes. Papillary thyroid cancer often develops along with benign thyroid diseases, especially nodular goiter and Hashimoto thyroiditis [18]. Hashimoto thyroiditis is a common autoimmune thyroid disease [19, 20]. Although the immediate relationship between papillary thyroid carcinoma and Hashimoto's thyroiditis is unclear, many scholars have hypothesized that the occurrence of Hashimoto's thyroiditis could stimulate hyperplasia of the thyroid follicular epithelium due to the loss of autoimmune mechanisms, which may lead to disorder and cancerous cell growth [21–23]. Here, we found that papillary carcinoma combined with Hashimoto's thyroiditis increased annually, which may contribute to the increase in papillary thyroid cancer. However, this mechanism requires further investigation.

In our study, we found that papillary thyroid carcinoma in younger patients tended to have lymph node metastasis ($P < 0.001$). This may be related to hormone secretion and rapid metabolism [23]. In addition, male sex, tumor size (>1 cm), and tumor presence in the contralateral lobe were independent risk factors for lymph node metastasis. Therefore, more caution should be exercised in these patients during the evaluation of the lymph nodes.

Currently, the etiology of this increase in TC is unclear. Many scholars believe that the improvement of inspection

technology, popularization of color Doppler ultrasound, application of high-resolution high-frequency probes, and improvement of health consciousness are improving the detection rate of asymptomatic and subclinical tumor [25, 26]. Some studies have shown that ionizing radiation is also a risk factor for an increase in thyroid cancer [27, 28]. Similarly, some studies have suggested that it may also be related to diet structure, lifestyle, environmental pollution, and autoimmunity [29]. However, these findings still lack mechanistic research, and the causes of the rising incidence remain controversial [30].

CONCLUSION

In conclusion, the findings of this retrospective analysis indicate that the number of thyroid carcinomas treated in our hospital has increased annually, with a prominent increase in PTC. The incidence in women was significantly higher than that in men and occurred mostly in patients aged 30–59 years. Thyroid malignancies often coexist with benign diseases. Male age, tumor size >1 cm, and bilateral tumors are risk factors for PTC lymph node metastasis. Our subsequent study will collect the sequencing data of the samples to further investigate the indicators affecting the prognosis of thyroid cancer. In our next study, it is worthwhile to further explore and study the clinical and pathological characteristics of thyroid cancer, so as to provide information for clinical diagnosis and treatment, and indicate the prognosis.

ETHICS AND CONSENT

The patient provided informed consent for the publication of this case. Data are available on request from the authors.

COMPETING INTERESTS

The authors have no competing interests to declare.

AUTHOR CONTRIBUTIONS

The respective role of each author:

Xiaomeng Wang: Collect the data and write the initial draft, Na Pan, Jie Cao and Weijiao Du visualization/data presentation. Weihong Zhang: Data curation. Shui Cao: critical review, commentary or revision—including pre- or post publication stages.

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PEER REVIEW

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