

Distribution Characteristics of Benign and Malignant Thyroid Nodules

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ABSTRACT

Introduction: The right thyroid lobe has a little bigger size and a few more number of cells than the left lobe. It is uncertain whether this anatomical variation may reflect the distribution differences of the malignant thyroid nodules.

Aim: To investigate the location differences and clinical characteristics of the benign and malignant thyroid nodules.

Materials and Methods: A total of 2194 participants with thyroid nodules were enrolled in this study. Colour Doppler was used to observe the parameters, including the number of nodules, nodule size, nodule shape, nodule capsule, internal echo and haemodynamics. The malignant thyroid nodules were diagnosed by thyroid ultrasonography and pathology. Statistical analysis was conducted with SPSS 16.0 software.

Results: The right lobes (46.5%) were more frequently encroached by Papillary Thyroid Carcinoma (PTC) than the left lobes and isthmus. The ratio of envelopes invaded by tumours was 45.6% for the right lobe, 40.4% for the left lobe, and 14% for the bilateral lobes. The ratio of lymph node metastases, which were encroached by PTC was approximately 24.2%. Adenoma, cyst and calcification were observed more frequently in the right lobes than in the left lobes.

Conclusion: The right lobe suffered from benign and malignant thyroid diseases more frequently than the left lobe. The right envelopes and lymph glands were more frequently encroached by PTC. More attention should be paid to the nodules on the right lobes.

Keywords: Papillary thyroid carcinoma, Relationship, Thyroid lobe

INTRODUCTION

Thyroid gland develops a right lobe, a left lobe and the isthmus. There are some differences between the right and left thyroid lobes in size, morphology, follicle structure and signaling pathways. The right thyroid lobe have a little bigger size and a few more number of cells than the left lobe [1,2]. Compared to the left lobe, the right one has a slightly higher activation index and more ability to express STAT3 and RAF1, which are significant for the development of thyroid glands [1-3].

The incidence of thyroid disease has increased over years. There are more than three million thyroid cancer patients in the world [4]. The thyroid carcinoma had been diagnosed in about 1.2% in 2017 in America [5]. Thyroid tumour is the fifth most common malignancy diagnosed in women recently. Thyroid carcinomas are the most common endocrine and neck tumours [6,7]. It was reported that thyroid tumours occur more frequently in the right lobe. The right lobe more often harbored the tumour initially [8]. In addition, thyroid nodules which are located on the upper pole can be considered to have a higher risk for malignancy than the nodules located elsewhere in the lobe [9]. These results may enhance the predictive value of thyroid nodule ultrasound for detecting malignancies.

More studies are needed to show the location differences of the benign or malignant thyroid nodules. The present study aimed to find out the malignancy rates of thyroid nodules and envelope invasion. The results can promote the clinical implication and the benefit for the patients and treatment strategy.

MATERIALS AND METHODS

The present retrospective study was conducted in Suqian First Hospital and Huai'an Second People's Hospital, from July 2017 to June 2018. It was approved by the ethics committee of the hospital (No. 20130223). This study was registered in Chinese Clinical Trial Register (ChiCTR-CCS-14004734).

The electronic medical records were used to select suitable patients who were older than 18 years and were examined for

thyroid ultrasonography or pathology. Totally, 4733 initial subjects (1582 males and 3151 females) were screened. Individuals without malignant or benign thyroid diseases, and with missing data such as gender, pathology and ultrasound results were excluded from this study. In the end, 2194 subjects qualified including 198 subjects with malignant tumour and 1996 subjects with benign nodules. The general clinical information and laboratory results including sex, age, pathology results and ultrasound results were collected. Of the 2194 consecutive subjects, 198 patients (50 males and 148 females) were diagnosed with Papillary Thyroid Carcinoma (PTC) by pathology. The other 1996 subjects (606 males and 1390 females) were diagnosed with thyroid nodules, thyroid adenomas, thyroid cysts, and thyroid calcifications by color Doppler.

STATISTICAL ANALYSIS

Statistical analysis was conducted with the SPSS 16.0 software (SPSS Inc., Chicago, IL). Continuous data were shown as the median±SD, and categorical variables such as sex, the incidence of malignant tumour or benign tumour, the position of the tumour envelope or lymph node are presented as proportions. The χ^2 test was used to compare the rate of thyroid disease between different lobes.

RESULTS

Totally, 2194 subjects were enrolled in the study, including 198 subjects with PTC and 1996 subjects with benign nodules. The mean age for patients with thyroid malignancies was 46.7 years (19-82 years), and that for patients with benign nodules were 51.9 years (18-98 years). The right lobes (46.5%) were more frequently encroached by PTC than the left lobes, bilateral lobes or isthmus [Table/Fig-1]. The right lobe suffered from malignant thyroid diseases more frequently than the left lobe.

Envelope invasion was more common in the right lobe (13.6%) than in the left lobe (11.6%) [Table/Fig-1]. Forty-eight subjects (24.2%) with PTC had lymph node invasion, 21 (43.8%) had lymph node invasion of the right lobe, 16 (33.3%) had lymph node invasion of the left lobe, and 11 (22.9%) had lymph node invasion of multiple

lobes [Table/Fig-1]. The envelopes and lymph of the right lobes were more frequently encroached by PTC. Furthermore, the envelope and lymph node were more commonly violated by the ipsilateral PTC [Table/Fig-2,3]. The rate of malignant tumours in the right thyroid lobe was greater than in the left lobe for both women and men [Table/Fig-4]. The rate of impaired lymph was similar for thyroid envelope, and the proportion of men was similar to women. There was a high rate of tumour, violated envelope and impaired lymph on the right side. When a subject had envelope invasion, the rate of lymph node invasion was 36.8%, which was significantly higher than those with no envelope invasion ($p=0.006$) [Table/Fig-1].

Location	Frequency		
	PTC	Envelope	Lymph
Left	72 (36.3%)	23 (40.3%)	16 (33.3%)
Right	92 (46.5%)	26 (45.6%)	21 (43.8%)
Isthmus	1 (0.5%)	0 (0%)	0 (0%)
Multiple	33 (16.7%)	8 (14.1%)	11 (22.9%)
Total	198 (100%)	57 (100%)	48 (100%)

[Table/Fig-1]: Location of papillary thyroid carcinoma, thyroid envelope invasion and thyroid lymph node invasion.

Multiple: two or three thyroid lobes were encroached by thyroid benign tumour

PTC	Envelope Invaded		
	Left	Right	Multiple
Left	21 (100%)	0 (0%)	0 (0%)
Right	0 (0%)	25 (92.6%)	2 (7.4%)
Multiple	2 (18.2%)	2 (18.2%)	7 (63.6%)

[Table/Fig-2]: The relationship between PTC and the thyroid envelope.

$\chi^2=85.16$; $p<0.001$

PTC	Lymph		
	Left	Right	Multiple
Left	12 (70.6%)	3 (17.6%)	2 (11.8%)
Right	2 (9.5%)	17 (81%)	2 (9.5%)
Multiple	2 (20%)	1 (10%)	7 (70%)

[Table/Fig-3]: The relationship between PTC and the thyroid lymph nodes.

$\chi^2=35.31$; $p<0.001$

PTC	Total	Male	Female
Left	72	21	51
Right	92	23	69
Isthmus	1	0	1
Multiple	33	6	27

[Table/Fig-4]: The relationship between thyroid lobe and gender of PTC.

Thyroid cysts were the most common (40.7%) benign thyroid tumours and occurred more frequently in the right lobe than in the left lobe. Additionally, thyroid adenoma and thyroid calcification occurred more frequently in the right lobe than in the left lobe [Table/Fig-5,6]. Therefore, clinicians should take more attentions for the right thyroid lobes. Four hundred and ninety-seven subjects had two or more kinds of benign thyroid tumours. Compared to thyroid cysts and thyroid adenomas, thyroid nodes were more likely to become calcified (6.7%).

Benign diseases	Frequency			Rate		
	Total	Male	Female	Total	Male	Female
Solid node	716	215	501	35.8%	35.5%	36.0%
Adenoma	796	234	562	39.8%	38.6%	32.2%
Cyst	812	257	555	40.7%	42.4%	39.9%
Calcification	179	50	129	8.9%	8.2%	9.2%

[Table/Fig-5]: Rate of thyroid nodes, thyroid adenomas, thyroid cysts, and thyroid calcifications.

	Left	Right	Isthmus	Multiple
Solid node	198 (27.6%)	235 (32.9%)	3 (0.4%)	280 (31.9%)
Adenoma	239 (30.0%)	288 (36.2%)	5 (0.6%)	264 (33.2%)
Cyst	265 (33.0%)	310 (38.7%)	4 (0.5%)	233 (27.8%)
Calcification	67 (37.4%)	79 (44.1%)	3 (1.7%)	30 (16.8%)

[Table/Fig-6]: Location of the thyroid nodes, thyroid adenomas, thyroid cysts, and thyroid calcifications.

DISCUSSION

Thyroid carcinomas are the most common neck and endocrine tumours. PTC accounts for more than 90% of all differentiated malignant thyroid tumours. It was reported that larger proportion of both benign and malignant tumours were presented in the right thyroid lobe [8].

In this study, the incidence of tumours in the right lobe was higher than in left thyroid one, but the value was not significantly different. The right lobe is larger than the left lobe, and a larger volume has more cells, indicating a higher risk of tumour development in the right lobe [10]. On the other hand, the thyroid volume of females is larger than that of males, and the rate of malignant tumours in the right thyroid lobe was greater than in the left lobe for both women and men [Table/Fig-4].

The right lobe has a higher activation index and more activation of STAT3 and RAF1 [3,11]. CD56 is a cell surface glycoprotein that is expressed in normal thyroid follicular cells and benign thyroid tumour cells. It has been found that Galectin 3 is a sensitive marker for malignancy, while the expression of CD56 decreases in patients with PTC [12]. There are more cells in the right thyroid lobe than in the left lobe, which results in an increase in the incidence of tumours along with a decrease in the expression of CD56.

Benign thyroid diseases, including thyroid cysts, thyroid nodes, and thyroid adenomas, are common among the general population. With the development of high-resolution colour Doppler, an increasing number of benign thyroid lesions have been detected. The detection rate for thyroid nodules is approximately 19%-68% by color Doppler with higher frequencies in women and elderly people than in the rest of the population [13]. In this study, thyroid cysts were the most common type of benign thyroid disease (40.7%) and had a higher incidence rate in females than in males, which was similar to that of thyroid adenoma, thyroid nodes and thyroid calcifications. This difference in incidence rate maybe due to the fact that women have larger thyroid glands and more thyroid follicles than men.

Thyroid nodes can be benign or malignant. In this study, only 6.7% of thyroid nodes were complicated with calcifications, which was significantly different from the percentage of normal tissue that has calcifications ($p<0.001$). A similar result was observed in thyroid adenomas and cysts. Therefore, we still need to pay attention to benign thyroid tumours. Furthermore, we found that multiple thyroid nodes are more likely to be complicated with thyroid calcifications than single nodes [Table/Fig-7]. Thyroid nodules located in the upper pole can be considered to have a higher risk for malignancy than the nodules located elsewhere in the lobe [9]. Thyroid-stimulating hormone stimulates thyroid follicular cells and lead to the overproduction and release of thyroid hormones by activating the Thyrotropin Receptor (TSHR). The abnormal thyroid follicles produce a number of cytokines, such as IL 1 β , 6, 12, 16,

Solid node	Calcification	
	Yes	No
Left	13 (6.6%)	185 (93.4%)
Right	14 (6.0%)	221 (94.0%)
Isthmus	0 (0%)	3 (100%)
Multiple	21 (7.5%)	259 (92.5%)

[Table/Fig-7]: The relation between solid node and calcification.

$\chi^2=18.84$; $p<0.001$

and 17, IFN- γ , TNF- α , and the CD40 ligand, all of which lead to inflammation and control the behaviour of thyroid epithelial cells [14,15]. TSHR is highly expressed and has a more precise location in the thyrocyte membrane in the right thyroid lobe than in the left [3]. Thyroid nodes and thyroid adenomas are solid nodules, and the right lobes have more thyroid follicle cells and gliocytes than the left. It is possible that solid and cystic tumours tend to occur in the right lobe. These phenomena may explain why the right thyroid lobe is easier to infiltrate.

LIMITATION

PTC is the focus of this study, however, benign thyroid disease and other malignant thyroid disease are equally important. Our results need to be validated on a larger number of subjects, probably in a multicenter study.

CONCLUSION

In summary, this study showed that the right lobe suffered from benign and malignant thyroid diseases more frequently than the left lobe. The envelopes and lymph node of the right lobes were more frequently encroached by PTC. So more attention is needed for PTC in right lobes.

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