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Original Article

Analysis of differences of ultrasound features in different courses of thyroid carcinoma

Jidong Liu[1,2], Litao Ruan[1], Bing Gong[2]

[1]Department of Ultrasonics, The First Affiliated Hospital of Medical College, Xi'an Jiaotong University, Xi'an 710061, Shaanxi Province, P. R. China; [2]Department of Ultrasonics, Jilin City Central Hospital, Jilin 132001, Jilin Province, P. R. China

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Abstract: Objective: To explore the changes of ultrasound features in patients with different courses of thyroid carcinoma, so as to provide a theoretical basis for the clinical treatment and diagnosis of thyroid carcinoma. Methods: A total of 160 patients with thyroid carcinoma treated in our hospital were enrolled and divided into the early stage group (n=76) and the advanced stage group (n=84) according to the results of pathological examination, and further grouped into the lymph node metastasis group (n=78) and the non-metastasis group (n=82). Another 80 patients with benign thyroid disease were enrolled as the benign group. All the enrolled subjects were subjected to ultrasound examination, and the differences of ultrasound features were compared between the different groups. Results: The average diameter of tumour and the proportion of nodular calcification and heterogeneous echo in the advanced stage group were significantly higher than those in the early stage group (P<0.05). The proportions of nodular calcification, heterogeneous echo, unsmooth margins, the aspect ratio of 1 or above, and irregular shapes in the malignant group were significantly higher than those in the benign group (P<0.05). The proportions of nodular calcification, heterogeneous echo, unsmooth margins, the aspect ratio of 1 or above, irregular shapes, multiple nodules, the largest diameter greater than 10 mm, rich blood flow, and absent halo in the lymph node metastasis group were significantly higher than those in the non-metastasis group (P<0.05). Conclusion: There were significant differences of ultrasound features in the different courses of thyroid carcinoma. Ultrasound examination can provide important reference for later clinical diagnosis and treatment.

Keywords: Thyroid carcinoma, different courses, ultrasound features, analysis, difference, exploration

Introduction

Thyroid carcinoma is a malignant tumour originating from thyroid tissue and is one of the most common types of tumours in the head and neck region [1]. The data show that the incidence of thyroid carcinoma worldwide is 3.0 per 100,000 women and 1.2 per 100,000 men [2]. In recent years, with the progress of global industrialization and the aggravation of environmental pollution, the incidence of thyroid carcinoma has being increasing year by year. According to data from the International Carcinoma Centre in 2012 [3], the incidence of thyroid carcinoma in men worldwide has reached 1.9 per 100,000, with an increase of nearly 26% compared with that in 2008, and the incidence of thyroid carcinoma in women has reached 6.1 per 100,000, with an increase of nearly 30% compared with that in 2008. Although the incidence of thyroid carcinoma in China is lower than the global level, it is also increasing gradually. The current incidence of thyroid carcinoma in China is three times of what it was 10 years ago [4].

Patients with thyroid carcinoma at the advanced stage may appear hoarseness, difficulties in breathing and swallowing and other symptoms. At the same time, the compression of tumour on nerves can also lead to Horner syndrome as well as the risk of the metastasis of distant organs. Therefore, the early intervention and treatment for patients with thyroid carcinoma are recommended clinically. Early diagnosis and intervention are important prerequisites for improving the prognosis of patients with thyroid carcinoma. The qualitative diagnosis of thyroid carcinoma is the reference standard for subsequent treatment options.

The traditional identification method for thyroid carcinoma is pathological examination, but it is rarely used due to invasive operation and poor repeatability [5]. In recent years, ultrasound imaging technology has gradually been popularized and applied in clinical practice. Due to the appearance of high-resolution probes, the resolution of ultrasound detection has been significantly improved compared with the past. Detection methods such as two-dimensional ultrasound and Doppler colour ultrasound have become important means to detect thyroid carcinoma [6]. A survey of 80 patients with thyroid nodules found that the accuracy rate of ultrasound TI-RADS classification for the detecting property of thyroid nodules was as high as 87.50%, and the accuracy rate could be increased to 98.75% if combined with real-time ultrasound detection [7]. Another investigation pointed out that ultrasound detection could be used to dynamically assess patients with thyroid carcinoma by monitoring the changes of ultrasound features of the patients, which has an important reference value for clinical treatment [8]. This study aimed to explore the differences of ultrasound features in patients with different courses of thyroid disease, so as to provide more detailed support for the clinical treatment of patients with thyroid carcinoma.

Materials and methods

General information

A total of 160 patients with thyroid carcinoma treated in our hospital from January 2019 to August 2020 were enrolled and divided into early stage group (n=76) and advanced stage group (n=84) according to pathological findings, and further grouped into lymph node metastasis group (n=78) and non-metastasis group (n=82). Another 80 patients with benign thyroid disease receiving physical examination in our hospital during the same period were enrolled as the benign group.

Inclusion criteria: (1) Subjects (except those in the benign group) diagnosed as thyroid carcinoma by pathological examination according to "Guidelines for the Treatment of Thyroid Carcinoma" [9]; (2) Patients with clear consciousness and were able to cooperate with the investigation; (3) Patients with complete medical records; (4) This study was conducted with approval by the Ethics Committee of the First Affiliated Hospital of Medical College, Xi'an Jiaotong University; (5) Patients voluntarily signed informed consent.

Exclusion criteria: (1) Patients combined with mental illness; (2) Patients combined with other malignant tumours; (3) Patients with previous thyroid surgery; (4) Patients with chemotherapy and radiotherapy; (5) Patients with chronic diseases such as myocardial infarction, stroke, and heart failure; (6) Patients combined with severe hepatic and renal dysfunction; (7) Patients combined with Parkinson's diseases, muscle sclerosis, *etc*. which could affect the investigation; (8) Patients combined with distant metastasis of carcinoma; (9) Patients with a history of anxiety and depression.

Elimination criteria: (1) Patients who voluntarily withdrew during the investigation; (2) Death cases during the investigation; (3) Patients who could not continue to participate in the research during the intervention period because of their deteriorated condition; (4) Patients who withdrew from the investigation for other reasons.

Interventional methods

All the enrolled subjects were first subjected to a routine physical examination by HI VISION Preius color ultrasound instrument. Patients were placed in the supine position with their heads tilted back to fully expose the tested site. The linear array probe was selected and set to 6-13 MHz. The instrument was set as thyroid detection mode. The detective depth and gain of the nodules were adjusted to optimize the image display. First, the lesions were examined by gray-scale ultrasound. Conventional transverse and longitudinal section were performed to carefully observe the location, size, shape, margin, internal echo, microcalcification, lymph node metastasis, and aspect ratio of tumours. The detection mode of Doppler ultrasound was then changed. The patients were told not to swallow or speak. 2 ml contrast medium and 5 ml saline were injected intravenously from the elbow vein of patients (pay attention to sequential injection). While the contrast medium was injected, the detection was started, and the changes of enhanced ultrasound features of the subject were recorded. The detective results were imported into the workstation by the instrument, and two experienced sonographers were invited for analysis. If the diagnosis results were

Table 1. Comparison of differences in general clinical data between the early stage group and the advanced stage group ($\bar{x}$ ± sd)/[n (%)]

General clinical data		Early stage group (n=76)	Advanced stage group (n=84)	t/X^2	*P*
Gender	Male	40	44	0.001	0.982
	Female	36	40		
Average age (years)		60.29±4.11	59.19±4.56	1.129	0.262
Average body weight (kg)		65.59±4.33	66.01±4.01	0.45	0.654
Average course of disease (years)		1.29±0.21	1.31±0.19	0.447	0.656
Hypertension	Yes	16	20	0.087	0.768
	No	60	64		
Diabetes mellitus	Yes	20	20	0.067	0.796
	No	56	64		

Table 2. Comparison of differences in general clinical data between the benign group and the malignant group ($\bar{x}$ ± sd)/[n (%)]

General clinical data		Benign group (n=80)	Malignant group (n=160)	X^2	*P*
Gender	Male	40	84	0.067	0.796
	Female	40	76		
Average age (years)		61.29±3.44	61.31±3.01	0.033	0.974
Average body weight (kg)		65.01±4.01	64.98±3.98	0.039	0.969
Average course of disease (years)		1.31±0.98	1.41±0.77	0.611	0.542
Hypertension	Yes	20	36	0.093	0.76
	No	60	124		
Diabetes mellitus	Yes	24	40	0.341	0.559
	No	56	120		

inconsistent, the superior physician would be asked to conduct a consultation and make a diagnosis.

Outcome measurement and evaluating standards

A total of 160 patients diagnosed with thyroid carcinoma by pathological examination were divided into early stage group (n=76) and advanced stage group (n=84), and then further divided into lymph node metastasis group (n=78) and non-metastatic group (n=82). Another 80 patients with benign thyroid disease receiving physical examination in our hospital were enrolled as the benign group. The differences of ultrasound features were compared between the early stage group and the advanced stage group, the lymph node metastasis group and the non-metastasis group, and the benign group and the malignant group.

Statistical analysis

SPSS 22.0 statistical software was used to analyze the data. For the data conforming to the normal distribution, the counting data were expressed as [n (%)] and analysed by the *Chi*-square test, and the measurement data were expressed as mean ± standard deviation (χ ± Sd) and analysed by the t test. *P*<0.05 was considered statistically significant [10].

Results

Comparison of differences in general clinical data between the different groups

There was no statistically significant difference in general clinical data such as gender, age, course of disease, marital status, *etc*. between the different groups (*P*>0.05) (**Tables 1**-**3**).

Differences in ultrasound features of thyroid carcinoma in the different stages

The average diameter of tumour and the proportions of nodular calcification and heterogeneous echo in the advanced stage group were significantly higher than those in the early stage group (*P*<0.05) (**Table 4**).

Table 3. Comparison of differences in general clinical data between the lymph node metastasis group and the non-metastasis group ($\bar{x}$ ± sd)/[n (%)]

General clinical data		Lymph node metastasis group (n=78)	Non-metastasis group (n=82)	X^2	*P*
Gender	Male	38	46	0.436	0.509
	Female	40	36		
Average age (years)		61.28±2.32	61.34±2.55	0.11	0.913
Average body weight (kg)		65.98±3.98	66.01±4.02	0.034	0.973
Average course of disease (years)		1.19±0.32	1.21±0.33	0.275	0.784
Hypertension	Yes	18	18	0.015	0.904
	No	60	64		
Diabetes mellitus	Yes	24	16	1.351	0.245
	No	54	66		

Table 4. Differences in ultrasound features of thyroid carcinoma in the different stages ($\bar{x}$ ± sd)/[n (%)]

Ultrasound features		Early stage group (n=76)	Advanced stage group (n=84)	t/X^2	*P*
Average diameter of tumours (mm)		6.19±2.11	10.82±1.23	12.129	<0.001
Nodular calcification	Yes	20 (26.32)	64 (74.42)	19.9	<0.001
	No	56 (73.68)	20 (23.81)		
Internal ultrasound	Homogeneous	20 (26.31)	16 (19.05)	6.219	0.008
	Heterogeneous	24 (31.58)	48 (57.14)		
	Hypoechoic	32 (42.11)	20 (23.81)		

Comparison of ultrasound features of thyroid diseases with different nature

The proportions of nodular calcification, heterogeneous echo, unsmooth margins, the aspect ratio of 1 or above, and irregular shapes in the malignant group were significantly higher than those in the benign group ($P<0.05$) (**Figure 1A** and **1B**, **Table 5**).

Analysis of the impact of lymph node metastasis on the ultrasound features of thyroid carcinoma

The proportions of nodular calcification, heterogeneous echo, unsmooth margins, the aspect ratio of 1 or above, irregular shapes, multiple nodules, the largest diameter greater than 10 mm, rich blood flow, and absent halo in the lymph node metastasis group were significantly higher than those in the non-metastasis group ($P<0.05$) (**Figure 1C** and **1D**, **Table 6**).

Discussion

The thyroid gland is one of the important endocrine organs in the human body, which is located on both sides of the trachea under the thyroid cartilage. It is named thyroid because it resembles shield armour [11]. The thyroid gland has the physiological function of controlling the body's energy consumption, producing protein, and regulating the secretion of other hormones. It is the largest endocrine gland in adults and plays an important role in the normal functioning, growth and development of the body. Thyroid carcinoma is a carcinoma that occurs in the thyroid. It is the most common malignant tumour in the endocrine system [12]. Its incidence accounts for about 1% of all malignant tumours. The epidemiological data in recent years show that the incidence of thyroid carcinoma is increasing year by year [12]. A multi-centre survey conducted from 1975 to 2006 indicated that the incidence of thyroid carcinoma in the United States increased from 4.9 per 100,000 to 11 per 100,000, with an even greater increase in the proportion of female patients, from 6 per 100,000 in 1975 to 16 per 100,000 in 2006 [13, 14]. According to the data of China Tumor Registration Center, from 1981 to 2001, the incidence of thyroid carcinoma in China increased from

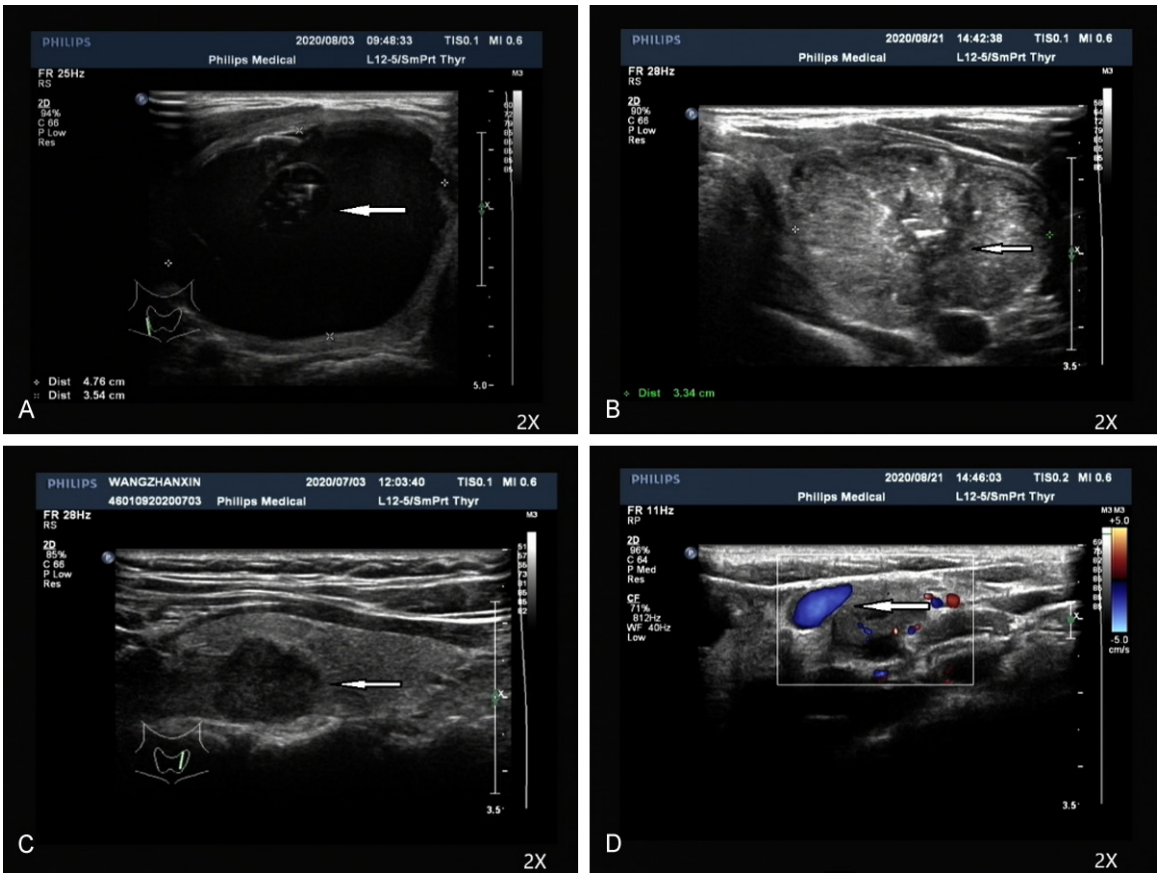

Figure 1. Analysis of different ultrasound features of thyroid carcinoma in the different stages. Thyroid cysts (benign lesions) had homogeneous internal echoes, unsmooth margins, and regular shapes (A). The advanced thyroid carcinoma had severe nodular calcification and heterogeneous internal echoes (B). The advanced thyroid carcinoma with lymph node metastasis had hypoechoic masses, regular shape, heterogeneous internal echoes, unsmooth margins, scattered edges (C), and rich blood flow (D).

Table 5. Comparison of ultrasound features of thyroid diseases of different nature [n (%)]

Ultrasound features		Benign group (n=80)	Malignant group (n=160)	X^2	*P*
Nodular calcification	Yes	20 (25.00)	84 (52.50)	3.947	0.047
	No	60 (75.00)	76 (47.50)		
Internal ultrasound	Homogeneous	46 (57.50)	36 (22.50)	9.189	<0.001
	Heterogeneous	20 (25.00)	72 (45.00)		
	Hypoechoic	14 (17.50)	48 (30.00)		
Margins	Smooth	56 (70.00)	48 (30.00)	17.376	<0.001
	Unsmooth	24 (30.00)	112 (70.00)		
Aspect ratio	≥1	24 (30.00)	110 (68.75)	16.238	<0.001
	<1	56 (70.00)	50 (31.25)		
Shape	Regular	48 (60.00)	46 (28.75)	10.93	0.001
	Irregular	32 (40.00)	114 (71.25)		

0.869 per 100,000 to 2543 per 100,000, with an increase of 193%. Many other studies have confirmed an increasing incidence of thyroid carcinoma in China, especially in coastal areas [15, 16]. The cause of thyroid carcinoma is still unclear, but most scholars and studies point out that thyroid carcinoma occurs under the influence of multiple factors. For example,

Table 6. Analysis of the impact of lymph node metastasis on the ultrasound features of thyroid carcinoma [n (%)]

Ultrasound features		Lymph node metastasis group (n=78)	Non-metastasis group (n=82)	X^2	*P*
Nodular calcification	Yes	68 (87.18)	16 (19.51)	36.7	<0.001
	No	10 (12.82)	66 (80.49)		
Internal ultrasound	Homogeneous	4 (5.13)	32 (39.01)	20.191	<0.001
	Heterogeneous	46 (58.97)	26 (31.71)		
	Hypoechoic	28 (35.90)	24 (29.27)		
Margins	Smooth	12 (15.38)	36 (43.90)	5.632	0.018
	Unsmooth	66 (84.62)	46 (56.10)		
Aspect ratio	≥1	70 (89.74)	40 (48.78)	15.611	<0.001
	<1	8 (10.26)	42 (51.22)		
Shape	Regular	18 (23.08)	28 (34.15)	1.196	0.274
	Irregular	60 (76.92)	54 (65.85)		
Number	Single	24 (30.77)	50 (60.98)	7.336	0.007
	Multiple	54 (69.22)	32 (39.02)		
The largest diameter (mm)	≤10	32 (41.03)	56 (68.29)	6.004	0.014
	>10	46 (58.97)	26 (31.71)		
Blood flow	Rich	64 (82.05)	20 (24.39)	26.648	<0.001
	Not rich	14 (17.95)	62 (75.61)		
Halo	Presence	18 (23.08)	58 (70.73)	18.202	<0.001
	Absence	60 (76.92)	24 (29.27)		

abnormal intake of iodine can lead to changes in thyroid structure and function, so iodine intake has a great influence on the occurrence and development of thyroid carcinoma. Another report pointed out that gender, age, genetic factors, *etc*. also affect thyroid carcinoma to a certain extent. In addition, a study reported that changes in dietary structure and adjustments in lifestyles in recent years were closely related to the incidence of thyroid carcinoma [17].

Accurate diagnosis is an important prerequisite for treatment. The commonly used diagnostic method for thyroid carcinoma is pathological examination, which is the gold standard for thyroid diagnosis at present. Pathological examination is an invasive operation with long detective cycle, high cost and poor repeatability. A simpler, faster and more accurate detection method has been sought in clinical practice [18]. In recent years, along with the continuous advancement of high-frequency ultrasound diagnostic technology and the improvement of quality of ultrasound imaging, the application of ultrasound in the detection of various diseases has been used more and more frequently. Thyroid ultrasound has now become a common detection method to differentiate the nature of thyroid, which is more and more widely used in the differentiation of nodular nature, preoperative examination of thyroid, and prognostic evaluation of thyroid surgery [19]. A study has shown that there are significant differences between malignant and benign thyroid nodules in terms of contour margin, calcification, internal echo, smooth margins, *etc*., suggesting that ultrasound can help differentiate the nature of thyroid nodules [20]. Another retrospective study showed that 40 patients with suspected thyroid carcinoma were diagnosed by pathological examination, and the accuracy of ultrasound differentiation reached 80.00% under double-blind conditions [21]. All these indicate that ultrasound has a good application value in thyroid examination, differentiation and diagnosis, and provides a solid theoretical basis for this study.

This study explored the differences of the ultrasound features in patients with different courses of thyroid carcinoma by setting up different groups. The results showed that the average diameter of tumour and the proportion of nodu-

lar calcification and heterogeneous echo in the advanced stage group were significantly higher than those in the early stage group, suggesting that there were significant differences of ultrasound features in patients with different stages of thyroid carcinoma. A study grouping patients with thyroid carcinoma according to TNM staging showed that the probability of nodular calcification in patients with T3-T4 stages was higher than that in patients with T1-T2 stages (90.00% vs 40.00%), and there was also a significant difference in the diameter of tumours between the two groups (7.10±0.43 mm vs 11.29±1.22 mm) [22], which was similar to the result of this study. The calcification of thyroid carcinoma can be divided into two categories: non-calcification and calcification. It is speculated that the causes of calcification are mostly related to the rapid proliferation of malignant cells and the death of some cells due to insufficient blood supply. An ultrasound study of 90 patients with thyroid cancer has indicated that diffuse microcalcification signs can be called as “snowstorm” sign, and the presence of the above lesions indicates that thyroid cancer cells have been in a state of obvious proliferation, which can be regarded as one of the clinical diagnostic signs of thyroid cancer [23]. In addition, the level of internal ultrasound is mostly related to the intercellular substance and the differentiated degree. A retrospective analysis of patients with thyroid cancer found that papillary cancer cells tended to have internal structural disorder changes due to rapid proliferation, thus the ultrasound inside the lesion often presented a heterogeneous state [24]. This is also confirmed by the comparison of differences of ultrasound features between benign and malignant thyroid lesions in this study. The differences of ultrasound features in benign and malignant lesions are also reflected in the margins, aspect ratios and morphology. The details are as following analysis: (1) Margins and morphology. Some scholars have pointed out that the smaller malignant thyroid nodules indicate the clearer boundary. However, as the nodules proliferate and spread outwards, the sharp margins will become blurred and appear smoother in ultrasound features, which is also confirmed in this study. (2) Aspect ratio. Aspect ratio is one of the important indicators reflecting the nature of thyroid nodules. Many studies have indicated that aspect ratio above 1 is highly specific for the prediction of thyroid carcinoma. It is speculated that the malignant cells in the anteroposterior aspect of nodule are more active in cell division in the early stage of thyroid carcinoma, while the malignant cells in the left posterior aspect are relatively static. This results in larger anterior and posterior diameter of the lesion than the left and right diameter, *i.e*., the aspect ratio greater than 1.

The impact of lymph node metastasis on the ultrasound features was also analysed in this study. It was found that the proportions of nodular calcification, heterogeneous echo, unsmooth margins, the aspect ratio of 1 or above, irregular shapes, multiple nodules, the largest diameter greater than 10 mm, rich blood flow, and absent halo in patients with lymph node metastasis were significantly higher than those in patients with non-metastasis. A study has revealed that the morphology of malignant thyroid nodules will have larger changes than benign nodules, which is also an important prerequisite for ultrasound to distinguish between benign and malignant thyroid nodules [25]. It is speculated that the presence of halo around the thyroid nodule is possibly related to the blood vessels and the capsule around the nodule. The presence of halo indicates that the nodule is growing or being compressed, and the capsule of the nodule is damaged due to the proliferation of nodule. This is also one of the commonly used reference indicators to differentiate the nature of nodules. Abundant blood flow often means sufficient blood supply, which is also a prerequisite for the proliferation and expansion of thyroid carcinoma cells. However, this indicator is not absolute. Papillary carcinoma, for example, often has no signal of internal blood flow due to its tight internal structure. This indicator needs to be combined with other detections to differentiate the nature of thyroids [26].

In summary, there are significant differences in ultrasound features in different courses of thyroid carcinoma. Ultrasound examination of patients with thyroid carcinoma can provide an important reference for later clinical diagnosis and treatment. The innovation of this study is to compare the ultrasound characteristics of thyroid cancer patients with different course of disease by grouping them according to pathological stage, lesion type and whether there is lymph node metastasis. The results are de-

tailed and reliable, which can provide theoretical basis for the follow-up study. The limitation of this study is that ultrasound features in different pathological types of thyroid carcinoma were not compared, resulting in the lack of specificity of some indicators. In view of the deficiency, the differences of ultrasound features in different pathological types of thyroid carcinoma will be carried out in the future so as to find out more accurate differential indicators of ultrasound for thyroid carcinoma, and provide reference for the clinical treatment of thyroid carcinoma.

Disclosure of conflict of interest

None.

Address correspondence to: Litao Ruan, Department of Ultrasonics, The First Affiliated Hospital of Medical College, Xi'an Jiaotong University, No. 277 Yanta West Road, Yanta District, Xi'an, Shaanxi Province, P. R. China. Tel: +86-029-85323610; E-mail: lijidong123452020@163.com; Bing Gong, Department of Ultrasonics, Jilin City Central Hospital, No. 4 Nanjing Street, Chuanying District, Jilin 132001, Jilin Province, P. R. China. Tel: +86-0432-62167069; E-mail: yangguang123012@163.com

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