ISSN 2618-1584 Vol. 6, Issue 2: 17-22, DOI: 10.25236/FMSR.2024.060203

Logistic regression analysis of ultrasound diagnosis of thyroid follicular adenoma and follicular carcinoma

Minghui Zhang[1,a,#], Yan Wang[1,b,#], Xuemei Wang[1,c], Zijun Yu[1,d], Ziyi Yang[1,e], Liang Sang[1,f,*]

[1]Department of Ultrasound, The First Hospital of China Medical University, Shenyang, 110001, China
[a]minghui__zhang@163.com, [b]2965841261@qq.com, [c]wxmlmt@163.com, [d]yzj18342650717@163.com, [e]918728828@qq.com, [f]20091213@cmu.edu.cn
[#]These authors contributed equally to this work and should be considered as co-first authors.
[*]Corresponding author

Abstract: *This study discussed the application of Logistic regression model in differential diagnosis of benign and malignant thyroid follicular tumors by high-frequency ultrasound. A total of 90 cases of pathologically confirmed thyroid follicular tumors were selected from January 2010 to November 2022, including 73 cases of thyroid follicular adenoma (FA) and 17 cases of thyroid follicular carcinoma (FTC). Analysis measures included age, sex, tumor location, size, aspect ratio, shape, boundary, halo, internal real part echo uniformity, calcification, cystic degeneration, and blood flow. The Logistic regression model was established through univariate and multifactor regression analysis, and the ROC curve of the model was plotted and the area under the curve was calculated. The results showed that there were 5 variables in Logistic regression analysis into the regression model, and the area under the ROC curve of the model was 0.903. The Logistic regression model of thyroid follicular tumors based on high-frequency ultrasound characteristics established in this study has good diagnostic effect and important clinical value in distinguishing benign and malignant thyroid follicular tumors.*

Keywords: *Thyroid; Follicular tumor; Ultrasound; Logistic regression*

1. Introduction

Thyroid nodules are a common form of thyroid disease in modern society, especially in adults where the incidence is higher, and are classified into benign and malignant nodules. In malignant nodules, follicular thyroid carcinoma is derived from the height of the follicular epithelium of the differentiated thyroid gland and is the second most common thyroid cancer after papillary thyroid carcinoma, accounting for approximately 6 - 10% of all thyroid cancers[1, 2]. However, follicular thyroid carcinoma is far more malignant than papillary thyroid carcinoma, including invasion, metastasis, and mortality. Distant metastases of FTC often occur as hematopoietic diffusion, with the most common sites being bone and lung[3]. Surgical resection is the primary clinical treatment and has a poor prognosis[4].

As benign follicular tumors, adenomas can be actively monitored without symptoms and surgery is not necessary. However, it is difficult to distinguish follicular carcinoma from adenoma in terms of clinical symptoms, imaging presentation, and even cytological pathology, leading to leakage and misdiagnosis of follicular carcinoma[5]. At the same time, some patients are concerned about the malignancy risk of nodules, and some benign adenomas have been operated on, creating a physical and financial burden[6]. With the rapid development of ultrasound technology, thyroid ultrasound plays an irreplaceable role in distinguishing benign from malignant tumors, and the American College of Radiology requires pre-operative ultrasound evaluation of thyroid nodules[7, 8]. Ultrasound is still challenging in the differential diagnosis of thyroid follicular neoplasms due to the similarity in appearance between FA and FTC. Therefore, increasing the pre-operative FTC detection rate as much as possible from the current level can guide clinician diagnosis and patient follow-up treatment.

In this study, multivariate binary logistic regression analysis was used to screen for grey-scale and color Doppler ultrasound features that could distinguish thyroid follicular adenoma from follicular carcinoma. We use surgical pathology as the gold standard for diagnosis and build a logistic regression model to compare the valuable features of ultrasound between the two groups of patients. The proposed method improves the accuracy of ultrasound diagnosis of thyroid follicular adenoma and thyroid follicular carcinoma and, therefore, provides certain clinical help for early diagnosis and treatment of

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thyroid follicular carcinoma.

2. Materials and Methods

2.1 Abbreviations and Acronyms

Follicular adenoma: FA

Follicular thyroid carcinoma: FTC

2.2 General Information

Ninety cases of thyroid follicular tumors confirmed by surgical pathology in our hospital during the last 10 years were selected, consisting of 30 males and 60 females, aged between 13 and 77 years, with an average age of 50.98 years and a median age of 52.50 years. Of the 90 patients, 17 had lesions in their thyroid follicular carcinoma and 73 had lesions in their thyroid follicular adenoma. All patients were successfully sampled and had complete clinical data, pre-operative ultrasound, and pathology results.

2.3 Instruments and Methods

Ultrasound instruments include the Supersonic AIXP and the Canon Aplio I900. Ultrasound images of selected cases were analyzed retrospectively. The analysis metrics include gender, age, tumor location, size, aspect ratio, morphology, boundaries, blood flow, calcification, halo, internal components, echo intensity of solid parts, and echo homogeneity of solid parts. All patients were divided into FA and FTC groups based on pathology results.

2.4 Statistical Analysis

The statistical software SPSS 26.0 was used. $\chi2$ test was used for enumeration data, and an independent sample t-test was used for univariate analysis of measurement data ($P \leq 0.05$ was set as statistically significant). Logistic regression was used for multivariate analysis, regression equations were established, and Hosmer and Lemeshow tests and ROC curves were performed to assess diagnostic efficacy. If the area under the curve (AUC) is 0.7-0.8, the model is average. If the AUC is 0.8-0.9, the model is good. If $AUC > 0.9$, the model is very good. $P < 0.05$ is considered statistically significant.

3. Results

3.1 Results of the univariate analysis

The results of the single-factor analysis are shown in Table 1. Between two groups of patients, aspect ratio, boundary, presence of calcification, solid part of the echo intensity, and blood flow index differences are statistically significant ($p < 0.05$). The comparison between FA and FTC is shown in Figure 1.

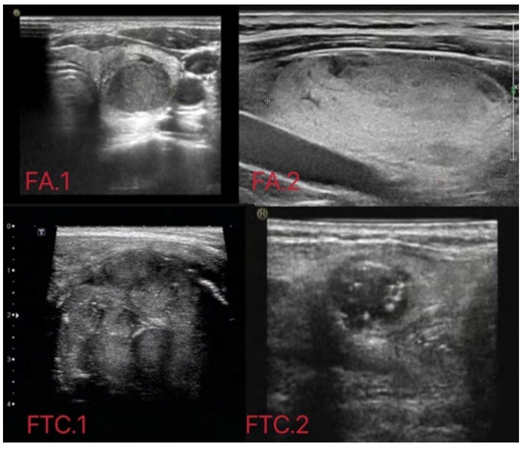

Figure 1: The comparison between FA and FTC.

ISSN 2618-1584 Vol. 6, Issue 2: 17-22, DOI: 10.25236/FMSR.2024.060203

Table 1: Results of univariate analysis of follicular thyroid tumors.

Project		FA	FTC	χ2[t]	P
gender	male	34.2(25/73)	29.4(5/17)	0.145	0.703
	famale	65.8(48/73)	70.6(12/17)		
age		49.11±13.302	59.00±14.138	0.242	0.624
location	left	46.6(34/73)	58.8(10/17)	1.676	0.433
	right	46.6(34/73)	41.2(7/17)		
	spondylolysis	6.8(5/73)	0(0/17)		
size		3.95±1.712	3.53±1,930	1.428	0.235
Aspect ratio	<1	93.2(68/73)	76.5(13/17)	4.263	0.039
	≥1	6.8(5/73)	23.5(4/17)		
regularity	regular	68.5(50/73)	64.7(11/17)	0.091	0.763
	irregular	31.5(23/73)	35.3(6/17)		
boundary	clear	90.4(66/73)	41.2(7/17)	21.816	<0.001
	not clear	9.6(7/73)	58.8(10/17)		
halo	no	78.1(57/73)	88.2(15/17)	0.888	0.346
	yes	21.9(16/73)	11.8(2/17)		
Internal echo uniformity	uniform	1.4(1/73)	0(0/17)	0.235	0.627
	uneven	98.6(72/73)	100(17/17)		
Presence of calcification	no	68.5(50/73)	29.4(5/17)	8.862	0.003
	yes	31.5(23/73)	70.6(12/17)		
internal components	mixed cystic and solid	67.1(49/73)	76.5(13/17)	0.562	0.453
	solid	32.9(24/73)	23.5(4/17)		
Blood flow situation	Marginal blood flow	30.1(22/73)	17.6(3/17)	13.729	0.003
	Central blood flow	30.1(22/73)	29.4(5/17)		
	Lack of blood supply	0(0/73)	17.6(3/17)		
	Mixed blood flow	39.7(29/73)	35.3(6/17)		
Solid echo intensity	Equal echo	61.6(45/73)	17.6(3/17)	12.247	0.002
	High echo	2.7(2/73)	0(0/17)		
	Low echo	35.6(26/73)	82.4(14/17)		

3.2 Results of the multivariate analysis

Table 2: Logistic regression analysis of risk factors for follicular thyroid carcinoma.

Independent variables	B	S.E.	Wald	df	Sig.	Exp(B)	95%C.I.for EXP(B)	
							lower	upper
Aspect ratio	0.697	0.991	0.494	1	0.482	2.007	0.288	13.987
boundary(not clear)	2.294	0.867	6.996	1	0.008	9.917	1.812	54.286
Presence of calcification(yes)	0.064	0.837	0.006	1	0.939	1.066	0.207	5.499
Blood flow situation(Mixed blood flow)	-.029	0.980	0.001	1	0.976	0.971	0.142	6.629
Solid echo intensity(low echo)	2.143	0.896	5.719	1	0.017	8.529	1.472	49.414
constant	3.850	1.055	13.329	1	0.000	0.021		

A total of 5 independent variables were screened into the logistic regression model, including aspect ratio, boundaries, presence or absence of calcification, echo intensity of solid parts, and blood flow. The results of the logistic regression model analysis are shown in Table 2, and 90 cases of thyroid nodules were predicted by this model. The regression value P ≥0.5 was predicted to be thyroid follicular carcinoma, and P <0.5 was predicted to be thyroid follicular adenoma, and the prediction accuracy was 81.1% (73/90). The logistic regression model and the probability prediction value of diagnosing thyroid

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follicular carcinoma were used to establish the ROC curve (Figure. 2 and Figure. 3). In the logistic regression model, the area under the ROC curves for aspect ratio, boundaries, presence or absence of calcification, solid part echo intensity, and blood flow are 0.583, 0.746, 0.695, 0.549, and 0.738, respectively. The area under the ROC curve for the prediction probability is 0.903 and the standard error is 0.033. P < 0.001, 95% confidence interval was (0.838 ~ 0.968), which proved that the fitting effect of the model was very good, and the effect of predicting benign and malignant thyroid follicular tumors was significant.

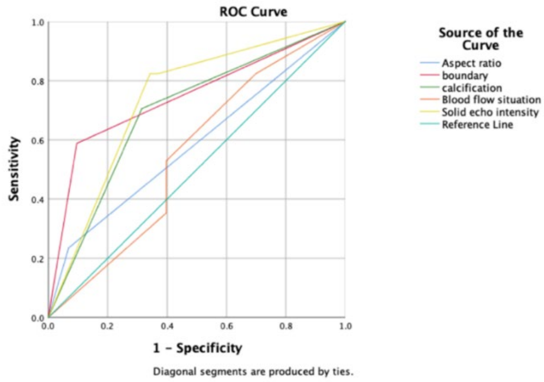

Figure 2: ROC curve of regression model.

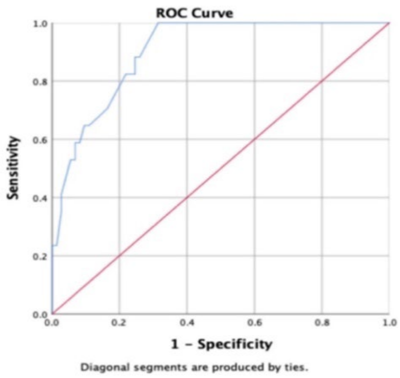

Figure 3: ROC curve of prediction probability of regression model

4. Discussion

Ultrasound is widely used in the diagnosis of thyroid disorders due to its unique advantages[9, 10]. The sonogram findings for thyroid follicular carcinoma and follicular thyroid adenoma were similar. Moreover, they are also so similar in cell morphology that even fine needle punctures are not sensitive enough to detect vascular or capsule invasion[11]. In patients for whom fine needle puncture and suspicion of FTC cannot be determined, a combination of ultrasound and other tests is more necessary to fully assess whether surgery or observation is necessary[12]. Therefore, it is important and difficult to accurately distinguish between benign and malignant thyroid follicular tumors before surgery. In this study, logistic regression was used to analyze the ultrasound characteristics of 90 follicular tumors, and univariate and logistic regression analyses were performed. Univariate analysis showed that the aspect ratio, boundary, calcification, echo intensity of the solid part, and blood flow of the lesions were statistically significant (P<0.05). Logistic regression analysis also indicates that unclear lesion boundaries and hypo-echoic solid echo paths are risk factors for FTC. The ROC curve was established by a logistic model and prediction probability, and the results showed that the model had good diagnostic performance (area under curve 0.903).

This study shows that the benign and malignant thyroid follicular tumors are not related to the gender, age, tumor location, size, morphology, presence or absence of halo, internal composition, and echo uniformity of the solid part, but there are differences in aspect of ratio, boundary, presence or absence of calcification, echo intensity of the solid part, and blood flow. Many previous studies[13-19] have shown that thyroid follicular tumors are most likely to occur in middle-aged and elderly women, with the largest diameter of the lesions >3cm, regular or irregular shape, halo rings, and accompanied by liquefy, with uneven solid parts and no typical or specific factors to distinguish benign and malignant tumors. The univariate factor analysis in this study is similar to the literature. One study showed that tumors located in the isthmus have a higher probability of FTC, which may be related to the narrow space in the isthmus where follicular tumors are more likely to invade the capsule during growth and eventually develop into follicular carcinoma. This study is in the isthmus, where the FTC sample size is set to zero. Past studies have yielded different results, and in the case of spondylolysis, the sample size may not be large enough to be aggregated. More cases need to be collected and discussed in the future.

The results of the multivariate analysis indicate that the unclear lesion boundaries in the solid part and the hypoechoic echo are risk factors for predicting FTC. Although 2D ultrasound features with calcification and mixed blood flow cannot be used as diagnostic criteria for FTC, their value cannot be completely ignored. FTC lesions are mostly ill-defined, which may be due to repeated invasion of the capsule and surrounding tissue by malignant tumor cells, resulting in blurred peripheral structures. Most of the literature on FTC calcification comes in a variety of forms, for coarse or microcalcification, and can also be without calcification[11, 15, 20-23]. It has been shown that the calcification of FTC is an independent influence factor. The results of this study show that calcification is not an independent predictor. This result is also of some significance for the diagnosis of FTC in comparison with calcification in calcified nodules, where there is no risk of FTC. The sonographer can include it in the diagnosis. In previous studies[24], FA is dominated by peripheral blood flow, the FTC blood flow signal is rich, and the local signal is mixed and disorderly, showing mixed blood flow. However, the results of this study do not reflect the high value of mixed blood flow in the diagnosis of FTC, which may be due to the high subjectivity of ultrasound diagnosis and the fact that the samples in this study are not operated by the same sonographer, resulting in some differences from previous reports. The aspect ratio of lesions ≥1 was found in FA (5/73) and FTC (4/17), indicating that this factor has strong specificity in ultrasound diagnosis of FTC, which is also reflected in other related literature. The results of the multivariate analysis in this study are quite different from those reported in the existing literature, which may be related to the different ways in which ultrasound features have been used in different literature to build logistic regression models and may also be related to sample size.

There are some limitations to this study. First, fewer cases were included because of the relatively low incidence of follicular cancer, and more cases could be included in the future to obtain more convincing results. Second, the cases in this study were diagnosed and described by multiple sonographers, which is highly subjective. In addition, the development of new ultrasound technologies may provide more diagnostic information for thyroid follicular tumors, which can be further studied in combination with elastography, contrast-enhanced ultrasound, and other indicators to provide more information for clinical treatment decisions.

5. Conclusions

FA and FTC share many similarities in clinical and ultrasound manifestations, and even FNA does not sensitively detect the presence of vascular or capsule invasion by tumor cells. From the analysis of this study, it can be concluded that there are still some differences between them in some aspects. FTC is characterized by ambiguous or ambiguous boundaries, solid hypoechoic and non-uniform echoes of solid components, most of which have various forms of calcification, abundant blood supply, and disordered blood flow. These features are beneficial for pre-operative differential diagnosis and avoid missing and misdiagnosis.

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ISSN 2618-1584 Vol. 6, Issue 2: 17-22, DOI: 10.25236/FMSR.2024.060203

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