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Original Article

Logistic regression analysis of texture features of thyroid calcification based on computed tomography images

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Abstract: Objective: To explore the value of computed tomography (CT) texture features in differentiating benign and malignant thyroid calcified nodules by using a logistic regression model. Methods: The non-contrast CT images of 60 patients pathologically diagnosed with thyroid calcification were selected. The size of the reconstruction field of view is 70 millimeters. One rectangle region of interest (ROI) covering thyroid calcifications was manually delineated for each CT image by a radiologist. The texture features, including mean pixel intensity, standard deviation (SD), maximum intensity, minimum intensity, skewness, kurtosis, were measured in the ROI. The diagnostic value of CT texture features were analyzed statistically and the logistic model was established. Results: There was no significant difference in maximum intensity between benign and malignant calcified nodules using Student's *t* test ($P > 0.05$). The mean pixel intensity, SD, minimum intensity, skewness and kurtosis were significantly different between benign and malignant calcified nodules ($P < 0.05$). According to the results of logistic regression analysis, the accuracy, sensitivity, specificity and area under receiver operating curve (AUC) are 0.833, 0.875, 0.893 and 0.951, respectively. Conclusions: Logistic regression model created in this study can be implied well in differentiating the malignancy of thyroid calcified nodule based on CT texture features.

Keywords: Computed tomography, thyroid, calcification, texture feature

Introduction

Thyroid nodule calcification is a common sign of thyroid disease, and calcification is significantly correlated with malignant tumors [1], accounting for 49.6-78.8% of malignant nodules, and 15.7-38.7% of benign nodules [2]. The reference standard for the clinical diagnosis of thyroid nodules is fine-needle aspiration biopsy. However, fine-needle aspiration biopsy is invasive, resulting in physical and psychological harm to the patients [3]. Imaging examination methods such as scintigraphy, ultrasonography (US), CT, and magnetic resonance (MRI) are currently used to evaluate thyroid nodules but they cannot reliably differentiate benign from malignant lesions [4, 5]. CT is one of the common imaging examination methods to diagnose the nature of thyroid calcification nodules, and the image characteristics of thyroid calcifications are closely related to the pathological results [6]. Naturally, CT images contain substantial objective information, with clinical values which the naked eyes may be unable to identify.

In previous studies, mathematical methods were used to intuitively describe the distribution and change rules of image pixels, and quantitative parameters are used to evaluate the image [7]. With the gradual maturity of machine learning algorithm systems, texture analysis technology is an important part of computer-aided diagnosis system, and has extensive research value [8]. Some researchers have discussed the difference of the texture features between thyroid nodules and normal tissues [2], and the important value of some

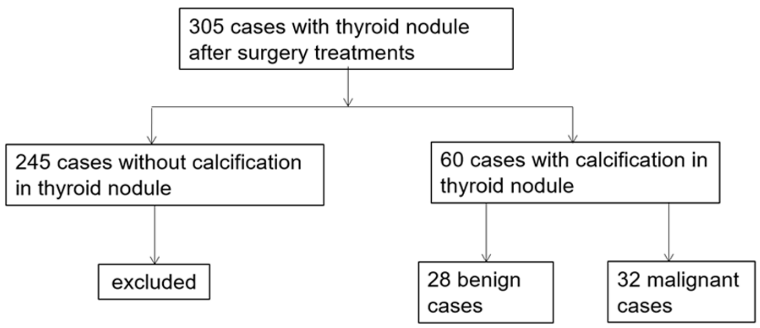

Figure 1. Flowchart of study population.

texture parameters in the diagnosis of thyroid cancer [9]. These studies used CT images reconstructed using a conventional field of view (FOV) (22~25 cm). It is not clear that if CT images with small FOV have high diagnostic value in identifying thyroid calcification. In addition, there are no reports discussing the relationship between the texture characteristics of calcified nodules and the differentiation between benign and malignant, or combining the texture characteristics parameters of multiple calcified nodules for analysis.

The purpose of this study was to investigate the value of CT calcified texture features in differentiating benign and malignant thyroid calcification nodules by logistic regression analysis.

Materials and methods

Clinical data

A retrospective review was performed on all 305 patients who underwent small imaging FOV plain scanning in the First People's Hospital in Hangzhou from January 2016 and June 2018. We excluded 245 cases without thyroid calcification, we identified 60 cases with calcification in the study group (**Figure 1**), including 28 cases with benign nodules and 32 cases with malignant ones (39 women and 21 men). The age ranged from 24 to 72 years, with a mean age of 50 (standard deviation, ±14 years). A typical calcified nodule was selected from CT images for each patient. Inclusion criteria are as follows: 1) incidental thyroid nodules; 2) without surgery or puncture biopsy; 3) no severe image artifact affecting observation and measurement; 4) definite pathological diagnosis. The study was approved by the institutional review board of the Hangzhou First People's Hospital, and informed consent was waived since this research was a retrospective study and the patient information was removed before processing.

Equipment and methods

All the CT images were generated from the Siemens Sensation 16-layer spiral CT (Siemens, Erlangen, Germany). The patients were required to lie in supine position with the neck extended as long as possible, and the scan range was from the oropharynx to the upper clavicle. The cross-sectional image of plain CT was selected, with the field of view (FOV) size of 70 millimeters and the image format was Digital Imaging and Communications in Medicine (DICOM). The scan parameters were: tube voltage 120 kV; tube current automatic regulation; 2~3 millimeter cross-sectional thickness; 2~3 millimeter cross-sectional distance; scan pitch 0.875; and 16×0.625 millimeter collimation.

Image analysis and data processing

The images were independently assessed by two radiologists. If the radiologists disagreed with each other, a senior radiologist would be invited to review the thyroid CT images and make final examination. Software of ImageJ 18.0 was used to extract the rectangle ROI covering thyroid calcification. If more than one calcification nodule was found in one patient, the most characteristic calcification nodules in CT images were selected (**Figure 2**). The following texture features of CT images were evaluated: mean pixel value, maximum intensity, minimum intensity, skewness, kurtosis, and standard deviation (SD) of pixel distribution.

Statistical analysis

Statistical analysis of the results was performed with SPSS 17.0. The Independent *t* test was used to determine the value of the measured data of six CT texture features in differentiating benign and malignant thyroid nodules. Binary logistic regression analysis was used to assess the association between the pathologic diagnosis and CT texture parameters. A logistic regression model was established according to

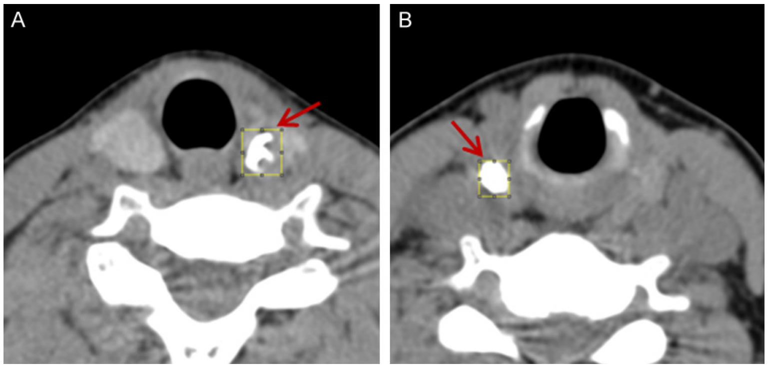

Figure 2. Typical calcified thyroid nodules. A. The goiter nodules of the left thyroid gland are associated with gross calcification. B. Papillary thyroid carcinoma with interstitial fibrosis and gross calcification at the right. Red arrow indicates the regions of interest.

the results of logistic regression analysis. The accuracy of the model can be obtained by testing the data of sixty ROIs. The ROC curve was obtained according to the results of binary logistic regression analysis. The accuracy, the sensitivity, specificity and AUC of benign and malignant thyroid diagnosis were analyzed.

Results

Comparison of benign and malignant thyroid nodules

The six image features were compared between benign and malignant thyroid nodules by independent *t* test (**Table 1**). The maximum intensity has no significant difference between two groups ($P = 0.280$). The mean intensity, standard deviation, minimum intensity, skewness and kurtosis have significant differences ($P < 0.05$). Skewness, Kurtosis and SD in the benign group are greater than the ones in the malignant group. Nevertheless, mean and minimum intensity are less than the malignant group.

Logistic regression analysis

The pathology results of benign and malignant thyroid nodules were used as dependent variables, and the six CT characteristic features were used as covariate variables. During logistic regression analysis, variable selection strategies including enter, forward, backward and stepwise were used and the strategy of enter was chosen for this method outperforming other strategies after comparing results. Based on the enter strategy, all the features were forced into the model. A satisfied fit model was achieved (Nagelkerke R Square = 0.764, -2Log likelihood = 31.956), and variables in the equation were shown in **Table 2**. Wald chi-square test for the corresponding *p* value, indicates that there is no significant difference in mean intensity, maximum intensity and kurtosis ($P > 0.05$), but there is significant difference in standard deviation, minimum and skewness ($P < 0.05$). The regression coefficients of standard deviation, minimum intensity, skewness and kurtosis are negative, indicating that the smaller these three parameters are, the greater the possibility of malignancy is, and the odds ratio is 0.861, 1.036 and 0.001, respectively; indicating that the three data sizes, the probability of malignancy is 0.861, 1.036 and 0.001 times of the probability of benign nodules.

From the **Table 2**, we set up a logistic regression equation (equation 1). The cut value is 0.5. If y is greater than 0.5, it was considered as malignant nodule. Otherwise, it was considered as benign. We presented the confusion matrix (**Figure 3**) to show the performance of the logistic regression model. The sensitivity and specificity and accuracy were 0.875, 0.89.3 and 0.833, respectively. The model performed effectively to discriminate benign nodules from malignant ones.

$$\mathrm{logit}(y) = 0.742-0.15x_1+0.035x_2-6.743x_3 \qquad (1)$$

Here, x_1, x_2 and x_3 indicate SD, minimum intensity and skewness respectively. Here, y is the predicted probability of the logistic regression model.

To evaluate the performance of logistic regression model, we applied the ROC curve to calculate the area of under the ROC curve. We achieved the predicted value by choosing probability option on the save panel of SPSS. The label and probability were applied to make the ROC curve, and the AUC was calculated (**Figure 4**).

Discussion

Thyroid nodule calcification refers to the calcium deposition in thyroid nodules. Calcification

Table 1. Statistical comparison of benign and malignant thyroid nodules characteristics

	Mean (HU)	SD (HU)	Min (HU)	Max (HU)	Skewness	Kurtosis
Benign	120.9±156.2	203.0±142.6	-152.6±370.9	703.6±411.9	1.0±1.1	1.3±2.4
Malignant	214.2±105.7	134.5±108.6	17.5±73.8	587.8±409.1	0.6±0.7	0.1±2.0
t value	-2.736	2.107	-2.385	1.090	2.010	2.031
p value	0.008	0.039	0.024	0.280	0.049	0.047

HU: Hounsfield unit.

Table 2. Variables in the equation on logistic regression analysis

	Coefficient	Standard Error	*p* value	Odds Ratio
Mean	0.032	0.020	0.106	1.033
SD	-0.150	0.053	0.004	0.861
Max	-0.013	0.014	0.341	0.987
Min	0.035	0.012	0.005	1.036
Skewness	-6.743	2.780	0.015	0.001
Kurtosis	-0.256	0.665	0.700	0.774
Constant	0.742	2.345	0.752	2.100

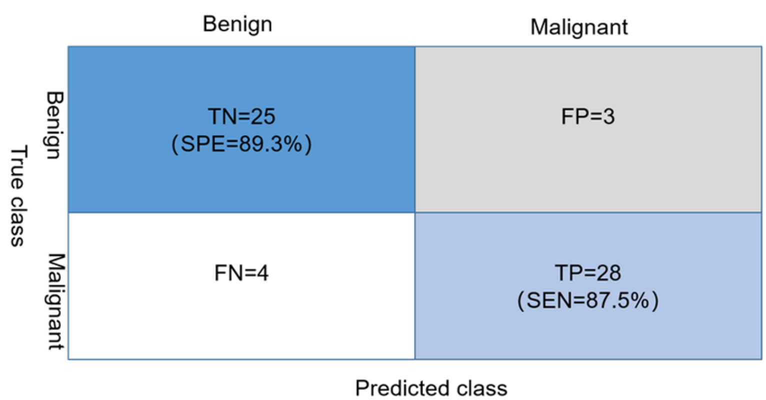

Figure 3. Confusion matrix of logistic model performance. FP indicates false positive; TP true positive; FN false negative; TN true negative; SEN sensitivity; SPE specificity.

is rare in benign thyroid diseases, usually due to nodular wall calcification or fibrous septal calcification after the absorption of inflammation and hematoma. In traditional clinical practice, ultrasound is often used to examine the thyroid gland. In the aspect of ultrasound, there have been studies on automatic identification of thyroid nodules and automatic identification of vascularization within the boundary [10-12]. However, such studies using CT are still immature [13, 14].

CT can also distinguish benign from malignant thyroid nodules [4, 15]. In terms of calcification, the current study by Liu W et al. shows that calcification has a high detection rate in malignant nodules. Han Z et al. previously used calcification signs in the identification of nodular goiter in the accuracy of 79.5%. In this experiment, the accuracy rate of identifying benign and malignant thyroid gland tissue was increased to 87.5% [16]. By establishing a Logistic model to compare with benign nodules, malignant thyroid nodules have a higher rate of calcification, and calcification mostly occurs in the interior of nodules. In addition, in the study on the types of thyroid calcification, a study showed that fine-grained calcification in thyroid nodules is an important sign of CT diagnosis of thyroid malignant nodules, and coarse-grained calcification in thyroid nodules is an important sign of CT diagnosis of benign thyroid nodules [17]. Most studies focus on the classification and distribution of calcification. This study attempted to analyze the texture of calcification. Texture analysis refers to the process of extracting texture feature parameters through certain image processing technology so as to obtain quantitative or qualitative description of texture. At present, studies have shown that dynamic enhanced liver texture analysis is of significance in the preliminary evaluation of colorectal cancer [18, 19]. In our study, texture analysis was used for thyroid calcification, where pixel value represents the number of pixels contained in the image. The higher the value is, the greater intensity the calcification will be, which is associated to the pathologic type of thyroid nodule. Skewness, kurtosis and standard deviation can reflect the distribution of pixel value. In this

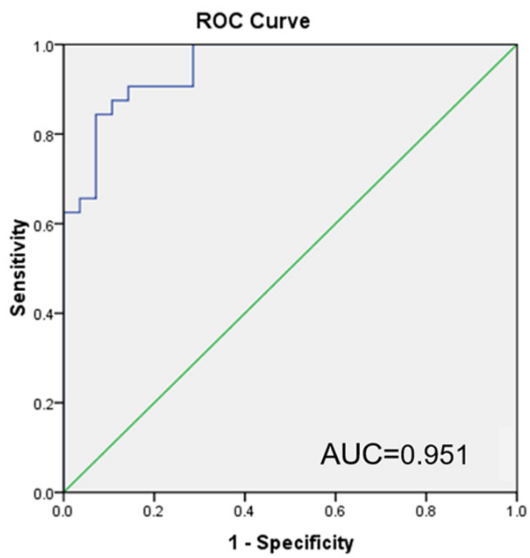

Figure 4. ROC curve of logistic regression analysis.

study, it was found by independent sample *t* test that skewness, kurtosis, minimum value, average pixel value and standard deviation of pixel distribution were of certain value in benign and malignant thyroid, while the maximum value of CT showed no significant difference in benign and malignant thyroid nodules ($P > 0.05$).

Logistic regression, also known as logistic regression analysis, is a generalized linear regression analysis model, commonly used in data mining, automatic diagnosis of diseases, economic forecasting and other fields. For example, to discuss the risk factors of causing diseases and predict the probability of occurrence of diseases based on the risk factors [20-23]. Therefore, in this experiment, logistic regression analysis was carried out on the parameters obtained from texture analysis, and Logistic model (equation 1) was obtained. The maximum approximation index was obtained through the obtained specificity and sensitivity. When Y is greater than this value, the probability of thyroid nodule being malignant is high. When Y is less than this value, thyroid nodules are more likely to be benign. Due to the difficulty in data collection, the sample size in this study is small. The thyroid calcification was not classified, and the size of thyroid calcification was different, leading to the inconsistent size of the selected area, which may have some impact on the classification results, which is the deficiency of this study. Finally, in the validation part of the model, this experiment only used the internal validation, and the obtained validation data is not comprehensive and rigorous enough. In the next step, we will collect new data, continue external verification of the established Logistic model, evaluate the model more comprehensively, and further improve the experiment.

Based on logistic regression model, this experiment carried out texture analysis of calcified nodules in CT images under small FOV scan of thyroid gland to provide reference opinions for the diagnosis of benign and malignant thyroid nodules, which has certain value in thyroid nodule diagnosis.

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Disclosure of conflict of interest

None.

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References

[1] Kim BK, Choi YS, Kwon HJ, Lee JS, Heo JJ, Han YJ, Park YH and Kim JH. Relationship between patterns of calcification in thyroid nodules and histopathologic findings. Endocr J 2013; 60: 155-60.

[2] Peng W, Liu C, Xia S, Shao D, Chen Y, Liu R and Zhang Z. Thyroid nodule recognition in computed tomography using first order statistics. Biomed Eng Online 2017; 16: 67.

[3] Baloch ZW, Fleisher S, LiVolsi VA and Gupta PK. Diagnosis of “follicular neoplasm”: a gray zone in thyroid fine-needle aspiration cytology. Diagn Cytopathol 2002; 26: 41-4.

[4] Nakadate M, Yoshida K, Ishii A, Koizumi M, Tochigi N, Suzuki Y, Ryu Y, Nakagawa T, Umehara I and Shibuya H. Is 18F-FDG PET/CT useful for distinguishing between primary thyroid lymphoma and chronic thyroiditis. Clin Nucl Med 2013; 38: 709-14.

[5] Lassau N, Estienne T, de Vomecourt P, Azoulay M, Cagnol J, Garcia G, Majer M, Jehanno E, Renard-Penna R, Balleyguier C, Bidault F, Cara-

mella C, Jacques T, Dubrulle F, Behr J, Poussange N, Bocquet J, Montagne S, Cornelis F, Faruch M, Bresson B, Brunelle S, Jalaguier-Coudray A, Amoretti N, Blum A, Paisant A, Herreros V, Rouviere O, Si-Mohamed S, Di Marco L, Hauger O, Garetier M, Pigneur F, Bergère A, Cyteval C, Fournier L, Malhaire C, Drape JL, Poncelet E, Bordonne C, Cauliez H, Budzik JF, Boisserie M, Willaume T, Molière S, Peyron Faure N, Caius Giurca S, Juhan V, Caramella T, Perrey A, Desmots F, Faivre-Pierre M, Abitbol M, Lotte R, Istrati D, Guenoun D, Luciani A, Zins M, Meder JF and Cotten A. Five simultaneous artificial intelligence data challenges on ultrasound, CT, and MRI. Diagn Interv Imaging 2019; 100: 199-209.

[6] Liu W, Dong X, Zhu C, Yang J, Yang J, Shao K, Yuan L, Chen H, Lu W and Zhu Y. Association between computed tomography-detected calcification and thyroid carcinoma. Neoplasma 2015; 62: 641-5.

[7] Liu C, Chen S, Yang Y, Shao D, Peng W, Wang Y, Chen Y and Wang Y. The value of the computer-aided diagnosis system for thyroid lesions based on computed tomography images. Quant Imaging Med Surg 2019; 9: 642-653.

[8] Song G, Xue F and Zhang C. A model using texture features to differentiate the nature of thyroid nodules on sonography. J Ultrasound Med 2015; 34: 1753-60.

[9] Schob S, Meyer HJ, Dieckow J, Pervinder B, Pazaitis N, Höhn AK, Garnov N, Horvath-Rizea D, Hoffmann KT and Surov A. Histogram analysis of diffusion weighted imaging at 3T is useful for prediction of lymphatic metastatic spread, proliferative activity, and cellularity in thyroid cancer. Int J Mol Sci 2017; 18.

[10] Bibicu D, Moraru L and Biswas A. Thyroid nodule recognition based on feature selection and pixel classification methods. J Digit Imaging 2013; 26: 119-28.

[11] Acharya UR, Faust O, Sree SV, Molinari F and Suri JS. ThyroScreen system: high resolution ultrasound thyroid image characterization into benign and malignant classes using novel combination of texture and discrete wavelet transform. Comput Methods Programs Biomed 2012; 107: 233-41.

[12] Keramidas EG, Maroulis D and Iakovidis DK. TND: a thyroid nodule detection system for analysis of ultrasound images and videos. J Med Syst 2012; 36: 1271-81.

[13] Baek HJ, Kim DW, Lee YJ, Choo HJ, Ahn HS, Lim HK and Ryu JH. Diagnostic accuracy of computed tomography for differentiating diffuse thyroid disease from normal thyroid parenchyma: a multicenter study. PLoS One 2018; 13: e0205507.

[14] Lee KH, Kim DW, Baek JW, Lee YJ, Choo HJ, Cho YJ, Lee SJ, Park YM, Jung SJ and Baek HJ. Comparison of computed tomography features between follicular neoplasm and nodular hyperplasia. Cancer Imaging 2016; 16: 31.

[15] Gao SY, Zhang XY, Wei W, Li XT, Li YL, Xu M, Sun YS and Zhang XP. Identification of benign and malignant thyroid nodules by in vivo iodine concentration measurement using single-source dual energy CT: a retrospective diagnostic accuracy study. Medicine (Baltimore) 2016; 95: e4816.

[16] Zhu D, Chen W, Xiang J and Han Z. Diagnostic value of CT artifacts for solitary coarse calcifications in thyroid nodules. Int J Clin Exp Med 2015; 8: 5800-5805.

[17] Zhang LX, Xiang JJ, Wei PY, Ding JW, Luo DC, Peng ZY and Han ZJ. Diagnostic value of computed tomography (CT) histogram analysis in thyroid benign solitary coarse calcification nodules. J Zhejiang Univ Sci B 2018; 19: 211-217.

[18] Ganeshan B, Burnand K, Young R, Chatwin C and Miles K. Dynamic contrast-enhanced texture analysis of the liver: initial assessment in colorectal cancer. Invest Radiol 2011; 46: 160-168.

[19] Ng F, Ganeshan B, Kozarski R, Miles KA and Goh V. Assessment of primary colorectal cancer heterogeneity by using whole-tumor texture analysis: contrast-enhanced CT texture as a biomarker of 5-year survival. Radiology 2013; 266: 177-184.

[20] Norton EC, Dowd BE and Maciejewski ML. Marginal effects-quantifying the effect of changes in risk factors in logistic regression models. JAMA 2019; 321: 1304-1305.

[21] Hughes G, Choudhury RA and McRoberts N. Summary measures of predictive power associated with logistic regression models of disease risk. Phytopathology 2019; 109: 712-715.

[22] Hsieh MH, Sun LM, Lin CL, Hsieh MJ, Hsu CY and Kao CH. Development of a prediction model for pancreatic cancer in patients with type 2 diabetes using logistic regression and artificial neural network models. Cancer Manag Res 2018; 10: 6317-6324.

[23] Ugwu C and Zewotir TT. Using mixed effects logistic regression models for complex survey data on malaria rapid diagnostic test results. Malar J 2018; 17: 453.