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Development and validation of a machine learning model for central compartmental lymph node metastasis in solitary papillary thyroid microcarcinoma via ultrasound imaging features and clinical parameters

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Abstract

Background Papillary thyroid microcarcinoma (PTMC) is the most common malignant subtype of thyroid cancer. Preoperative assessment of the risk of central compartment lymph node metastasis (CCLNM) can provide scientific support for personalized treatment decisions prior to microwave ablation of thyroid nodules. The objective of this study was to develop a predictive model for CCLNM in patients with solitary PTMC on the basis of a combination of ultrasound radiomics and clinical parameters.

Methods We retrospectively analyzed data from 480 patients diagnosed with PTMC via postoperative pathological examination. The patients were randomly divided into a training set ($n=336$) and a validation set ($n=144$) at a 7:3 ratio. The cohort was stratified into a metastasis group and a nonmetastasis group on the basis of postoperative pathological results. Ultrasound radiomic features were extracted from routine thyroid ultrasound images, and multiple feature selection methods were applied to construct radiomic models for each group. Independent risk factors, along with radiomics features identified through multivariate logistic regression analysis, were subsequently refined through additional feature selection techniques to develop combined predictive models. The performance of each model was then evaluated.

Results The combined model, which incorporates age, the presence of Hashimoto's thyroiditis (HT), and radiomics features selected via an optimal feature selection approach (percentage-based), exhibited superior predictive efficacy, with AUC values of 0.767 (95% CI: 0.716–0.818) in the training set and 0.729 (95% CI: 0.648–0.810) in the validation set.

Conclusion A machine learning-based model combining ultrasound radiomics and clinical variables shows promise for the preoperative risk stratification of CCLNM in patients with PTMC. However, further validation in larger, more diverse cohorts is needed before clinical application.

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Clinical trial number Not applicable.

Keywords Papillary thyroid carcinoma, Lymph node metastasis, Ultrasound, Machine learning

Background

Papillary thyroid microcarcinoma (PTMC) is the most common malignant subtype of thyroid cancer and is defined as papillary carcinoma with a maximum diameter of ≤ 1 cm [1]. While PTMC is generally associated with a favorable prognosis, its local invasiveness and propensity for lymph node metastasis present significant challenges in diagnosis, treatment, and long-term management [2]. Central compartment lymph node metastasis (CCLNM) is one of the most common metastatic pathways in PTMC and is closely linked to disease recurrence and progression, making it a critical prognostic factor in the management of this disease [3]. Although PTMC typically progresses slowly and is associated with low mortality rates, CCLNM remains a major predictor of recurrence, lateral neck lymph node metastasis, and mortality in PTMC patients [4, 5].

In recent years, thermal ablation techniques, including radiofrequency ablation, have gained increasing acceptance in the treatment of PTMC. These techniques provide therapeutic outcomes comparable to those of traditional surgical resection while significantly improving patients' quality of life [6–8]. Several international clinical guidelines now recommend thermal ablation as a first-line treatment for patients with thyroid microcarcinoma who do not exhibit regional or distant lymph node metastasis [9, 10]. Therefore, accurate preoperative assessment of CCLNM is essential for optimizing treatment strategies and improving patient outcomes.

Current research indicates that patients with PTMC are at risk for early cervical lymph node metastasis, with the incidence of CCLNM reaching approximately 40% [11, 12]. However, despite its widespread use, conventional ultrasound is limited in detecting CCLNM because of anatomical interference from the thyroid and trachea [13]. The sensitivity of ultrasound for detecting central compartment metastasis has been reported to be 33.2%, with a specificity of 85.7%, resulting in an overall accuracy of only approximately 40% [14, 15]. These limitations highlight the need for more reliable and accurate diagnostic methods.

With the rapid advancements in artificial intelligence (AI) and machine learning (ML), ultrasound radiomics has been identified as a promising tool for enhancing diagnostic accuracy in thyroid diseases. Radiomics involves the extraction of quantitative features from medical images, revealing underlying pathophysiological information that is not visible to the naked eye. When combined with ML, radiomics enables the development of predictive models for precise disease diagnosis and prognosis. Notably, ultrasound radiomics is considered to have great potential in improving preoperative diagnostic accuracy, risk stratification, and personalized treatment planning for thyroid diseases [16, 17].

Although radiomics has been successfully applied in predicting distant metastasis, malignancy risk, and lymph node involvement in thyroid cancers, no studies have specifically focused on its application for predicting CCLNM in patients with PTMC. This study aims to address this gap by developing a machine learning model that integrates ultrasound radiomics with clinical and ultrasound parameters. The relevant imaging features are to be extracted, and advanced feature selection techniques are to be employed to construct a robust predictive model for the noninvasive assessment of CCLNM in PTMC. This approach is expected to provide valuable insights for personalized treatment strategies and contribute to the growing field of precision medicine in the management of thyroid cancer.

Methods

Patient selection and data acquisition

A retrospective analysis of the clinical data of patients with papillary thyroid carcinoma who visited the Thyroid and Breast Surgery Department of Yichang Central People's Hospital between January 2020 and September 2024 was performed. A total of 480 patients were enrolled according to the established inclusion and exclusion criteria, comprising 123 males and 357 females aged between 18 and 60 years, with a mean age of 41 ± 9 years. This study was approved by the Medical Ethics Committee of Yichang Central People's Hospital, with a waiver of informed consent (ethical approval number: 2025-074-01).

The inclusion criteria were as follows:

① age ≥ 18 and ≤ 60 years;

② patients with solitary papillary thyroid microcarcinoma who underwent fine-needle aspiration cytology (FNAC) in our department; and.

total thyroidectomy and lymphadenectomy (central and/or lateral compartments) were performed on all patients, with postoperative pathology confirming papillary thyroid carcinoma.

The exclusion criteria were as follows:

① poor image quality;

② previous thyroid surgery or I^{131} treatment;

③ incomplete clinical and imaging data;

④ multifocal thyroid lesions;

and ⑤ distant metastasis.

Ultrasound image acquisition and preprocessing

Examinations were performed via a Mindray Resona R9s ultrasound diagnostic system equipped with a linear probe operating at frequencies ranging from 7.5 MHz to 18 MHz. Multiplanar imaging of the thyroid was conducted, with the largest longitudinal axis of the nodule serving as the reference plane. All the images were stored in DICOM format. Scans were conducted prior to fine-needle aspiration (FNA) via the same ultrasound system by interventional ultrasound physicians, who were formally trained in thyroid imaging and had over five years of clinical experience. The operators were blinded to the study design and patient allocation. A standardized imaging protocol was applied, and the largest transverse cross-section of each nodule was acquired to ensure consistency and minimize subjectivity in image selection.

Clinical parameter collection

Clinical data, including age, sex, body mass index (BMI), TRAb, T3, T4, TSH, TPOAb, carcinoembryonic antigen, thyroglobulin antibody, and the presence of Hashimoto's thyroiditis (HT), were collected. Preoperative fine-needle aspiration cytology was performed on all patients, and those with cytological results indicative of papillary thyroid carcinoma were initially selected for inclusion. Patients were subsequently enrolled on the basis of predefined inclusion and exclusion criteria. The diagnosis of HT was confirmed through histopathological examination of surgical samples.

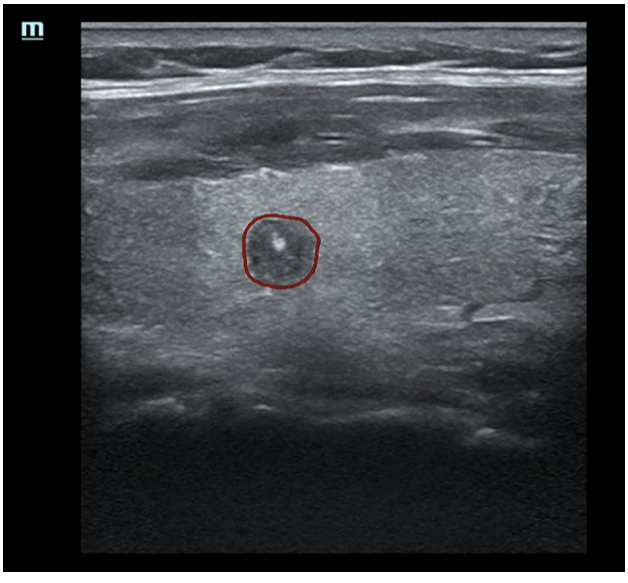


Fig. 1 Ultrasound image of a thyroid nodule with the region of interest (ROI) outlined in red. The image shows the characteristics of the nodule, which are analyzed for radiomic feature extraction in the study

Feature extraction, feature selection, and modeling

Thyroid nodules were accurately delineated by an experienced ultrasonographer, and regions of interest (ROIs) were defined accordingly (Fig. 1). The images were then imported into the Beijing Medical Intelligent Research Platform, where 1,125 radiomic features were automatically extracted. The extracted features were initially preprocessed via min–max normalization. Optimal feature selection was then performed through percentage-based filtering, followed by dimensionality reduction via Lasso regression for classification. Finally, a predictive model for CCLNM in patients with PTMC was developed via logistic regression algorithms.

Statistical analysis and model evaluation

Statistical analysis was conducted via SPSS 26.0 software. Continuous variables with a normal distribution were expressed as the mean ± standard deviation (± s) and were compared via the independent-samples t test. Nonnormally distributed continuous variables were expressed as medians (interquartile ranges) and were compared via the Mann–Whitney U test. Categorical variables were expressed as frequencies (percentages) and were analyzed via the chi-square (χ^2) test. A P value of < 0.01 was considered statistically significant for univariate analysis. The threshold of $P < 0.01$ was chosen intentionally to reduce the risk of false positives (Type I errors) and to enhance the reliability of the selected predictors in the multivariate model. This more stringent criterion is widely accepted in clinical prediction modeling to ensure more confidence in variable selection.

The performance of each model was evaluated by constructing receiver operating characteristic (ROC) curves and calculating the area under the curve (AUC) in both the training and validation datasets. The calibration of the predictive models was assessed via the Hosmer–Lemeshow goodness-of-fit test, with a P value > 0.05 considered to indicate good calibration. A P value of > 0.05 suggests that there is no statistically significant difference between the predicted and observed outcomes, which indicates a good model fit.

Results

Patient characteristics

A total of 480 patients with PTMC were included in the study, comprising 242 patients with CCLNM and 238 without CCLNM. Statistically significant differences in age, sex, and the presence of HT were observed between the two groups. The patients were randomly divided into a training set ($n = 336$) and a validation set ($n = 144$) at a 7:3 ratio. No significant differences were found in the clinical variables between the training and validation sets, indicating that the distributions of the baseline characteristics were well balanced (Table 1).

Table 1 Comparison of clinical parameters between the relapse and nonrelapse groups

Characteristic	total	CCLNM positive(242)	CCLNM negative(238)	t/Z/X²	*p*
Age(year)	41 ± 9	38 ± 9	43 ± 8	-5.137	< 0.001
Sex, n(%)				7.376	0.007
Male	123(25.6)	75(31.0)	48(20.2)		
Female	357(74.4)	167(69.0)	190(79.8)		
HT n (%)				29.495	< 0.001
Yes	94(19.6)	71(29.3)	23(9.7)		
No	386(80.4)	171(70.1)	215(90.3)		
Tg	(14.7,16.9)	(14.4,19.2)	(15.0,13.9)	-1.575	0.115
TRAb	(1.7,5.1)	(1.7,5.3)	(1.8,5.0)	-0.237	0.812
T4	(15.4,2.6)	(15.4,2.5)	(15.4,2.7)	-0.846	0.397
T3	(5.2,0.8)	(5.3,0.9)	(5.2,0.7)	-2.838	0.005
TSH	(2.3,1.8)	(2.3,1.6)	(2.4,2.0)	-0.376	0.707
CEA	(1.3,1.2)	(1.2,1.2)	(1.3,1.1)	-0.164	0.870
TGAb	(5.6,15.7)	(12.0,19.5)	(1.0,14.8)	-2.837	0.005
TPOAb	(0.3,0.4)	(0.3,0.6)	(0.3,0.3)	-1.777	0.076

Multivariate logistic regression analysis

After the exclusion of collinear variables with statistical significance in the univariate analysis, multivariate logistic regression was conducted. Hashimoto's thyroiditis and age were identified as independent predictors of CCLNM in patients with PTMC. The regression coefficient for HT was 0.598 (95% CI: 0.548–0.649; $P < 0.001$), and for age, it was 0.340 (95% CI: 0.292–0.389; $P < 0.001$). Gender also showed a significant association, with a regression coefficient of 0.446 (95% CI: 0.395–0.497; $P = 0.040$). Receiver operating characteristic curve analysis revealed that the AUC was 0.632 (95% CI: 0.582–0.681) for age, 0.599 (95% CI: 0.548–0.650) for HT, and 0.705 (95% CI: 0.659–0.751) for the combined predictive model (Fig. 2).

Model construction and comparison

A total of 1,125 radiomic features were subjected to seven distinct feature selection methods to develop predictive models for CCLNM in PTMC. Model performance was evaluated via the AUC. In addition to radiomic features, independent clinical risk factors—age and HT—were incorporated into the models. Seven combined models were constructed on the basis of different feature selection strategies, and their performances were subsequently compared. The model developed via the percentage-based feature selection method exhibited the highest performance and was selected as the optimal model. As shown in Fig. 3, age was identified as the most important predictor, followed by radiomic features such as Maximum Diameter and Sphericity, as well as the presence of HT.

A radiomic score (RadScore) was generated through a linear combination of six selected features, including

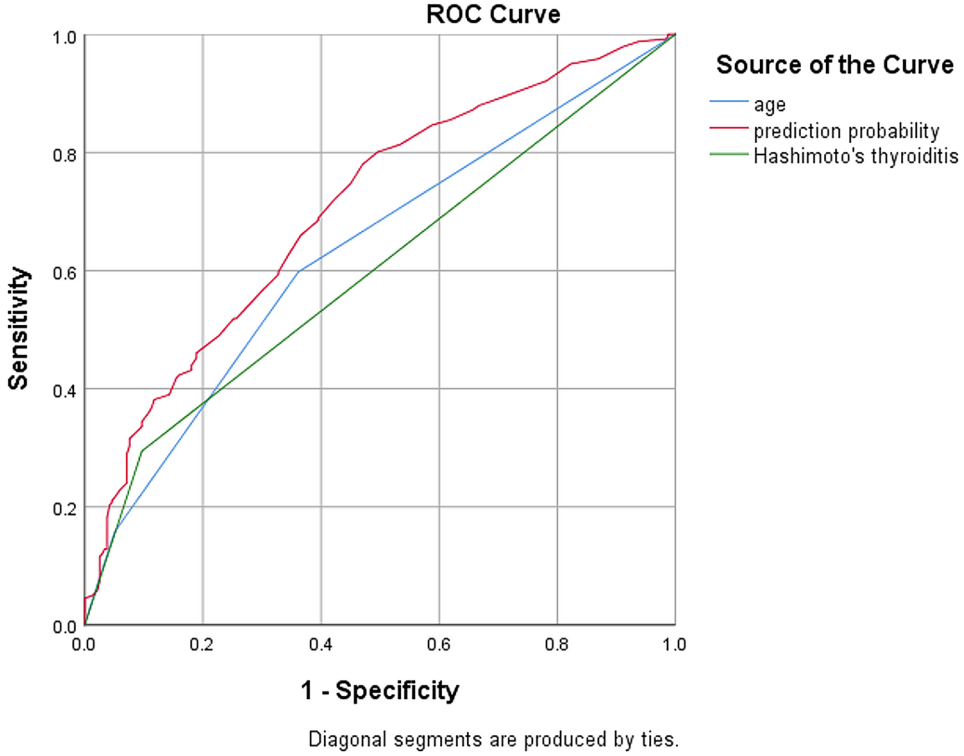


Fig. 2 ROC curve analysis of clinical parameters for predicting central lymph node metastasis in patients with thyroid micropapillary carcinoma. The graph compares the diagnostic performance of three factors: age (blue curve), HT (green curve), and the combined prediction probability (red curve)

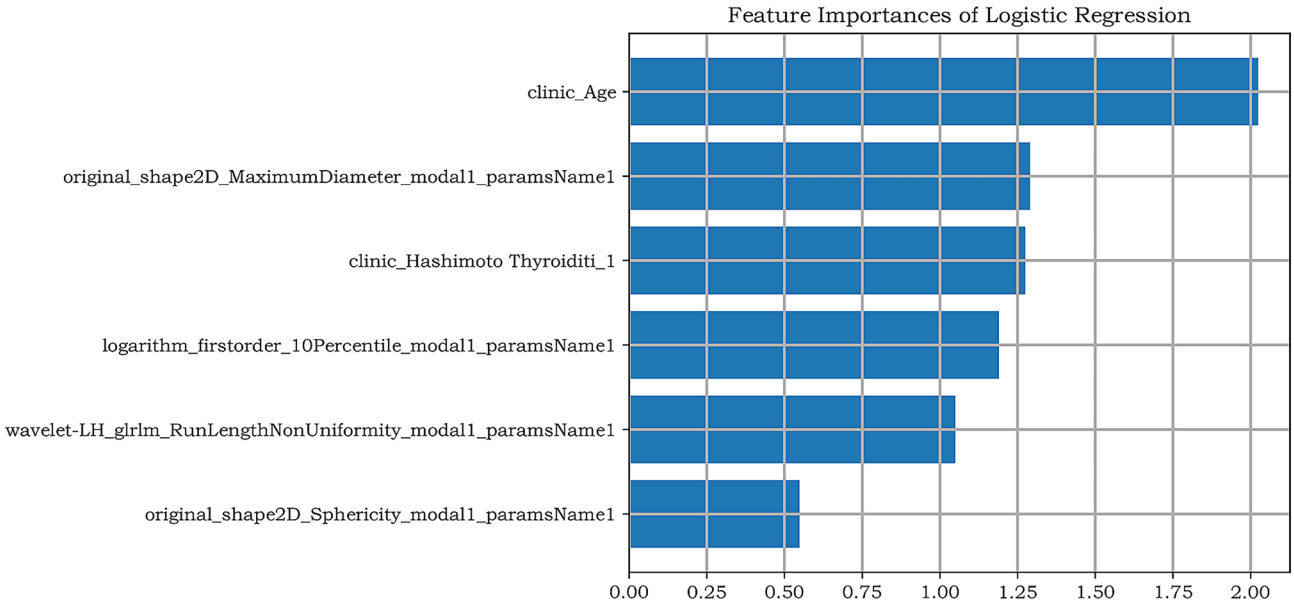


Fig. 3 Feature importance rankings from the logistic regression model for predicting central cervical lymph node metastasis in papillary thyroid microcarcinoma. Both clinical and radiomic features were included. Radiomic features were extracted via the Darwin platform (http://www.yizhun-ai.com/)

both radiomic and clinical variables. The formula for the RadScore was as follows:

$$
\begin{aligned}
&\boldsymbol{RadScore} = \\
&-2.025 \times clinic_Age \\
&+1.291 \times original_shape2D \\
&\quad_MaximumDiameter_modal1_paramsName1 \\
&+1.275 \times clinic_HashimotoThyroiditis_1 \\
&+1.190 \times logarithm_firstorder_10Percentile \\
&\quad_modal1_paramsName1 \\
&+1.049 \times wavelet-LH_glrlm \\
&\quad_RunLengthNonUniformity \\
&\quad_modal1_paramsName1 \\
&-0.549 \times original_shape2D_Sphericity \\
&\quad_modal1_paramsName1 \\
&+0.209
\end{aligned}
$$

For the training cohort, the AUC was 0.767 (95% CI: 0.716–0.818), the recall was 0.556 (95% CI: 0.481–0.629), and the accuracy was 0.708. For the validation cohort, the AUC was 0.729 (95% CI: 0.648–0.810), the recall was 0.753 (95% CI: 0.644–0.838), and the accuracy was 0.674. These results indicated robust discriminative performance, with the model demonstrating enhanced sensitivity in identifying positive cases in the validation cohort.

The relative importance of each feature within the logistic regression model was visualized (Fig. 4). Model calibration was evaluated via the Hosmer–Lemeshow goodness-of-fit test, which demonstrated acceptable calibration for both the training set ($Z = 5.909$, $P = 0.052$) and the validation set ($Z = 2.523$, $P = 0.283$) (Fig. 5).

Discussion

In the present study, the combination of ultrasound radiomics and clinical parameters substantially improved the predictive performance of CCLNM in patients with PTMC. Central compartment lymph node metastasis, which has been reported in approximately 34–60% of PTMC patients, represents a pivotal determinant of disease progression and long-term prognosis [18, 19]. The identification of independent risk factors—specifically patient age and the presence of HT—was demonstrated to be critically important for individualized risk stratification. In preoperative settings, particularly prior to microwave ablation of thyroid nodules, the application of the proposed predictive model may enable more precise estimation of metastatic risk. This, in turn, may assist in optimizing clinical decision-making, tailoring treatment strategies, reducing unnecessary surgical interventions, and ultimately enhancing patient outcomes.

Risk factors for central lymph node metastasis

Multivariate analysis identified younger age as an independent risk factor for CCLNM in patients with PTMC. This association is in accordance with previous studies [20]. Younger patients tend to present with larger tumors and a higher incidence of thyroid capsule invasion, suggesting more aggressive local behavior [21]. Furthermore, increased susceptibility to genetic alterations in younger individuals may contribute to earlier tumor onset and more rapid progression [22].

A significantly higher rate of lymph node metastasis has been observed in male patients than in female patients. While male sex has consistently been recognized as a risk

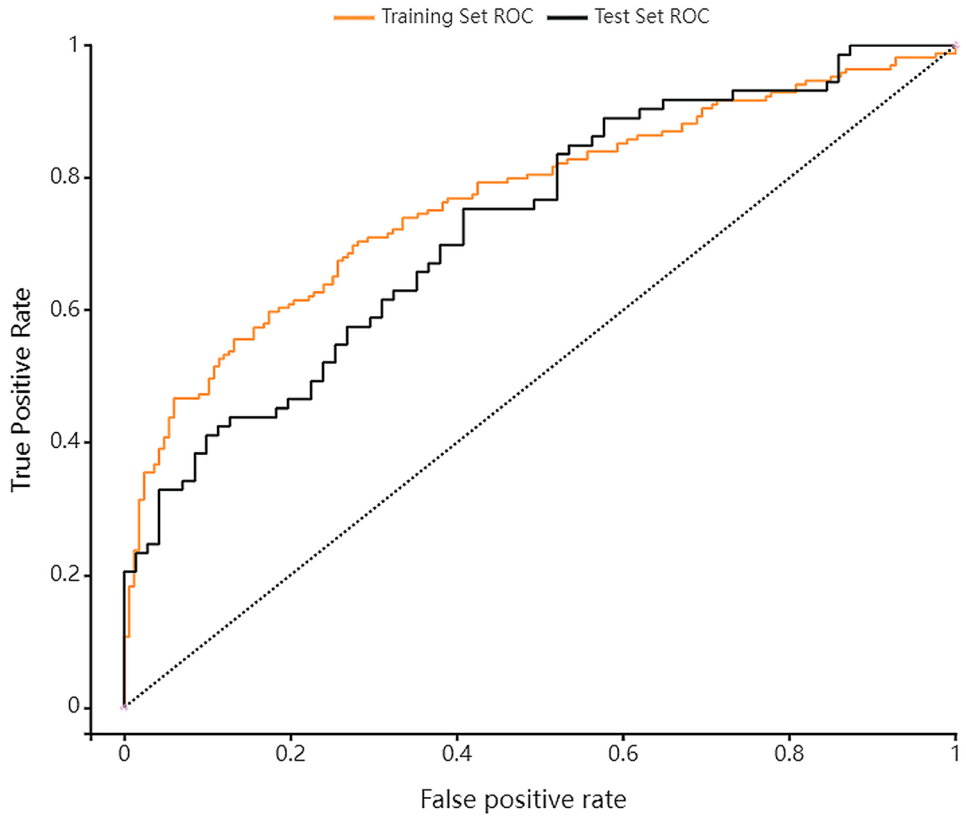


Fig. 4 ROC curve comparison of the model developed using radiomic features from ultrasound data and independent risk factors for predicting central lymph node metastasis in patients with thyroid micropapillary carcinoma. (**a**) ROC curve for the model applied to the training set (orange curve), (**b**) ROC curve for the model applied to the test set (black curve)

factor for lymph node metastasis in patients with PTMC, the underlying mechanisms remain unclear. Further investigation is needed to elucidate the role of sex-related biological differences in the development of CCLNM.

Relationship between HT and lymph node metastasis

Hashimoto's thyroiditis is a common autoimmune thyroid disorder, and its association with papillary thyroid carcinoma has been widely acknowledged. In the present study, HT was identified as an independent risk factor for CCLNM in patients with PTMC. Although the relationship between HT and PTC, particularly with respect to lymph node metastasis, remains controversial, some studies have proposed that chronically elevated TSH levels in HT patients may promote follicular epithelial cell proliferation, thereby accelerating the development of PTMC [23]. Conversely, other studies suggest that HT may exert a protective effect, delaying lymph node metastasis and extrathyroidal invasion in patients with PTMC [24, 25].

The findings of the present study support the hypothesis that HT is an independent risk factor for CCLNM, which is consistent with results from several other centers [26–28]. Lubin et al. [28] suggested that background HT, through increased expression of programmed death-ligand 1 (PD-L1), may promote lymph node metastasis. While the precise mechanisms underlying the coexistence of HT and PTC remain incompletely understood, it is hypothesized that the chronic inflammatory microenvironment in HT may modulate tumor invasiveness and metastatic characteristics through immune responses and cytokine alterations. Further studies are warranted to explore the role of HT in PTMC, particularly in relation to its impact on CCLNM.

The role of ultrasound radiomics in predicting lymph node metastasis

The present study suggests that ultrasound radiomics holds significant promise for predicting CCLNM in patients with PTMC. The area under the curve for the ultrasound-only model was 0.695 (95% CI: 0.639–0.751) in the training set and 0.668 (95% CI: 0.580–0.756) in the test set. When combined with clinically independent risk factors, such as age and HT, the predictive performance of the model improved. Ultrasound radiomics, an emerging quantitative imaging technique, extracts tumor features such as morphology, texture, and echogenicity to

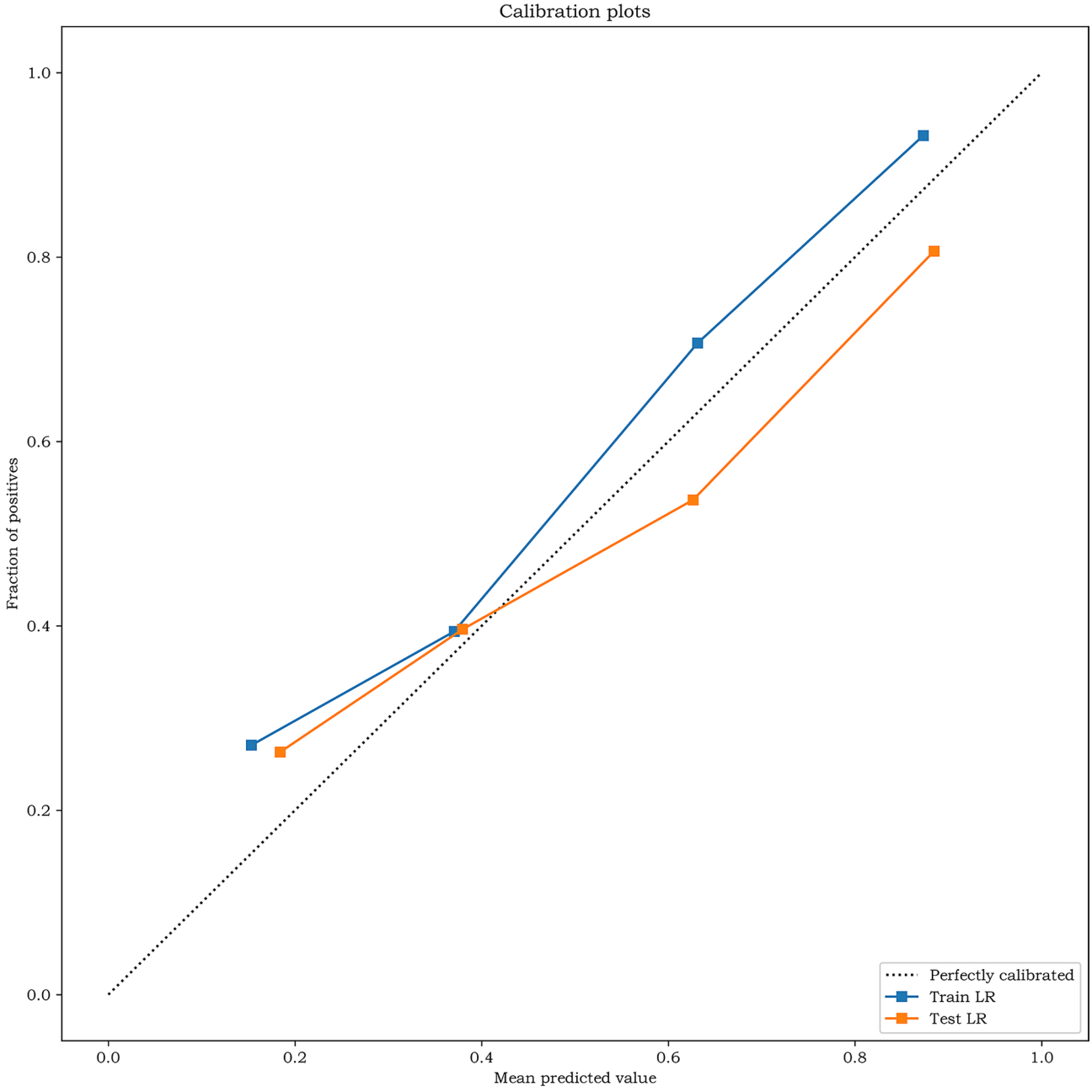


Fig. 5 Calibration plots of the model for predicting central lymph node metastasis in patients with thyroid micropapillary carcinoma. The points illustrate the alignment between the model's predicted probabilities and the actual observed outcomes in both the training and test datasets

provide more precise information for predicting lymph node metastasis in thyroid cancer patients.

Although most existing studies do not differentiate between unifocal and multifocal PTMC [29–31], the focus of the present study was on the risk of CCLNM in unifocal PTMC. The results demonstrated that combining ultrasound radiomics with clinical parameters can further increase the prediction accuracy. Thus, ultrasound radiomics not only offers valuable support for preoperative lymph node metastasis assessment in patients undergoing microwave ablation but also provides a solid foundation for the development of personalized treatment plans.

Study limitations and future directions

This study has several acknowledged limitations. First, its retrospective, single-center design and modest sample size ($n = 480$) may introduce selection bias and limit generalizability. Although the cohort was rigorously selected from 2,933 consecutive cases to ensure data quality and

homogeneity, this stringent inclusion may have constrained variability and reduced the external applicability of the model.

Second, the current analysis did not incorporate molecular markers, genetic profiles, or postoperative pathological details, which are increasingly recognized as influential in nodal metastasis risk stratification. Their absence may partially account for the model's moderate predictive performance.

Moreover, while the use of machine learning-based radiomics for predicting central compartment lymph node metastasis (CCLNM) in papillary thyroid microcarcinoma (PTMC) appears promising, the AUC values indicate that the model is not yet suitable for clinical deployment. The intent of this study was to explore feasibility rather than to offer a ready-to-use clinical tool.

To address these limitations, future research should focus on constructing prospective, multicenter datasets, incorporating more diverse clinical and biological variables (e.g., BRAF/TERT mutations and the Ki-67 index), and validating models across external cohorts. These steps are essential for enhancing model generalizability, performance stability, and clinical translatability.

Conclusions

The combined model integrating ultrasound radiomics and clinical parameters showed good potential in predicting CCLNM in unifocal PTMC patients. However, the model's performance, as indicated by the AUC values, is not yet sufficient for clinical application. The main goal of this study was to assess the feasibility of using machine learning-based radiomics for CCLNM prediction. Future studies should focus on refining the model with a larger, more diverse dataset and incorporating additional imaging, pathological, and molecular data to improve its stability, standardization, and clinical applicability.

Abbreviations

PTMC	Papillary thyroid microcarcinoma
CCLNM	Central compartment lymph node metastasis
RFA	Radiofrequency ablation
AI	Artificial intelligence
ML	Machine learning
FNAC	Fine-needle aspiration cytology
BMI	Body mass index
HT	Hashimoto's thyroiditis
ROI	Regions of interest
LR	Logistic regression
ROC	Receiver operating characteristic
AUC	Curves, area under the curve
TSH	Thyroid-stimulating hormone
PD-L1	Programmed death-ligand 1

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Author contributions

Haiyang Han, Heng Sun contributed equally to this paper. Authors' contributions Haiyang Han, Heng Sun: Formal analysis; Haiyang Han, Heng Sun: Investigation; Chang Zhou, Li Wei: Methodology; Haiyang Han, Heng Sun: Project administration; Chang Zhou, Li Wei: Resources; Haiyang Han, Heng Sun, Liang Xu，Dian shen and Wenshu Hu: Software; Chang Zhou: Supervision; Liang Xu，Dian shen and Wenshu Hu: Validation; Haiyang Han, Heng Sun: Writing -original draft; Chang Zhou, Li Wei, Liang Xu: Writing-review & editing. All authors reviewed the manuscript.

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Data availability

The datasets generated and/or analysed during the current study are not publicly available due to the hospital policy but are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This retrospective study was approved by the Medical Ethics Committee of Yichang Central People's Hospital, with a waiver of informed consent (ethical approval number: 2025-074-01).

Human participants

We confirm that all procedures involving human participants were conducted in accordance with relevant institutional and national guidelines and regulations.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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