Original Article

Prediction model construction of cervical central lymph node metastasis in papillary thyroid carcinoma combined with Hashimoto's thyroiditis utilizing conventional ultrasound and elastography

Jie Zhao, Ling-Min Li, Liang Gao, Hui Zhang, Lei Zhou, Xiao-Li Zhu, Meng-Ying Li, Jian-Hong Wang

Department of Ultrasound, Xi'an People's Hospital (Xi'an Fourth Hospital), Xi'an, China

Contributions: (I) Conception and design: JH Wang; (II) Administrative support: JH Wang; (III) Provision of study materials or patients: J Zhao; (IV) Collection and assembly of data: J Zhao, LM Li, L Gao, H Zhang, L Zhou, MY Li, XL Zhu; (V) Data analysis and interpretation: J Zhao, LM Li, L Gao, H Zhang, L Zhou, MY Li, XL Zhu; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Jian-Hong Wang, MD. Department of Ultrasound, Xi'an People's Hospital (Xi'an Fourth Hospital), 21 Jiefang Road, Xincheng District, Xi'an 710000, China. Email: sonowangyy@126.com.

Background: When papillary thyroid carcinoma (PTC) is accompanied by Hashimoto's thyroiditis (HT), it is often challenging for preoperative ultrasound to distinguish between central lymph node enlargement caused by PTC metastasis and inflammatory reaction due to HT. However, central lymph node metastasis (CLNM) is closely associated with the risk of PTC recurrence after surgery. In this study, we developed a model to predict in patients with PTC combined with HT, based on conventional ultrasound characteristics and shear wave elastography (SWE) quantitative parameters of the primary lesion. We aimed to evaluate its predictive value to provide a useful reference for clinical decisions regarding central lymph node dissection.

Methods: This retrospective study included ultrasound data for 181 PTC patients with concurrent HT (totaling 215 nodules), confirmed by surgical pathology at our hospital and routinely undergoing central neck lymph node dissection. All enrolled PTC patients were randomly divided into training and test groups at a 7:3 ratio. Then, patients in each group were further segregated into two distinct cohorts: the CLNM group and the non-CLNM group as per the gold standard of pathology assessment. Subsequent statistical analysis of conventional ultrasound characteristics pertaining to primary foci alongside quantitative parameters derived from SWE, facilitated the identification of independent risk factors associated with CLNM. Then, a nomogram model was constructed, and its predictive value was evaluated. The test group was used for internal validation.

Results: Univariate analysis results in the training group indicated that nodule size, multiplicity, location, capsular invasion, and Emax were significantly associated with CLNM (all $P<0.05$). Multivariate analysis further identified nodule size, multiplicity, location, capsular invasion, and Emax as independent risk factors for CLNM (all $P<0.05$). Based on the multivariate analysis results, a nomogram model was developed to predict the occurrence of CLNM in PTC patients with HT. Receiver operating characteristic (ROC) curve analysis showed high predictive accuracy for CLNM, with an area under the ROC curve (AUC) of 0.837 in the training group and 0.882 in the test group. Calibration curves demonstrated good fit, closely aligning with the diagonal, indicating strong consistency in predicting CLNM.

Conclusions: The nomogram model, based on primary lesion ultrasound characteristics and SWE quantitative parameters in PTC patients with HT, may aid clinicians in preoperatively predicting the likelihood of CLNM in PTC patients.

Keywords: Central lymph node metastasis (CLNM); Hashimoto's thyroiditis; papillary thyroid carcinoma (PTC); shear wave elastography (SWE); prediction model

Submitted Jul 02, 2024. Accepted for publication Dec 09, 2024. Published online Dec 27, 2024.
doi: 10.21037/gs-24-271
View this article at: https://dx.doi.org/10.21037/gs-24-271

Introduction

Thyroid carcinoma represents a prevalent malignancy within the endocrine system, exhibiting an upward trajectory in incidence rates in recent times. Papillary thyroid carcinoma (PTC), constituting 80–90% of thyroid carcinoma cases, stands as the predominant histopathological subtype (1). Notably, patients with PTC commonly manifest lymph node metastasis, predominantly observed as central lymph node metastasis (CLNM) (2). Hashimoto's thyroiditis (HT), or chronic lymphocytic thyroiditis, typifies an autoimmune disease characterized by extensive infiltration of lymphocytes into the thyroid gland often culminating in inflammatory enlargement and central lymph node involvement. However, when PTC is combined with HT, preoperative ultrasound often struggles to distinguish whether central lymph node enlargement is due to metastatic spread from PTC or an inflammatory response caused by HT. In most cases, the lymph nodes appear as rounded enlargements (3,4). However, CLNM is closely associated with the risk of recurrence following PTC surgery (5,6).

A significant association has been identified between ultrasound imaging features of the primary PTC lesion and CLNM (7-9), while other evidence has suggested a strong correlation between primary lesion SWE quantitative parameters and CLNM (10). However, few studies have explored the relationship between these factors and CLNM in cases where PTC is combined with HT. Hence, in our study, we aimed to explore the interplay between ultrasound characteristics of primary foci, quantitative parameters derived from shear wave elastography (SWE), and CLNM in patients presenting with concurrent PTC and HT. By interpreting these relationships, we aim to develop a predictive model that can furnish clinical evidence for the implementation of central lymph node dissection thereby mitigating the risk of over-treatment. Ultimately, our objective is to furnish a more precise and tailored therapeutic approach for PTC patients concurrently afflicted with HT, thereby enhancing treatment efficacy and augmenting the quality of life for these patients. We present this article in accordance with the TRIPOD reporting checklist (available at https://gs.amegroups.com/article/view/10.21037/gs-24-271/rc).

Highlight box

Key findings

- The nomogram model, based on primary lesion ultrasound features and shear wave elastography (SWE) quantitative parameters in patients with papillary thyroid carcinoma (PTC) combined with Hashimoto's thyroiditis (HT), can assist clinicians in predicting the likelihood of central lymph node metastasis in PTC patients preoperatively.

What is known and what is new?

- Some studies suggest a significant correlation between the ultrasound characteristics of primary PTC lesions and central lymph node metastasis. Others have found a notable association between primary lesion SWE quantitative parameters and central lymph node metastasis. However, few studies have investigated the relationship between these two factors and central lymph node metastasis in PTC patients with concurrent HT.
- This study aims to explore the relationship between primary lesion ultrasound features, SWE quantitative parameters, and central lymph node metastasis in PTC patients with HT. Based on this relationship, a predictive model is constructed to guide decisions on central lymph node dissection, helping to avoid overtreatment.

What is the implication, and what should change now?

- In cases of PTC combined with HT, when preoperative ultrasound shows enlarged, rounded central lymph nodes, the ultrasound features of the primary.

Methods

Patients

We conducted a retrospective analysis of the ultrasound data from patients diagnosed with PTC combined with HT who underwent surgical treatment with routine cervical central lymph node dissection at Xi'an People's Hospital (Xi'an Fourth Hospital) between January 2019 and October 2023. A total of 181 patients, comprising 215 nodes, were enrolled in this study. The age of the patients ranged from 5 to 70 years, with a mean age of 46.50±9.57 years. All enrolled PTC patients were randomly divided into training and test groups at a 7:3 ratio. Then, patients in each group were further categorized into two groups based on pathology results: the CLNM group

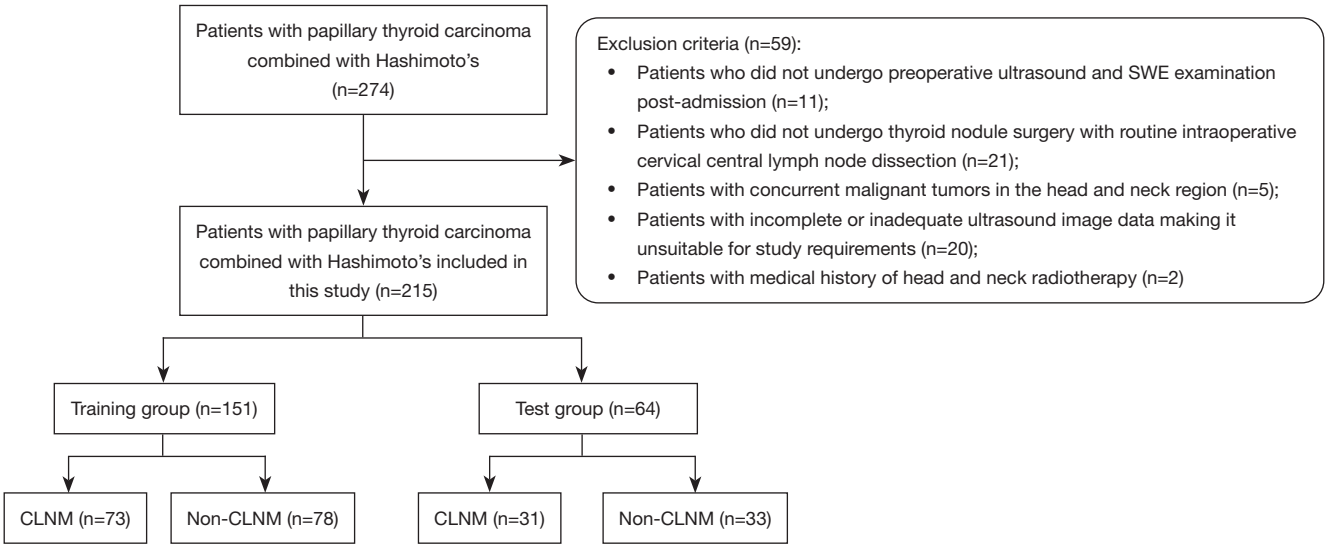

Figure 1 Flowchart of enrollment and grouping. CLNM, central lymph node metastasis; SWE, shear wave elastography.

(comprising 104 nodes) and non-CLNM group (comprising 111 nodes) with pathology serving as the gold standard. A flowchart of enrollment and grouping is shown in *Figure 1*.

Inclusion criteria were: (I) patients who underwent preoperative ultrasound and SWE examination post-admission with complete image data available; (II) patients who underwent thyroid nodule surgery with routine intraoperative cervical central lymph node dissection (11).

Exclusion criteria were: (I) patients with concurrent malignant tumors in the head and neck region; (II) patients with incomplete or inadequate ultrasound image data making it unsuitable for study requirements; (III) patients with medical history of head and neck radiotherapy.

Instruments and methods

Instruments

The ultrasound data utilized in this study were obtained using the Aixplorer ultrasound machine manufactured by SuperSonic Imagine (Aix-en-Provence, France). The imaging was conducted with a linear array probe model SLl5-4, featuring a frequency range of 4–15 MHz.

Study methods

Patients were arranged in a supine position with neck elevated to fully expose the thyroid region. A routine ultrasound scan was performed to assess thyroid nodules including observations regarding the quantity, location, depth, size, orientation (both vertical and horizontal). Additionally, characteristics such as structure (solid, cystic solid, and cystic) echogenicity (hyper-echoic, iso-echoic, hypo-echoic, extremely hypo-echoic), calcification (no calcification, coarse calcification, peripheral calcification), margins (well-defined, indistinct, irregular), and capsule (invasive, non-invasive) of the nodules were meticulously evaluated during the examination.

Following the conventional ultrasound examination, the SWE mode was activated, and the region of interest (ROI) was meticulously selected to encompass the entire nodule along with surrounding normal thyroid tissue. Throughout the examination, patients were instructed to hold their breath while the probe was gently placed without exerting any pressure. Once the image was stabilized and properly framed, a 2-mm-diameter Q-BOX was positioned at the firmest region within the nodules. Quantitative SWE parameters including the Young's modulus maximum (Emax), the mean (Emean), and the minimum (Emin) were then acquired. To ensure data accuracy, three measurements were obtained and subsequently averaged.

Image acquisition and evaluation were conducted collaboratively by two senior sonographers. In case of disagreement, a third senior sonographer was consulted to facilitate discussion and ultimately achieve a consensus regarding the assessment.

Statistical analysis

SPSS version 26.0 and R software version 4.1.3 were

utilized for statistical analysis. All enrolled PTC patients were randomly divided into training and test groups at a 7:3 ratio. The study began with univariate analysis of primary foci features and quantitative SWE parameters of the training group. Quantitative data were expressed as $\bar{x} \pm s$ and comparison between groups was conducted using independent samples *t*-test. Categorical data were expressed as n (%), and comparison between groups was performed using Chi-squared test or Fisher's exact test. Following this, logistic regression analysis was utilized to conduct multifactorial analysis on statistically significant indicators identified in univariate analysis aiming to determine independent risk factors of CLNM. Subsequently, a nomogram model was constructed based on the results of logistic regression analysis and validated using the test group (12-14). The diagnostic efficacy of the model was assessed by generating receiver operating characteristic (ROC) curves, while calibration curves were plotted to assess the model's prediction compliance. A statistical significance level of P<0.05 was applied throughout the statistical analyses.

Ethical statement

This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). It was approved by the Ethics Committee of Xi'an People's Hospital (Xi'an Fourth Hospital) (No. KJLL-Z-K-2024008). Since this study was retrospective and did not involve direct contact with study participants, the ethics committee waived the requirement for informed consent.

Results

Univariate analysis of CLNM in PTC patients when accompanied by HT

Univariate analysis of the training group revealed significant associations between CLNM and several factors including nodule size, multiplicity, location, capsule invasion, and Emax (all P<0.05). Specifically, larger nodule diameter, multiple nodules located in the isthmus, capsule invasion, and higher Emax were observed to be associated with an increased tendency for CLNM (as summarized n *Table 1*).

Multifactorial analysis of CLNM in PTC patients when accompanied by HT

Multifactorial analysis of the training group demonstrated that nodule size, multiplicity, location, capsule invasion, and Emax emerged as independent risk factors for CLNM (all with P<0.05) (as indicated in *Table 2*).

Nomogram model construction of CLNM in PTC patients when accompanied by HT

The nomogram model for predicting CLNM in PTC patients combined with HT was constructed based on the results of multifactorial analysis. In this model, the presence of CLNM was defined as the dependent variable, while the six independent risk factors identified were defined as independent variables. Each predictive indicator was assigned a score within the model, and cumulative total score corresponded to the predicted risk value (*Figure 2*).

The accuracy of the model in predicting CLNM was assessed using ROC analysis. The area under the ROC curve (AUC) for the training set was 0.837 (95% confidence interval: 0.773–0.901). For the test set, the AUC was 0.882 (95% confidence interval: 0.803–0.960) (*Figure 3*).

Additionally, calibration curves of the training and test groups were generated to evaluate the alignment between the actual observations and the probabilistic prediction made by the nomogram model. The calibration curve was close to the diagonal line, which signifies good fitting, affirming the consistency of the model in predicting CLNM (*Figure 4*).

Discussion

PTC generally carries a favorable prognosis, but it is often accompanied with CLNM (15). International experts typically do not recommend prophylactic central lymph node dissection for low-risk PTC patients who clinically or radiologically show negative lymph nodes. Domestic experts also tend to adopt a conservative approach in such cases (15-17). Nonetheless, research has indicated recurrence rates of PTC ranging from 8% to 25% postoperatively, with CLNM being a primary contributing factor (5,18). Ultrasound serves as the primary imaging modality for preoperative diagnosis of CLNM in PTC patients. Accurate evaluation of central lymph nodes preoperatively is crucial to prevent recurrence resulting from misdiagnosis via ultrasound. Central lymph nodes are situated around the trachea and suprasternal fossa. However, due to gas interference and patients' individual conditions, direct ultrasound diagnosis rates of CLNM are low, particularly in PTC patients with concurrent HT. In this subgroup, the

Table 1 Univariate analysis of CLNM in PTC patients when accompanied by HT

Variables	Non-CLNM (n=111)	CLNM (n=104)	Statistical value	P
Nodule size (cm)	0.82±0.58	1.35±0.74	−5.872	<0.001
Multiple			4.665	0.03
No	59 (53.2)	40 (38.5)		
Yes	52 (46.8)	64 (61.5)		
Location			20.336	<0.001
Isthmus	2 (1.8)	13 (12.5)		
Upper pole	21 (18.9)	36 (34.6)		
Middle pole	36 (32.4)	18 (17.3)		
Lower pole	52 (46.8)	37 (35.6)		
Depth			1.921	0.69
Shallow	41 (36.9)	40 (38.5)		
Middle	11 (9.9)	7 (6.7)		
Deep	39 (35.1)	32 (30.8)		
Shallow-deep	20 (18.0)	25 (24.0)		
Orientation			0.014	0.90
Horizontal	45 (40.5)	43 (41.3)		
Vertical	66 (59.5)	61 (58.7)		
Structure			0.144	0.71
Solid	108 (97.3)	102 (98.1)		
Predominantly solid	3 (2.7)	2 (1.9)		
Echogenicity			1.392	0.50
Iso-echoic	1 (0.9)	3 (2.9)		
Hypo-echoic	70 (63.1)	61 (58.7)		
Extreme hypo-echoic	40 (36.0)	40 (38.5)		
Calcification			1.434	0.49
No	38 (34.2)	29 (27.9)		
Gross calcification	7 (6.3)	5 (4.8)		
Microcalcification	66 (59.5)	70 (67.3)		
Edge			3.336	0.07
Smooth	13 (11.7)	5 (4.8)		
Blurred or irregular	98 (88.3)	99 (95.2)		
Capsule invasion			32.931	<0.001
No	65 (58.6)	21 (20.2)		
Yes	46 (41.4)	83 (79.8)		
Emax (kPa)	51.96±21.51	65.69±25.84	−4.219	<0.001
Emean (kPa)	40.64±16.11	41.28±16.55	−0.287	0.77
Emin (kPa)	25.86±11.35	25.45±11.38	0.266	0.79

Data are presented as mean ± standard deviation or n (%). CLNM, central lymph node metastasis; PTC, papillary thyroid carcinoma; HT, Hashimoto thyroiditis.

Table 2 Multifactorial analysis of CLNM in PTC patients when accompanied by HT

Indicator	β	SE	Wald	P	Exp(B)	95% CI
Size (cm)	1.044	0.336	9.656	0.002	2.84	1.470–5.485
Emax (kPa)	0.021	0.009	5.915	0.02	1.022	1.004–1.040
Multiple occurrence	0.966	0.348	7.680	0.006	2.627	1.327–5.201
Location	0.336	0.140	5.715	0.02	1.399	1.062–1.842
Capsule invasion	1.673	0.355	22.145	0.001	5.327	2.654–10.691

CLNM, central lymph node metastasis; PTC, papillary thyroid carcinoma; HT, Hashimoto thyroiditis; SE, standard error; CI, confidence interval.

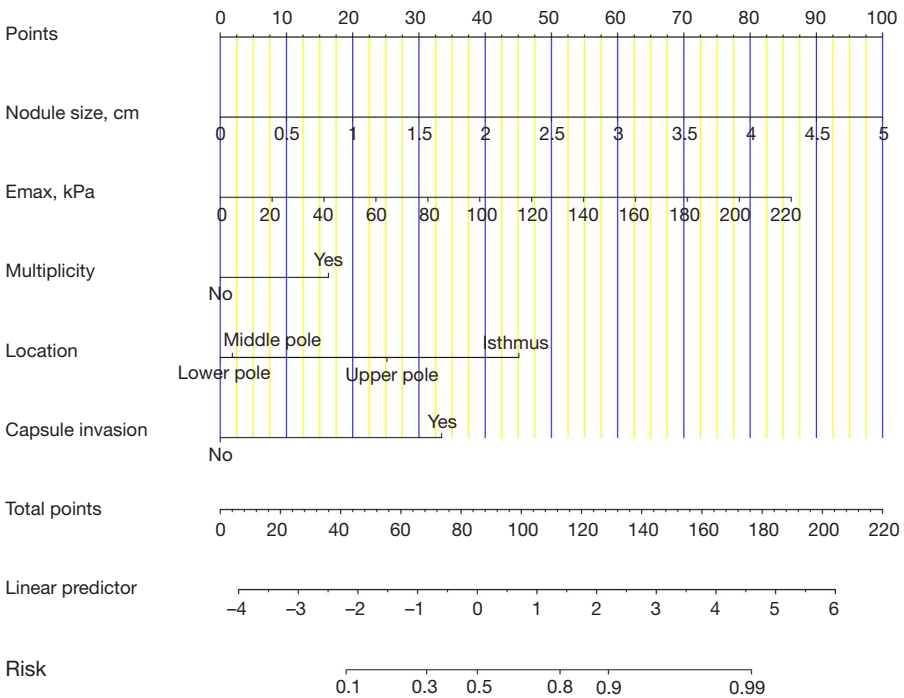

Figure 2 Predictive nomogram of risk of CLNM in PTC patients when accompanied by HT. CLNM, central lymph node metastasis; PTC, papillary thyroid carcinoma; HT, Hashimoto thyroiditis.

presence of numerous inflammation-stimulated reactive hyperplasia lymph nodes in the central region significantly hampers ultrasound diagnosis sensitivity.

Studies have indicated a preoperative misdiagnosis rate of CLNM in patients with PTC via ultrasound ranging from 30% to 70% (19,20), which is consistent with our findings, showing that only 64 cases of thyroid metastasis were diagnosed preoperatively through ultrasound. Despite the low direct detection rate of CLNM by ultrasound, its depiction of primary foci of PTC is typically clear and reliable. However, the relationship between PTC combined with HT and CLNM has not been explored enough. Therefore, in this study we aimed to investigate this relationship focusing on routine ultrasound features of primary foci, quantitative parameters of SWE and their association with CLNM in patients with PTC with concurrent HT. Our results indicated that larger nodule size, multiple nodules, isthmus location, capsule invasion, and larger Emax were all identified as independent risk factors for CLNM. Based on these findings we constructed a prediction model that demonstrated high accuracy in predicting CLNM.

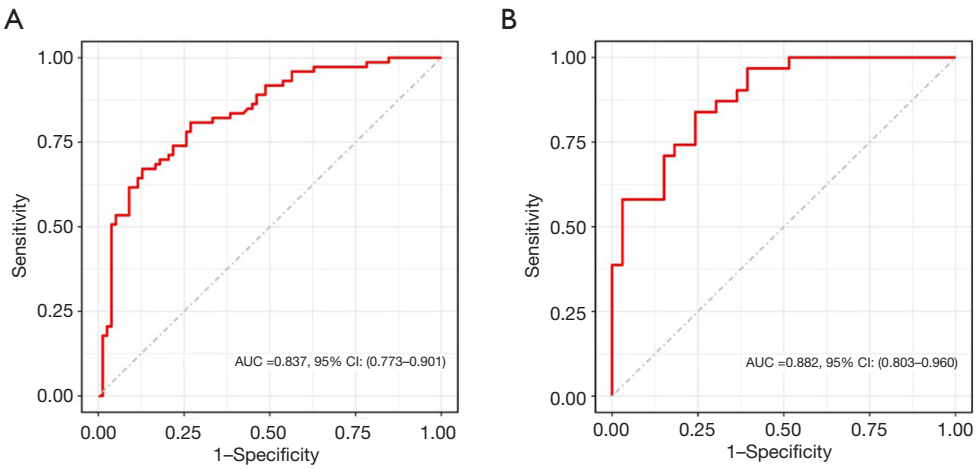

Figure 3 ROC of the predictive nomogram model of CLNM in PTC patients when accompanied by HT. (A) Training set; (B) test set. AUC, area under the curve; CI, confidence interval; ROC, receiver operating characteristic; CLNM, central lymph node metastasis; PTC, papillary thyroid carcinoma; HT, Hashimoto thyroiditis.

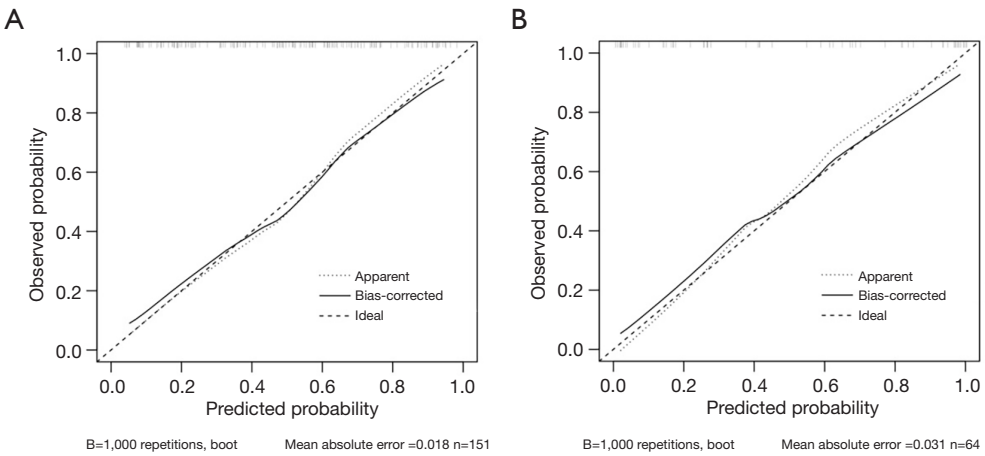

Figure 4 Calibration curve of the nomogram model. (A) Training set; (B) test set.

It is commonly observed that many thyroid nodules are multifocal, with prevalence rates ranging from approximately 18% to 87% (21). Several studies have confirmed that multifocal PTC is indeed associated with CLNM, which aligns with the findings of this study (22-24). From a biological perspective, tumor cells in multifocal PTC tend to be more invasive, spreading faster, and are more prone to developing CLNM. Additionally, considering tumor burden, having multiple nodules results in a higher overall tumor burden and consequently increases the risk of metastasis, despite the maximum diameter of individual nodes in multifocal PTC often being smaller than those in solitary PTC (25).

Several studies have highlighted thyroid capsule invasion as a significant risk factor for CLNM in PTC, consistent with the findings of this study (26-28). Another research has suggested that diagnosing CLNM may involve considering capsule invasion up to 25% of the total capsule of the tumor-capsule interface (21). The thyroid capsule comprises both a true capsule consisting of the outer thyroid membrane and a false capsule composed of cervical visceral fascia. The false capsule is present only on the medial side of lateral lobes and posterior side of the isthmus. Consequently, most of the thyroid gland is covered

solely by the outer thyroid membrane which is composed of thin fibrous tissue and is prone to being breached by tumor tissues. This makes it more likely for tumor tissues to invade central lymph nodes via the lymphatic vessels (29).

According to reports, CLNM is positively correlated with node size, where the larger the nodule the higher the CLNM probability (30,31). Certain studies have also reported that nodules larger than 1 cm in diameter were a risk factor for CLNM, which is consistent with this study (32). This could be attributed to the secretion of vascular endothelial growth factor by malignant nodules, which stimulates neo-vascularization, accelerating nodule growth and facilitating further infiltration (33).

Several studies have indicated that isthmus nodules are more susceptible to extra-glandular invasion and CLNM when compared to lobar nodules, which corroborates with the results of our study (34). Additionally, some researchers have suggested that bilateral central lymph node dissection should be considered a standard procedure for isthmus tumors (35). The recommendation may be attributed to the proximity of isthmus nodules to the thyroid capsule, making them more likely to cause damage to it during tumor growth.

In this study, a larger nodal Emax was associated with a higher likelihood of CLNM which aligns with the findings of Wang *et al.* (36). This relationship may be attributed to the degree of nodal fibrosis, which is known to promote tumor aggressiveness. Elastography, by assessing tissue stiffness, can indirectly indicate the extent of tissue fibrosis and may also suggest the presence of lymph node metastasis (30,32,37).

Conclusions

The decision to perform cervical central lymph nodes dissection in PTC patients who also have HT, hinges on the development of CLNM. Therefore, it is of great clinical significance to establish an individual-specific prediction model for CLNM in patients with PTC who also have HT. In this study, through multifactorial regression analysis, we constructed a nomogram model integrating five independent risk factors including node size, multiplicity, location, capsule invasion, and Emax to visualize the risk of CLNM in different patients. The model demonstrated a favorable predictive value for CLNM with an AUC of 0.846, as evaluated by ROC analysis.

However, there are several limitations in this study. Firstly, being a retrospective single-center study, the sample size was limited, necessitating future expansion for validation in multicenter prospective studies. Additionally, this study considered multiple PTC nodules within the same patient as separate samples, potentially failing to account for the influence of other cancer foci on the model. Further analysis and exploration of this aspect will be crucial in future prospective studies.

Acknowledgments

Funding: None.

Footnote

Reporting Checklist: The authors have completed the TRIPOD reporting checklist. Available at https://gs.amegroups.com/article/view/10.21037/gs-24-271/rc

Data Sharing Statement: Available at https://gs.amegroups.com/article/view/10.21037/gs-24-271/dss

Peer Review File: Available at https://gs.amegroups.com/article/view/10.21037/gs-24-271/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://gs.amegroups.com/article/view/10.21037/gs-24-271/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). It was approved by the Ethics Committee of Xi'an People's Hospital (Xi'an Fourth Hospital) (No. KJLL-Z-K-2024008). Since this study was retrospective and did not involve direct contact with study participants, the ethics committee waived the requirement for informed consent.

References

1. Miranda-Filho A, Lortet-Tieulent J, Bray F, et al. Thyroid cancer incidence trends by histology in 25 countries: a population-based study. Lancet Diabetes Endocrinol 2021;9:225-34.
2. Zhou SL, Guo YP, Zhang L, et al. Predicting factors of central lymph node metastasis and BRAF(V600E) mutation in Chinese population with papillary thyroid carcinoma. World J Surg Oncol 2021;19:211.
3. Ragusa F, Fallahi P, Elia G, et al. Hashimotos' thyroiditis: Epidemiology, pathogenesis, clinic and therapy. Best Pract Res Clin Endocrinol Metab 2019;33:101367.
4. Fang F, Gong Y, Liao L, et al. Value of Contrast-Enhanced Ultrasound for Evaluation of Cervical Lymph Node Metastasis in Papillary Thyroid Carcinoma. Front Endocrinol (Lausanne) 2022;13:812475.
5. Min Y, Huang Y, Wei M, et al. Preoperatively Predicting the Central Lymph Node Metastasis for Papillary Thyroid Cancer Patients With Hashimoto's Thyroiditis. Front Endocrinol (Lausanne) 2021;12:713475.
6. Liu Y, Lv H, Zhang S, et al. The Impact of Coexistent Hashimoto's Thyroiditis on Central Compartment Lymph Node Metastasis in Papillary Thyroid Carcinoma. Front Endocrinol (Lausanne) 2021;12:772071.
7. Du J, Yang Q, Sun Y, et al. Risk factors for central lymph node metastasis in patients with papillary thyroid carcinoma: a retrospective study. Front Endocrinol (Lausanne) 2023;14:1288527.
8. Chang L, Zhang Y, Zhu J, et al. An integrated nomogram combining deep learning, clinical characteristics and ultrasound features for predicting central lymph node metastasis in papillary thyroid cancer: A multicenter study. Front Endocrinol (Lausanne) 2023;14:964074.
9. Gao X, Luo W, He L, et al. Predictors and a Prediction Model for Central Cervical Lymph Node Metastasis in Papillary Thyroid Carcinoma (cN0). Front Endocrinol (Lausanne) 2021;12:789310.
10. Guo JN, Song LH, Yu PY, et al. Ultrasound Elastic Parameters Predict Central Lymph Node Metastasis of Papillary Thyroid Carcinoma. J Surg Res 2020;253:69-78.
11. Shaha AR, Tuttle RM. Frozen section of central lymph nodes in thyroid cancer. Gland Surg 2022;11:637-9.
12. Zhao D, Li W, Zhang X. Development and validation of a nomogram for preoperative prediction of ipsilateral cervical central lymph node metastasis in papillary thyroid cancer: a population-based study. Gland Surg 2024;13:528-39.
13. Zou Y, Shi Y, Bi H, et al. A nomogram for risk stratification of central cervical lymph node metastasis in patients with papillary thyroid carcinoma. Quant Imaging Med Surg 2024;14:5084-98.
14. Duan S, Yang Z, Wei G, et al. Nomogram for predicting the risk of central lymph node metastasis in papillary thyroid microcarcinoma: a combination of sonographic findings and clinical factors. Gland Surg 2024;13:1016-30.
15. China Anti-Cancer Association Committee of Thyroid Oncology. China Anti-Cancer Association guidelines for holistic integrative management of thyroid cancer (2022 abridged version). Chinese Journal of Clinical Oncology 2023;50:325-30.
16. Bible KC, Kebebew E, Brierley J, et al. 2021 American Thyroid Association Guidelines for Management of Patients with Anaplastic Thyroid Cancer. Thyroid 2021;31:337-86.
17. Durante C, Hegedüs L, Czarniecka A, et al. 2023 European Thyroid Association Clinical Practice Guidelines for thyroid nodule management. Eur Thyroid J 2023;12:e230067.
18. Li Y, Tian J, Jiang K, et al. Risk factors and predictive model for recurrence in papillary thyroid carcinoma: a single-center retrospective cohort study based on 955 cases. Front Endocrinol (Lausanne) 2023;14:1268282.
19. Woo CG, Sung CO, Choi YM, et al. Clinicopathological Significance of Minimal Extrathyroid Extension in Solitary Papillary Thyroid Carcinomas. Ann Surg Oncol 2015;22 Suppl 3:S728-33.
20. Yu X, Song X, Sun W, et al. Independent Risk Factors Predicting Central Lymph Node Metastasis in Papillary Thyroid Microcarcinoma. Horm Metab Res 2017;49:201-7.
21. Guang Y, He W, Zhang W, et al. Clinical Study of Ultrasonographic Risk Factors for Central Lymph Node Metastasis of Papillary Thyroid Carcinoma. Front Endocrinol (Lausanne) 2021;12:791970.
22. Liang J, Zeng W, Fang F, et al. Clinical analysis of Hashimoto thyroiditis coexistent with papillary thyroid cancer in 1392 patients. Acta Otorhinolaryngol Ital 2017;37:393-400.
23. Gui CY, Qiu SL, Peng ZH, et al. Clinical and pathologic predictors of central lymph node metastasis in papillary thyroid microcarcinoma: a retrospective cohort study. J Endocrinol Invest 2018;41:403-9.

24. Rui ZY, Liu Y, Zheng W, et al. A retrospective study of the risk factors and the prognosis in patients with papillary thyroid carcinoma depending on the number of lymph node metastasis. Clin Exp Med 2021;21:277-86.
25. Feng JW, Qu Z, Qin AC, et al. Significance of multifocality in papillary thyroid carcinoma. Eur J Surg Oncol 2020;46:1820-8.
26. Luo Y, Zhao Y, Chen K, et al. Clinical analysis of cervical lymph node metastasis risk factors in patients with papillary thyroid microcarcinoma. J Endocrinol Invest 2019;42:227-36.
27. Huang XP, Ye TT, Zhang L, et al. Sonographic features of papillary thyroid microcarcinoma predicting high-volume central neck lymph node metastasis. Surg Oncol 2018;27:172-6.
28. Wu X, Li B, Zheng C, et al. Risk factors for central lymph node metastases in patients with papillary thyroid microcarcinoma. Endocr Pract 2018;24:1057-62.
29. Zhu M, Zheng W, Xiang Y, et al. The relationship between central lymph node metastasis and the distance from tumor to thyroid capsule in papillary thyroid microcarcinoma without capsule invasion. Gland Surg 2020;9:727-36.
30. Zhao W, He L, Zhu J, et al. A nomogram model based on the preoperative clinical characteristics of papillary thyroid carcinoma with Hashimoto's thyroiditis to predict central lymph node metastasis. Clin Endocrinol (Oxf) 2021;94:310-21.
31. Zhong M, Zhang Z, Xiao Y, et al. The Predictive Value of ACR TI-RADS Classification for Central Lymph Node Metastasis of Papillary Thyroid Carcinoma: A Retrospective Study. Int J Endocrinol 2022;2022:4412725.
32. Liu C, Xiao C, Chen J, et al. Risk factor analysis for predicting cervical lymph node metastasis in papillary thyroid carcinoma: a study of 966 patients. BMC Cancer 2019;19:622.
33. Sisdelli L, Cordioli MICV, Vaisman F, et al. AGK-BRAF is associated with distant metastasis and younger age in pediatric papillary thyroid carcinoma. Pediatr Blood Cancer 2019;66:e27707.
34. Ramundo V, Lamartina L, Falcone R, et al. Is thyroid nodule location associated with malignancy risk? Ultrasonography 2019;38:231-5.
35. Li G, Lei J, Peng Q, et al. Lymph node metastasis characteristics of papillary thyroid carcinoma located in the isthmus: A single-center analysis. Medicine (Baltimore) 2017;96:e7143.
36. Wang L, Zheng W, She T. Predictive value of shear wave elastography in cervical lymph node metastasis of papillary thyroid carcinoma. China Medical Herald 2021;18:143-6.
37. Yang Z, Heng Y, Lin J, et al. Nomogram for Predicting Central Lymph Node Metastasis in Papillary Thyroid Cancer: A Retrospective Cohort Study of Two Clinical Centers. Cancer Res Treat 2020;52:1010-8.

Cite this article as: Zhao J, Li LM, Gao L, Zhang H, Zhou L, Zhu XL, Li MY, Wang JH. Prediction model construction of cervical central lymph node metastasis in papillary thyroid carcinoma combined with Hashimoto's thyroiditis utilizing conventional ultrasound and elastography. Gland Surg 2024;13(12):2325-2334. doi: 10.21037/gs-24-271