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Pretreatment level of circulating tumor cells is associated with lymph node metastasis in papillary thyroid carcinoma patients with ≤ 55 years old

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Abstract

Objective To investigate the relationship of pretreatment of circulating tumor cells (CTCs) and cervical lymph node metastasis (LNM) (central LNM (CLNM) and lateral LNM (LLNM)) in papillary thyroid carcinoma (PTC) patients with ≤ 55 years old.

Methods Clinicopathological data (CTCs level, Hashimoto's thyroiditis, thyroid function, multifocal, tumor size, invaded capsule, clinical stage, and LNM) of 588 PTC patients with ≤ 55 years old were retrospectively collected. The relationship of CLNM, LLNM and the clinical features of patients was analyzed. Univariate and multivariate logistic regression analyses were used to evaluate the relationship between the CTCs and CLNM, LLNM.

Results There were 273(46.4%) and 89(15.1%) patients with CLNM and LLNM, respectively. Patients with CLNM had higher proportions of multifocality, tumor size > 1 cm, invaded capsule, and positive CTCs level than those without (all $p < 0.05$). Patients with LLNM had higher proportions of multifocality, tumor size > 1 cm, and invaded capsule than those without (all $p < 0.05$). Logistic regression analysis showed that multifocality (odds ratio (OR): 1.821, 95% confidence interval (CI): 1.230–2.698, $p = 0.003$), tumor size > 1 cm (OR: 3.444, 95% CI: 2.296–5.167, $p < 0.001$), invaded capsule (OR: 1.699, 95% CI: 1.167–2.473, $p = 0.006$), and positive CTCs level (OR: 1.469, 95% CI: 1.019–2.118, $p = 0.040$) were independently associated with CLNM; and multifocality (OR: 2.373, 95% CI: 1.389–4.052, $p = 0.002$), tumor size > 1 cm (OR: 5.344, 95% CI: 3.037–9.402, $p < 0.001$), and invaded capsule (OR: 2.591, 95% CI: 1.436–4.674, $p = 0.002$) were independently associated with LLNM.

Conclusions Preoperative CTCs positive was associated with CLNM in PTC patients with ≤ 55 years old, but not LLNM.

Keywords Circulating tumor cells, Papillary thyroid carcinoma, Central lymph node metastasis, Lateral lymph node metastasis

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Introduction

Thyroid cancer is a common malignant tumor of the head and neck, as well as one of the most common endocrine malignancies [1]. Due to the wide application and sensitivity of thyroid disease diagnosis technology, the detection rate of thyroid cancer is getting higher and higher, and the incidence of thyroid cancer is increasing [2, 3]. Differentiated thyroid carcinoma (DTC) accounts for the vast majority of thyroid malignancies, mainly including papillary thyroid carcinoma (PTC) and follicular thyroid carcinoma (FTC) [4, 5], of which PTC is the most common subtype [6]. Thyroid surgery is the most important treatment method for PTC. The main purpose of thyroid surgery is to resect thyroid cancer lesions, adjacent affected tissues, organs, and metastatic lymph nodes to prepare for postoperative radioactive iodine (RAI) treatment [7]. PTC is an inert cancer, and although the prognosis is good, about 10–30% of patients will have tumor recurrence and progression after initial treatment [8]. Cervical lymph node metastases (LNM), such as central lymph node metastasis (CLNM) and lateral lymph node metastasis (LLNM), have been shown to be the factors for poor prognosis of PTC, and patients with LNM have an increased risk of recurrence and decreased survival [9].

The biological behavior and clinical features of malignancies vary across ages, not only in the general spectrum of cancers, but also in individual cancer types and individual patients [10, 11]. Unlike most cancer stages, thyroid cancer is a tumor with age as the main stratifying factor, and age is independent from other factors [12]. Compared with older PTC patients, younger PTC patients have a higher incidence of larger tumor size, multifocality, LNM, and distant metastasis, and a higher recurrence rate of cervical lymph nodes [13–15]. In PTC patients younger than 55 years of age, LNM significantly affected disease-free survival (DFS) [16]. Wang et al. found that LLNM was a predictor of recurrence in PTC patients < 45 years of age [17]. Although various studies on age as a prognostic factor for PTC have used different age cut-off values, most studies have shown that the effect of LNM on prognosis in young patients is different with older patients. However, what are the risk factors for LNM in young PTC patients? It is a clinical problem worth studying.

The eighth edition of the American Joint Committee on Cancer/Union for International Cancer Control tumor-node-metastasis (AJCC/UICC TNM) staging system uniformly sets the cut-off age for DTC at 55 years [18, 19]. Tumor cells that survive in circulation after breaking through the blood vessel barrier are called circulating tumor cells (CTCs). CTCs are tumor biomarkers that are released into peripheral blood circulation from primary or metastatic sites spontaneously or due to clinical procedures [20]. At present, CTC has been widely used for early screening, disease monitoring, and prognosis assessment of solid tumors, especially breast cancer, lung cancer and colorectal cancer [20–22]. There was a correlation between the level of CTCs and the stage of thyroid cancer [23]. Yu et al. found that high level of CTCs was associated with CLNM in PTC [24]. It is understood that the relationship between CTCs and LNM in young PTC patients is still unclear. Therefore, this study retrospectively analyzed the relationship between cervical LNM and clinicopathological features in PTC patients with ≤ 55 years old, especially the level of CTCs before treatment. The aim of this study was to identify risk factors for cervical LNM in young patients with PTC.

Materials and methods

Subjects

The clinical records of 588 PTC patients with ≤ 55 years old who were hospitalized in Meizhou People's Hospital, from June 2022 to April 2023 were retrospectively analyzed. Inclusion criteria were as follows: (1) ≤ 55 years old; (2) the diagnosis of PTC was confirmed by histopathological examination; (3) patients without other tumors; and (4) there were complete medical records. Exclusion criteria were as follows: (1) patients with other malignant tumor diseases; (2) cases with other pathological types of thyroid cancer; and (3) cases with dysfunction of important organs. This study was supported by the Ethics Committee of the Meizhou People's Hospital.

Data collection

Clinical medical records of the PTC patients with ≤ 55 years old were collected, such as age, gender, preoperative circulating tumor cells (CTCs), Hashimoto's thyroiditis, thyroid function, multifocality, tumor size, invaded capsule, clinical stage, and LNM. The tumor size group was divided into two groups: PTC with tumor size ≤ 1 cm and tumor size > 1 cm [25, 26]. Peripheral blood CTCs were detected by reverse transcription-polymerase chain reaction (RT-PCR) technique using the CytoploRare Kit (Genosaber Biotech, Shanghai, China). The red blood cells and the vast majority of white blood cells were depleted using the negative enrichment method to obtain folate receptor-positive cells. The folate receptor-positive cells were then labeled with specific small molecule probes. Finally, the oligonucleotides in folic acid receptor binding small molecule probes were quantitatively detected by polymerase chain reaction (PCR) using a specific primer designed for small molecule probes and Taqman fluorescent probes. Folate receptor Unit (FU) per 3mL (FU/3mL) as defined in the manufacturer's manual, was used to represent the level of FR + CTC in 3 mL of peripheral blood. According to the threshold set in the CTC test kit instructions, CTC ≥ 8.7 FU/3mL (folate

receptor-positive CTCs unit in 3mL blood) is considered to be positive for CTC levels, and CTC < 8.7 FU/3mL is negative.

Statistical analysis

The relationship of CLNM, LLNM and the clinicopathological features of PTC patients was evaluated by χ^2 test or Fisher's exact test. Univariate analysis and multivariate logistic regression analysis were used to evaluate the relationship between the clinicopathological features and LNM in PTC patients, based on estimating the odds ratios (OR) and their 95% confidence intervals (CIs). And gender, Hashimoto's thyroiditis, thyroid function, multifocality, lesion diameter, invaded capsule, and clinical stage were selected as covariates in the multivariate logistic regression analysis for the association between CTCs and LNM. The goodness of fit of the model was examined. SPSS statistical software version 26.0 (IBM Inc., USA) was used for data analysis. $p < 0.05$ as statistically significant.

Table 1 The clinicopathological features of PTC patients

Clinicopathological features	PTC patients ($n = 588$)
Gender	
Male, n (%)	110 (18.7%)
Female, n (%)	478 (81.3%)
Hashimoto's thyroiditis	
No, n (%)	431 (73.3%)
Yes, n (%)	157 (26.7%)
Thyroid function	
Normal, n (%)	526 (89.5%)
Abnormal, n (%)	62 (10.5%)
Multifocal	
No, n (%)	408 (69.4%)
Yes, n (%)	180 (30.6%)
Tumor size	
≤ 1 cm, n (%)	401 (68.2%)
> 1 cm, n (%)	189 (31.8%)
Invaded capsule	
No, n (%)	333 (56.6%)
Yes, n (%)	255 (43.4%)
T stage	
T1-T2, n (%)	542 (92.2%)
T3-T4, n (%)	46 (7.8%)
CLNM	
No, n (%)	315 (53.6%)
Yes, n (%)	273 (46.4%)
LLNM	
No, n (%)	499 (84.9%)
Yes, n (%)	89 (15.1%)
Preoperative CTCs (FU/3mL)	
< 8.7	238 (40.5%)
≥ 8.7	350 (59.5%)

PTC, papillary thyroid carcinoma; CLNM, central lymph node metastasis; LLNM, lateral lymph node metastasis; CTC, circulating tumor cell; FU, folate receptor unit

Results

Clinicopathological features of PTC patients

In the study, there were 110 (18.7%) male patients and 478 (81.3%) were female patients. There were 157 (26.7%) PTC patients had Hashimoto's thyroiditis, and 62 (10.5%) had abnormal thyroid function. There were 180 (30.6%), 189 (31.8%), and 255 (43.4%) patients with multifocality, tumor size > 1 cm, and invaded capsule, respectively. And 273 (46.4%), and 89 (15.1%) PTC patients had CLNM and LLNM, respectively. There were 238 (40.5%) patients with preoperative CTCs < 8.7 FU/3mL, and 350 (59.5%) patients had preoperative CTCs ≥ 8.7 FU/3mL (Table 1).

Comparison of clinical features among PTC patients with or without CLNM

There were 273 (273/588, 46.4%) PTC patients with CLNM, and 315 (315/588, 53.6%) without. PTC patients with CLNM had a lower proportion of abnormal thyroid function (7.7% vs. 13.0%) ($p = 0.043$), and had higher proportions of multifocality (40.7% vs. 21.9%) ($p < 0.001$), tumor size > 1 cm (48.7% vs. 17.1%) ($p < 0.001$), invaded capsule (55.7% vs. 32.7%) ($p < 0.001$), T3-T4 stage (13.2% vs. 3.2%) ($p < 0.001$), and positive CTCs level (≥ 8.7 FU/3mL) (65.2% vs. 54.6%) ($p = 0.011$) than those in PTC patients without CLNM. There were no statistically significant differences in distribution of gender, and proportion of Hashimoto's thyroiditis between PTC patients with and without CLNM (Table 2).

Comparison of clinical features among PTC patients with or without LLNM

There were 89 (89/588, 15.1%) PTC patients with LLNM, and 499 (499/588, 84.9%) without. PTC patients with LLNM had a lower proportion of female (69.7% vs. 83.4%) ($p = 0.003$), and had higher proportions of multifocality (55.1% vs. 26.3%) ($p < 0.001$), tumor size > 1 cm (74.2% vs. 24.2%) ($p < 0.001$), invaded capsule (76.4% vs. 37.5%) ($p < 0.001$), and T3-T4 stage (29.2% vs. 4.0%) ($p < 0.001$) than those in PTC patients without LLNM. There were no statistically significant differences in proportions of Hashimoto's thyroiditis, abnormal thyroid function, and positive CTCs level between PTC patients with and without LLNM (Table 3).

Logistic regression analysis of risk factors of CLNM and LLNM

The results of univariate analysis showed that multifocality (odds ratio (OR): 2.443, 95% confidence interval (CI): 1.704–3.501, $p < 0.001$), tumor size > 1 cm (OR: 4.592, 95% CI: 3.149–6.695, $p < 0.001$), invaded capsule (OR: 2.586, 95% CI: 1.849–3.616, $p < 0.001$), T3-T4 stage (OR:

Table 2 Comparison of clinicopathological features among PTC patients with and without CLNM

Clinicopathological features	CLNM		*p* values
	No (*n* = 315)	Yes (*n* = 273)	
Gender			
Male, n (%)	55(17.5%)	55(20.1%)	0.458
Female, n (%)	260(82.5%)	218(79.9%)	
Hashimoto's thyroiditis			
No, n (%)	234(74.3%)	197(72.2%)	0.576
Yes, n (%)	81(25.7%)	76(27.8%)	
Thyroid function			
Normal, n (%)	274(87.0%)	252(92.3%)	0.043
Abnormal, n (%)	41(13.0%)	21(7.7%)	
Multifocal			
No, n (%)	246(78.1%)	162(59.3%)	< 0.001
Yes, n (%)	69(21.9%)	111(40.7%)	
Tumor size			
≤ 1 cm, n (%)	261(82.9%)	140(51.3%)	< 0.001
> 1 cm, n (%)	54(17.1%)	133(48.7%)	
Invaded capsule			
No, n (%)	212(67.3%)	121(44.3%)	< 0.001
Yes, n (%)	103(32.7%)	152(55.7%)	
T stage			
T1-T2, n (%)	305(96.8%)	237(86.8%)	< 0.001
T3-T4, n (%)	10(3.2%)	36(13.2%)	
Preoperative CTCs (FU/3mL)			
< 8.7	143(45.4%)	95(34.8%)	0.011
≥ 8.7	172(54.6%)	178(65.2%)	

PTC, papillary thyroid carcinoma; CLNM, central lymph node metastasis; CTC, circulating tumor cell; FU, folate receptor unit

Table 3 Comparison of clinicopathological features among PTC patients with and without LLNM

Clinicopathological features	LLNM		*p* values
	No (*n* = 499)	Yes (*n* = 89)	
Gender			
Male, n (%)	83(16.6%)	27(30.3%)	0.003
Female, n (%)	416(83.4%)	62(69.7%)	
Hashimoto's thyroiditis			
No, n (%)	368(73.7%)	63(70.8%)	0.603
Yes, n (%)	131(26.3%)	26(29.2%)	
Thyroid function			
Normal, n (%)	442(88.6%)	84(94.4%)	0.132
Abnormal, n (%)	57(11.4%)	5(5.6%)	
Multifocal			
No, n (%)	368(73.7%)	40(44.9%)	< 0.001
Yes, n (%)	131(26.3%)	49(55.1%)	
Tumor size			
≤ 1 cm, n (%)	378(75.8%)	23(25.8%)	< 0.001
> 1 cm, n (%)	121(24.2%)	66(74.2%)	
Invaded capsule			
No, n (%)	312(62.5%)	21(23.6%)	< 0.001
Yes, n (%)	187(37.5%)	68(76.4%)	
T stage			
T1-T2, n (%)	479(96.0%)	63(70.8%)	< 0.001
T3-T4, n (%)	20(4.0%)	26(29.2%)	
Preoperative CTCs (FU/3mL)			
< 8.7	203(40.7%)	35(39.3%)	0.816
≥ 8.7	296(59.3%)	54(60.7%)	

PTC, papillary thyroid carcinoma; LLNM, lateral lymph node metastasis; CTC, circulating tumor cell; FU, folate receptor unit

4.633, 95% CI: 2.253–9.526, $p < 0.001$), and positive CTCs level (OR: 1.558, 95% CI: 1.116–2.174, $p = 0.009$) were associated with CLNM. And multifocality (OR: 1.821, 95% CI: 1.230–2.698, $p = 0.003$), tumor size > 1 cm (OR: 3.444, 95% CI: 2.296–5.167, $p < 0.001$), invaded capsule (OR: 1.699, 95% CI: 1.167–2.473, $p = 0.006$), and positive CTCs level (OR: 1.469, 95% CI: 1.019–2.118, $p = 0.040$) were independently associated with CLNM in multivariate regression logistic analysis (Table 4).

The results of univariate analysis showed that male (OR: 2.183, 95% CI: 1.311–3.634, $p = 0.003$), multifocality (OR: 3.441, 95% CI: 2.166–5.467, $p < 0.001$), tumor size > 1 cm (OR: 8.964, 95% CI: 5.346–15.031, $p < 0.001$), invaded capsule (OR: 5.403, 95% CI: 3.206–9.104, $p < 0.001$), and T3-T4 stage (OR: 9.884, 95% CI: 5.215–18.734, $p < 0.001$) were associated with LLNM. Multivariate regression logistic analysis showed that male (OR: 2.087, 95% CI: 1.125–3.869, $p = 0.020$), multifocality (OR: 2.373, 95% CI: 1.389–4.052, $p = 0.002$), tumor size > 1 cm (OR: 5.344, 95% CI: 3.037–9.402, $p < 0.001$), invaded capsule (OR: 2.591, 95% CI: 1.436–4.674, $p = 0.002$), and T3-T4 stage (OR: 3.027, 95% CI: 1.430–6.405, $p = 0.004$) were independently associated with LLNM (Table 4).

Discussion

Thyroid cancer is more likely to occur in patients with thyroid nodules ≤ 55 years of age [27, 28]. Thyroid nodules in younger patients have a higher risk of developing into malignant nodules than older patients, but thyroid cancer in younger patients is well differentiated and the prognosis is significantly better than older patients [29]. Young patients are not sensitive to chemotherapy and radiotherapy, and surgery is the main treatment method [30, 31]. Radical cervical lymph node dissection in young patients with thyroid cancer may increase complications and affect patients' quality of life [32, 33]. The selection of surgical scope for young thyroid cancer patients should be individualized according to LNM, so as to avoid postoperative complications affecting the quality of life [34, 35].

The total CTCs in thyroid cancer patients is a biomarker to predict the prognosis of patients [36]. Some studies suggest that the mesenchymal transformation of thyroid carcinoma epithelial cells promotes the metastasis and invasion of thyroid cancer [37–39]. And the CTCs detected in PTC patients are predominantly mesenchymal or epithelial-mesenchymal phenotypes [40, 41]. Therefore, CTCs have the potential to reflect the level of

Table 4 Logistic regression analysis of risk factors of CLNM and LLNM

Variables	CLNM				LLNM			
	Univariate		Multivariate		Univariate		Multivariate	
	OR (95% CI)	*p* values	OR (95% CI)	*p* values	OR (95% CI)	*p* values	OR (95% CI)	*p* values
Preoperative CTCs (≥ 8.7/<8.7, FU/3mL)	1.558 (1.116–2.174)	0.009	1.469 (1.019–2.118)	0.040	1.058 (0.667–1.678)	0.810	0.808 (0.468–1.393)	0.442
Gender (male/female)	1.193 (0.788–1.806)	0.405	0.986 (0.619–1.569)	0.951	2.183 (1.311–3.634)	0.003	2.087 (1.125–3.869)	0.020
Hashimoto's thyroiditis (yes/no)	1.114 (0.773–1.607)	0.561	1.041 (0.693–1.563)	0.846	1.159 (0.704–1.909)	0.561	1.052 (0.580–1.908)	0.866
Thyroid function (abnormal/normal)	0.557 (0.320–0.968)	0.038	0.669 (0.367–1.221)	0.191	0.462 (0.180–1.186)	0.108	0.619 (0.217–1.764)	0.369
Multifocal (yes/no)	2.443 (1.704–3.501)	< 0.001	1.821 (1.230–2.698)	0.003	3.441 (2.166–5.467)	< 0.001	2.373 (1.389–4.052)	0.002
Tumor size (> 1 cm/≤1 cm)	4.592 (3.149–6.695)	< 0.001	3.444 (2.296–5.167)	< 0.001	8.964 (5.346–15.031)	< 0.001	5.344 (3.037–9.402)	< 0.001
Invaded capsule (yes/no)	2.586 (1.849–3.616)	< 0.001	1.699 (1.167–2.473)	0.006	5.403 (3.206–9.104)	< 0.001	2.591 (1.436–4.674)	0.002
T stage (T3-T4/T1-T2)	4.633 (2.253–9.526)	< 0.001	1.672 (0.751–3.723)	0.208	9.884 (5.215–18.734)	< 0.001	3.027 (1.430–6.405)	0.004

PTC, papillary thyroid carcinoma; CLNM, central lymph node metastasis; LLNM, lateral lymph node metastasis; CTC, circulating tumor cell; FU, folate receptor unit; OR, odds ratio; CI, confidence interval

metastasis and invasion of thyroid cancer. Han et al.. have used molecular beacon probes to target epithelial-mesenchymal CTCs and detect corresponding cell markers to predict the location of distant metastases of tumor cells [42]. Xu et al. showed that CTC was a good diagnostic marker for thyroid nodules [43]. Wang et al. found that patients with high CTCs level had poor progression-free survival (PFS) [36]. At present, the relationship of CTCs and LNM in PTC remains unclear. In terms of CTCs level and tumor metastasis in PTC patients, Li et al. found that the early recurrence and metastasis rate of PTC patients with high CTCs level was significantly higher than that of patients with low CTCs level [41]. Qiu et al. revealed that high CTCs level correlate with distant metastases [44]. High CTCs level was associated with CLNM in papillary thyroid microcarcinoma (PTMC) [24]. In this study, preoperative CTCs ≥ 8.7 FU/3mL was a risk factor for CLNM in PTC patients with ≤ 55 years old, but not LLNM. In terms of mechanism, CTCs may be to invade the lymphatic and circulatory system in the presence of hypoxia and starvation [45], and through interactions with blood cells and immune cells [46, 47]. The presence of high CTC levels means that more CTC is likely to invade the lymphatic system. Present study enriches the data on the evaluation value of CTCs in the progression of thyroid cancer. The National Comprehensive Cancer Network (NCCN) 2022 Clinical Practice Guidelines for thyroid Cancer state that central lymph node dissection is not recommended for patients with clinically negative lymph nodes [48]. For clinical node-negative patients without high risk factors, individual management is feasible. The results of this study suggest that CTC may be one of the potential indicators for predicting CLNM risk in PTC patients with ≤ 55 years old.

In this study, multifocality, tumor size > 1 cm, and invaded capsule were associated with CLNM in PTC patients with ≤ 55 years old. Multifocality is a common phenomenon in PTC and is an independent risk factor for CLNM, which is consistent with most previous research reports [49–52]. Multifocal PTC is formed by the spread of tumor cells in the main nodules in the glands, and it is more invasive and has an increased risk of LNM [53]. Jiang et al. found that the tumor invasiveness of multifocal PTC with a diameter > 1 cm was significantly higher than that of PTC with a diameter < 1 cm [54]. However, the relationship between multifocality and CLNM in young PTC patients has been less studied. This study provides the corresponding evidence for it. Larger tumor size is thought to be associated with CLNM [55–58]. This study is consistent with previous findings. In terms of capsular invasion, it is also considered by some studies to be a risk factor for CLNM [59–61]. It can be seen that these risk factors for CLNM in PTC also apply to young PTC patients.

Moreover, male, multifocality, tumor size > 1 cm, invaded capsule, and T3-T4 stage were associated with LLNM in PTC patients with ≤ 55 years old in this study. Some studies suggest that the incidence of LNM in male PTC patients is significantly higher than that in female patients [62, 63]. Feng et al. found that male was a risk factor for LLNM in PTMC patients [64]. Therefore, more attention should be paid to the risk of LLNM in male PTC patients and the selection of the scope of dissection during surgery, although the sample size of male patients

included in this study was not large. In terms of multifocality, it is considered to be a risk factor for LLNM [65, 66]. Some studies have shown that larger tumor size is related to LLNM [67, 68]. Tumor size is generally positively correlated with the risk of LLNM, and the rate of metastasis increases with the increase of maximum tumor diameter [62]. Some studies have suggested that the maximum tumor diameter > 1.0 cm is a risk factor for LLNM [69–71]. Wu et al. suggested that the cutoff value of the maximum tumor diameter should be > 0.7 cm [66]. Kim et al. reported that PTC > 2–3 cm was an independent risk factor for LLNM [72]. In addition, capsular invasion is an independent risk factor for LLNM [65, 73, 74]. Yan et al. suggested that patients with extra-thyroid aggression were more likely to develop LLNM [75]. Moreover, T stage is associated with LLNM [65]. It follows that these risk factors for LLNM in PTC patients are the same in young PTC patients.

This study provides one piece of evidence that high preoperative CTCs level was a risk factor for CLNM in PTC patients with ≤ 55 years old. Some of the risk factors (multifocality, tumor size > 1 cm, and invaded capsule) for LNM in PTC patients also apply to younger PTC patients, and the risk factors for CLNM and LLNM differ. Therefore, attention should be paid to the risk of CLNM and LLNM in young PTC patients and the selection of the scope of lymph node dissection during surgery. However, this study has some limitations: (1) it is a single-center retrospective study and the sample size is small, and a large central cohort study is needed to verify the conclusions obtained; (2) this study is a retrospective study, due to the limitation of clinical data, the indicators collected in this study are not very comprehensive, so more clinical indicators need to be included to optimize the construction of clinical prediction model for LNM in PTC patients with ≤ 55 years old; (3) due to the small tumor load and inert biological behavior of most thyroid cancers, the sensitivity and specificity of CTCs detection methods are limited [21, 76], and the relationship between CTCs level and LNM may be biased. In addition, there is a possibility that ctc levels in PTC patients in remission will continue to increase [23]; (4)at present, there is a lack of recognized high sensitivity and specificity detection methods. There are many CTCs detection techniques, and different CTCs sorting, enrichment and analysis methods will produce different results, so there is a possibility that different detection techniques may cause differences in research results. Therefore, the LNM risk prediction model based on CTC level, including more indicators and large samples will be more clinically significant.

Conclusions

In summary, preoperative CTCs positive (≥ 8.7 FU/3mL) may be a risk factor for CLNM in PTC patients with ≤ 55 years old, but not LLNM. Multifocality, tumor size > 1 cm, and invaded capsule may be associated with both CLNM and LLNM in PTC patients with ≤ 55 years old. It provides valuable reference data for the risk assessment of CLNM and LLNM in PTC patients with ≤ 55 years old. Of course, it still needs to be confirmed by more in-depth researches.

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Author contributions

Ming Yu, Yeqian Lai, and Yuedong Wang contributed to study concept and design. Ming Yu, Jiaqin Deng, Yihua Gu, Yeqian Lai, and Yuedong Wang collected clinical data. Ming Yu, and Yuedong Wang contributed to analyze the data. Ming Yu contributed to prepare the manuscript. All authors approved the final version to be published.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

This study was conducted according to the Declaration of Helsinki and approved by the Human Ethics Committees of Meizhou People's Hospital.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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