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Original Article

Hormonal correlation with abnormal thyroid function and their auxiliary diagnostic value in breast cancer

Yun Cai[1], Yi Liu[1], Ye Sun[1], Yu Ren[2]

[1]Department of Traditional Chinese Medicine, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an 710061, Shaanxi, China; [2]Department of Breast Surgery, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an 710061, Shaanxi, China

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Abstract: Objective: To investigate the association between thyroid hormone levels and pathological characteristics in patients with breast cancer. Methods: A retrospective analysis was conducted on 120 breast cancer patients who received treatment at the First Affiliated Hospital of Xi'an Jiaotong University between January 2020 and December 2023. A total of 100 healthy individuals undergoing routine physical examinations were enrolled as the control group. Serum levels of free triiodothyronine (FT3), free thyroxine (FT4), thyroid-stimulating hormone (TSH), thyroglobulin antibody (TG-Ab), and Thyroid peroxidase antibody (TPO-Ab) were measured and compared between the two groups. The diagnostic performance of thyroid hormones for breast cancer was evaluated using receiver operating characteristic (ROC) curve analysis, and correlations between thyroid hormone levels and pathological features of breast cancer were further analyzed. Results: No significant differences were observed in serum FT3, TSH, T3, or T4 levels between the two groups (P = 0.446, 0.594, 0.405 and 0.781, respectively). Compared with healthy controls, patients with breast cancer were observed to have significantly higher FT4 levels and substantially higher TPO-Ab levels, despite both parameters remaining within their normal reference ranges (all P < 0.001). ROC analysis demonstrated that the areas under the curve (AUCs) of FT4 and TPO-Ab for predicting breast cancer were 0.701 and 0.805, respectively. Furthermore, FT4 levels were significantly associated with tumor size, clinical stage, and lymph node metastasis (all P < 0.001). TPO-Ab levels were significantly correlated with tumor size, clinical stage, lymph node metastasis, and the expression of estrogen receptor (ER) and progesterone receptor (PR) (P = 0.006, 0.015, 0.046, 0.048 and 0.017, respectively). Follow-up analysis further revealed that clinical stage, lymph node metastasis, postoperative radiotherapy and chemotherapy, ER and PR expression, as well as FT4 and TPO-Ab levels, were independent factors influencing breast cancer recurrence. Conclusion: Serum FT4 and TPO-Ab levels are closely associated with the occurrence, progression, and specific pathological features of breast cancer, demonstrating favorable diagnostic and predictive value. Moreover, they may serve as important potential biomarkers for evaluating the risk of recurrence in patients with breast cancer.

Keywords: Thyroid hormones, breast cancer, diagnostic performance, pathological characteristics, clinical assessment

Introduction

Breast cancer is the most common malignancy and a leading cause of cancer incidence among women worldwide. Its incidence has been increasing globally, making it a major public health challenge [1, 2]. The risk of developing breast cancer increases with age, with the highest incidence observed in women aged 40 to 60 years [3, 4]. Previous studies have demonstrated that multiple factors contribute to the pathogenesis of breast cancer, including genetic mutations (such as BRCA gene alterations), hormonal imbalances, reproductive history, obesity, unhealthy lifestyle behaviors, and environmental exposures. In addition, the incidence of breast cancer in Asian countries, including China, has risen more rapidly than the global average, and the age of onset tends to be younger [5, 6]. Given these trends, enhancing public awareness of early breast cancer detection and promoting regular breast screening are

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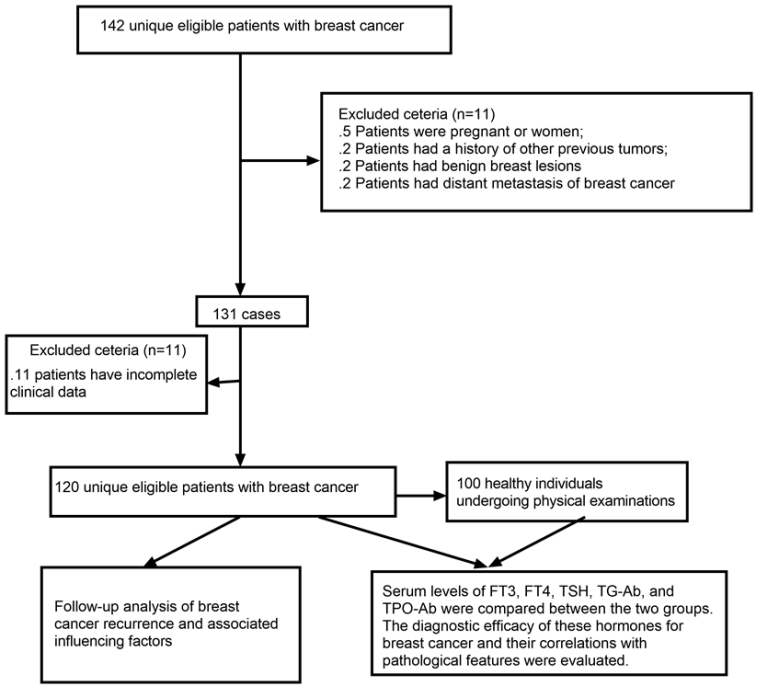

Figure 1. Flow chart of patient enrollment.

of great importance for achieving early diagnosis, reducing mortality, and improving patients' quality of life.

Recent studies have demonstrated a significant association between breast cancer and thyroid disorders, particularly hypothyroidism and autoimmune thyroiditis, with their underlying mechanisms involving shared endocrine and immune regulatory pathways. Estrogen not only promotes the initiation and progression of breast cancer but also stimulates the proliferation of thyroid follicular cells, contributing to the development of thyroid nodules and carcinogenesis [7]. The incidence of thyroid cancer in women is approximately three times higher than that in men, further suggesting the potential role of sex hormones in thyroid tumorigenesis [8]. Among the parameters reflecting thyroid function, thyroid-stimulating hormone (TSH), free thyroxine (FT4), free triiodothyronine (FT3), and thyroid peroxidase antibody (TPO-Ab) are considered key indicators. These biomarkers are not only used to assess thyroid functional status, such as hyperthyroidism or hypothyroidism, but are also closely associated with the regulation of the tumor microenvironment and the progression of various malignancies.

Although several studies have suggested an association between thyroid hormones and the development of breast cancer, most previous research has been limited to incidence comparisons or preliminary analyses of single hormone indicators. Systematic investigations examining multiple thyroid hormone parameters - such as TSH, FT3, FT4, and TPO-Ab - in relation to the diagnosis and pathological characteristics of breast cancer, including molecular subtypes, lymph node metastasis, and TNM stage, remain scarce. Moreover, few studies have explored the combined diagnostic efficacy of these parameters [9]. Therefore, this study focuses on thyroid hormone related parameters to comprehensively evaluate their associations with the clinicopathological features of breast cancer. The aim of this work is to elucidate their potential roles in auxiliary diagnosis and prognostic assessment from a multidimensional perspective.

General data and methods

Study population

A retrospective analysis was conducted on 120 patients with breast cancer who received treatment at the First Affiliated Hospital of Xi'an Jiaotong University between January 2020 and December 2023. In addition, 100 healthy individuals who underwent routine physical examinations were enrolled as the control group. Details are presented in **Figure 1**.

Inclusion criteria

Patients were included if they met the following criteria: (1) aged between 18 and 80 years; (2) newly diagnosed with breast cancer; (3) had complete clinical data, including detailed medical history, preoperative and postoperative laboratory tests, imaging findings, and pathological reports.

Exclusion criteria

Exclusion criteria were as follows: (1) pregnancy or lactation; (2) incomplete clinical data; (3) his-

tory of other malignancies; (4) benign breast lesions; (5) presence of distant metastasis at diagnosis; (6) obesity (BMI > 28 kg/m^2).

This study was approved by the Institutional Ethics Committee of The First Affiliated Hospital of Xi'an Jiaotong University.

Data retrieval

Baseline characteristics, preoperative blood test results, and pathological findings of all patients were obtained from the hospital's electronic medical record system. Thyroid Hormone Assays: All enrolled participants underwent fasting venous blood collection in the morning following admission. Blood samples were sent to the Department of Laboratory Medicine of our hospital for analysis. Serum levels of TSH, FT4, FT3, T3, and T4 were measured using an electrochemiluminescence immunoassay (ECLIA) on a Cobas 6000 automated analyzer (Roche Diagnostics International Ltd.). The reference ranges were as follows: TSH, 0.35-4.94 mIU/L; FT4, 9.01-19.04 pmol/L; FT3, 2.63-5.70 pmol/L; T3, 0.89-2.44 nmol/L; T4, 67.0-163.0 nmol/L.

Body Mass Index (BMI) Classification: According to the Guidelines for the Prevention and Control of Overweight and Obesity in Chinese Adults, BMI < 18.5 kg/m^2 was defined as underweight, 18.5-23.9 kg/m^2 as normal weight, 24.0-27.9 kg/m^2 as overweight, and ≥ 28 kg/m^2 as obesity.

Histopathological Analysis: All postoperative tumor specimens were examined histopathologically to determine the nature of the lesions and the molecular subtypes of breast cancer. Immunohistochemistry was further performed to assess the expression of estrogen receptor (ER), progesterone receptor (PR), Ki-67, and human epidermal growth factor receptor 2 (HER2). Pathological results were reported as either negative ("-") or positive ("+"). All assays were conducted using a fully automated Roche immunoassay analyzer with an optimized polymer detection system and epitope retrieval reagents.

Follow-up

In this study, breast cancer recurrence was defined as either local recurrence-referring to tumor reappearance in the ipsilateral breast, chest wall, or regional lymph nodes-or distant metastasis, defined as the dissemination of cancer cells to distant organs such as the bone, lung, liver, or brain. Recurrence and metastasis were confirmed through imaging examinations (e.g., ultrasound, CT) and/or pathological evaluation following initial radical treatment.

Follow-up was performed through outpatient visits, telephone interviews, and home visits until June 2025. The follow-up period was calculated from the date of surgery, with the first recorded recurrence or metastasis serving as the endpoint event.

Statistical analysis

All data were analyzed using SPSS version 22.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD) and compared between groups using the independent-samples t test. Categorical variables were presented as numbers (n) and compared using the chi-square test. Univariate analysis was performed to identify potential high-risk factors associated with breast cancer. Variables showing statistical significance were further subjected to multivariate logistic regression analysis. The receiver operating characteristic (ROC) curve analysis was applied to evaluate the diagnostic performance of variables with statistical significance in logistic regression analysis. The DeLong test was applied to compare the diagnostic efficacy between individual predictors and combined models. A P value < 0.05 was considered statistically significant.

Results

Comparison of baseline characteristics between the two groups

There were no significant differences between the two groups in terms of age, BMI, comorbidities, or reproductive history, indicating good comparability (all P > 0.05). Detailed baseline characteristics are summarized in **Table 1**.

Pathological types of breast cancer

Among the 100 patients, postoperative pathological examination identified invasive ductal carcinoma as the most prevalent subtype, followed by ductal carcinoma in situ, invasive lobular carcinoma, adenocarcinoma, and other

Table 1. Comparison of baseline data of the two groups

Category	Breast cancer group (n = 100)	Control group (n = 100)	Statistical value	P
Age	58.5±7.8	59.0±7.7	-0.456	0.649
BMI	23.2±2.7	23.5±2.8	-0.771	0.441
Age at menarche	13.3±1.4	13.2±1.3	0.523	0.601
Reproductive history	92	90	0.244	0.621
Menopause (Yes/No)	55	59	0.326	0.568
History of hypertension	24	21	0.258	0.611
History of diabetes	11	8	0.523	0.469

Note: BMI, body mass index.

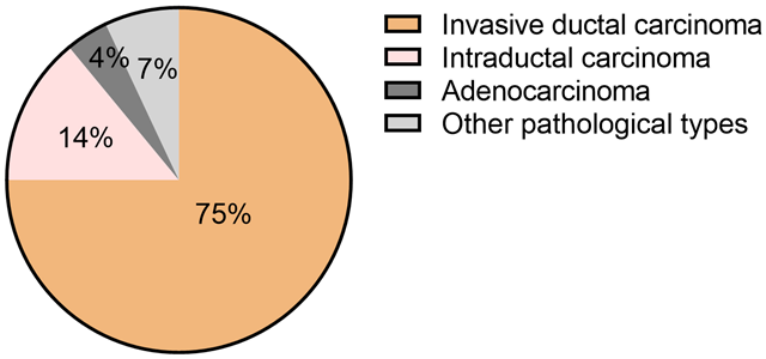

Figure 2. Distribution of pathological subtypes among the study cohort.

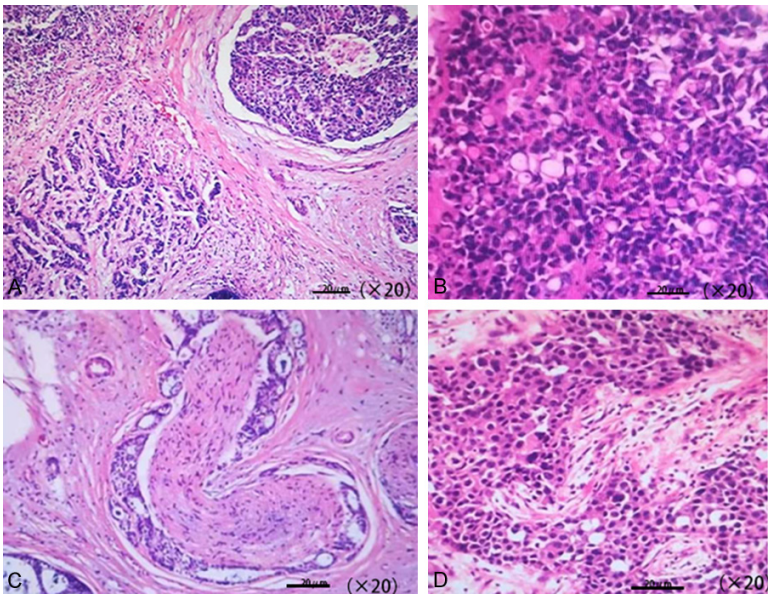

Figure 3. Representative histopathological images of common breast cancer types. A. Non-specific invasive ductal carcinoma; B. Invasive lobular carcinoma; C. Invasive ductal carcinoma; D. Non-specific invasive ductal carcinoma. Scale bar: 20 μm; Objective magnification: 40×.

pathological types. The distribution and proportion of pathological types are shown in **Figures 2** and **3**.

Comparison of peripheral blood inflammatory markers between the two groups

No significant differences were observed between the two groups in peripheral blood leukocyte count, interleukin-6 (IL-6), or C-reactive protein (CRP) levels (all P > 0.05). Details are presented in **Figure 4**.

Comparison of liver and renal function, serum albumin, and total protein between the two groups

There were no significant differences between the two groups in liver function parameters (ALT/AST), renal function parameters [serum creatinine (Scr)/blood urea nitrogen (BUN)], serum albumin, or total protein levels (all P > 0.05). Details are presented in **Table 2**.

Comparison of peripheral blood thyroid hormones between the two groups

No significant differences were observed between the two groups in FT3, TSH, T3, or T4 levels (P > 0.05). However, compared with the healthy control group, breast cancer patients had significantly higher serum FT4 and TPO-Ab levels, although both values remained within their respective normal range (both P < 0.05). Details are presented in **Table 3**.

Association between thyroid hormones and breast cancer and evaluation of diagnostic performance

Logistic regression analysis identified serum FT4 and TPO-Ab as independent risk factors for breast cancer, with odds ratios (ORs) of 1.422 (95% CI: 1.032-1.940) and 1.377 (95% CI: 1.117-1.845), respectively (both P < 0.05).

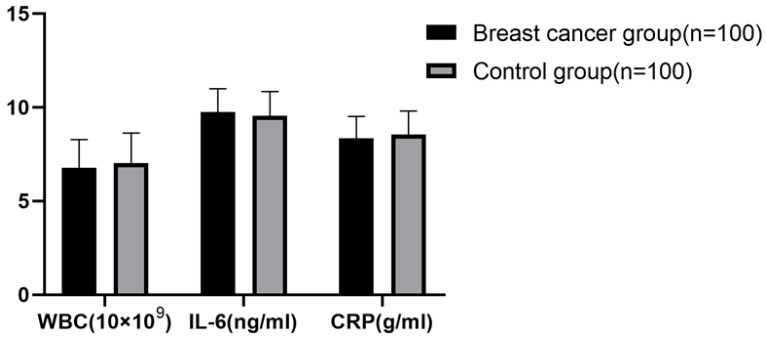

Figure 4. Comparison of inflammatory markers between the two groups. Note: WBC, white blood cell; IL-6, interleukin-6; CRP, C-reactive protein.

Table 2. Comparison of liver and kidney function and protein levels between the two groups

Category	Breast cancer group (n = 100)	Control group (n = 100)	Statistical value	P
ALT (U/L)	23.6±7.5	24.0±7.4	-0.333	0.740
AST (U/L)	25.1±8.1	25.0±8.0	-0.380	0.705
Scr (μmol/L)	78.5±4.7	78.1±4.4	0.621	0.535
BUN (mg/dl)	11.5±2.2	11.4±2.3	0.314	0.754
TP (g/L)	72.4±3.7	72.3±3.2	0.204	0.838
Alb (g/L)	37.4±1.6	37.5±1.7	-0.428	0.669

Note: ALT, alanine aminotransferase; AST, aspartate aminotransferase; Scr, serum creatinine; BUN, blood urea nitrogen; TP, total protein; Alb, albumin.

Table 3. Comparison of thyroid hormones between the two groups

Category	Breast cancer group (n = 100)	Control group (n = 100)	Statistical value	P
T3 (μmol/L)	1.74±0.75	1.82±0.73	-0.764	0.446
T4 (μmol/L)	98.45±32.18	96.06±31.05	0.534	0.594
TSH (μmol/L)	2.66±1.75	2.46±1.64	0.834	0.405
FT3 (μmol/L)	4.74±1.72	4.81±1.83	-0.279	0.781
FT4 (μmol/L)	14.86±2.84	10.43±2.72	11.265	< 0.001
TPO-Ab (μmol/L)	53.40±11.92	39.51±12.71	7.971	< 0.001

Note: T3, triiodothyronine; T4, thyroxine; TSH, thyroid-stimulating hormone; FT3, free triiodothyronine; FT4, free thyroxine; TPO-Ab, thyroid peroxidase antibody.

Table 4. Diagnostic performance of FT4 and TPO-Ab

Category	AUC	95% CI	Cut-off	Compare	Delong test	P
FT4	0.701	0.538-0.865	71.4	Vs combine	-5.990	< 0.001
TPO-Ab	0.805	0.664-0.946	28.7	Vs combine	-4.887	< 0.001
FT4+TPO-Ab	0.868	0.747-0.988	-	-	-	-

Note: FT4, free thyroxine; TPO-Ab, thyroid peroxidase antibody.

Further analysis demonstrated good diagnostic performance for both FT4 and TPO-Ab. The Hosmer-Lemeshow test yielded a chi-square value of 3.040 (P = 0.932), indicating that the predictive model was well-calibrated and stable. The calibration curve derived from the multivariate model also showed strong concordance between observed and predicted probabilities of breast cancer occurrence. Detailed results are presented in **Table 4** and **Figures 5**, **6**.

Association of FT4 and TPO-Ab levels with clinicopathological features in breast cancer patients

Serum FT4 levels in breast cancer patients were significantly associated with tumor size, clinical stage, and lymph node metastasis (all P < 0.05). Additionally, TPO-Ab levels were significantly correlated with tumor size, clinical stage, lymph node metastasis, and the expression of ER and PR (all P < 0.05). Details are presented in **Table 5**.

Analysis of factors associated with breast cancer recurrence

By the end of the follow-up period, 20 patients experienced recurrence. Univariate analysis revealed that recurrent cases differed significantly from non-recurrent cases with respect to tumor size, breast cancer stage, lymph node metastasis, postoperative radiotherapy and chemotherapy, HER2 and PR expression, as well as FT4 and TPO-Ab levels, whereas no significant differences were observed for age, family history, or tumor location. Multivariate analysis identified breast cancer stage, lymph node metastasis, postoperative radiotherapy and chemotherapy, ER and PR expression, and FT4 and

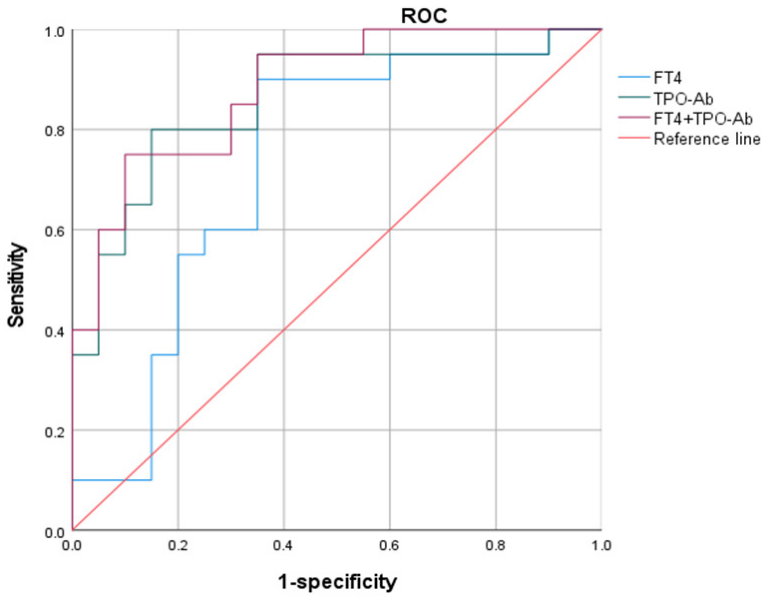

Figure 5. Receiver operating characteristic (ROC) curves for FT4 and TPO-Ab in predicting breast cancer. Note: FT4, free thyroxine; TPO-Ab, thyroid peroxidase antibody.

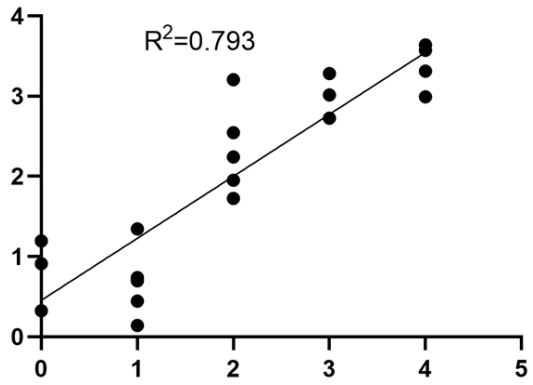

Figure 6. Comparison of the consistency between the observed and predicted probabilities of breast cancer occurrence.

TPO-Ab levels as independent factors associated with breast cancer recurrence. Details are presented in **Tables 6-8**.

Discussion

Thyroid disorders, among the most common endocrine diseases, mainly include hyperthyroidism, hypothyroidism, and thyroid nodules. According to World Health Organization data, the global incidence of thyroid disorders is rising, particularly in women, with prevalence rates reaching up to 10% [10, 11]. Breast cancer, on the other hand, is the most prevalent malignancy among women, with over 2 million new cases diagnosed worldwide each year, posing a major threat to female health. Recent evidence suggests that thyroid hormones, beyond their central role in metabolic regulation, may influence the development and function of breast tissue, potentially contributing to breast carcinogenesis [12]. Moreover, patients with thyroid disorders often exhibit heightened immune activity, and such immune dysregulation may be closely related to breast cancer development. Specifically, individuals with autoimmune thyroid diseases, such as Hashimoto's thyroiditis, often present with markedly elevated antibody levels, which may trigger immune-mediated attacks on breast tissue and promote malignant transformation [13]. Collectively, these observations highlight the importance of investigating the immunological and endocrine links between thyroid disorders and breast cancer, which may provide valuable insights into the pathogenesis of breast cancer. Previous studies have confirmed an association between thyroid hormones and breast cancer; however, these investigations exhibit several notable limitations. Most were conducted with small sample sizes and employed single-center retrospective designs, which limit the generalizability of their conclusions. Moreover, statistical analyses often fail to adjust for key confounding factors, such as BMI and menopausal status. Many studies also focus on a single hormone parameter, such as TSH, and lack systematic analyses exploring the relationships between multiple thyroid hormone indicators and specific pathological features of breast cancer, including molecular subtypes and lymph node metastasis. In addition, the combined diagnostic performance of these parameters is rarely assessed, which restricts their translational and clinical utility [14].

Previous studies have indicated a connection between thyroid dysfunction and breast cancer [15]. Consistent with this, our study revealed elevated peripheral blood levels of FT4 and

Table 5. Association of FT4 and TPO-Ab levels with clinicopathological features in breast cancer patients

Factor	Cases	FT4	t	P	TPO-Ab		χ^2	P
					Positive	Negative		
Age (years)			-0.055	0.956			0.557	0.456
≥ 50	59	17.18±1.78			20	22		
< 50	41	17.20±1.81			32	26		
Tumor diameter (cm)			5.942	< 0.001			7.466	0.006
≥ 2	56	17.14±1.56			37	19		
< 2	44	15.23±1.64			17	27		
Tumor staging			7.087	< 0.001			5.915	0.015
I&II	67	18.25±1.56			38	25		
III&IV	33	16.00±1.49			13	24		
Lymph node metastasis			3.655	< 0.001			3.980	0.046
Yes	32	19.00±2.35			36	19		
No	68	17.25±2.41			21	24		
ER			1.056	0.293			3.896	0.048
(-)	25	18.03±2.88			9	21		
(+)	75	17.43±2.74			36	34		
PR			0.595	0.553			5.745	0.017
(-)	21	18.11±2.76			5	16		
(+)	79	17.70±2.82			39	40		

Note: FT4, free thyroxine; TPO-Ab, thyroid peroxidase antibody; ER, estrogen receptor; PR, progesterone receptor.

Table 6. Univariate analysis of factors associated with breast cancer recurrence

Factor	Non-recurrence (n = 20)	Recurrence (n = 80)	Statistical value	P
Age	56.8±5.6	57.0±5.8	-0.154	0.881
Menopause	8	30	0.770	0.380
Age at menarche	14.2±2.0	14.8±2.8	-1.173	0.244
Tumor diameter	3.8±1.2	2.5±1.0	5.467	< 0.001
Lymph node metastasis	12	25	5.673	0.172
Family history	5	12	1.134	0.287
Tumor location (left/right)	10/10	38/42	0.040	0.841
Tumor staging			1.010	0.315
I/II	7	38		
III/IV	13	42		
Postoperative chemoradiotherapy	13	28	5.953	0.147
ER (+)	11	20	6.732	0.009
PR (+)	10	22	4.219	0.040
FT4	19.8±2.0	17.7±1.9	4.870	< 0.001
TPO-Ab	56.87±12.5	46.97±11.9	3.520	0.001

Note: FT4, free thyroxine; TPO-Ab, thyroid peroxidase antibody; ER, estrogen receptor; PR, progesterone receptor.

TPO-Ab in breast cancer patients compared with healthy controls, with both markers demonstrating promising diagnostic value. This observation may be explained by several mechanisms. FT4, the biologically active form of thyroid hormone, directly regulates cellular metabolism, proliferation, and differentiation. Elevated FT4 levels have been shown to promote breast cancer initiation and progression via multiple pathways. For example, thyroid hormones can bind to thyroid hormone receptors on cancer cells, activating downstream signal-

Table 7. Variable assignment

Variable	Assignment
Breast cancer stage	0 = stage I-II; 1 = stage III-IV
Lymph node metastasis	0 = yes; 1 = No
Tumor diameter	In situ value
Postoperative chemoradiotherapy	0 = yes; 1 = No
ER (+)	0 = yes; 1 = No
PR (+)	0 = yes; 1 = No
FT4	In situ value
TPO-Ab	In situ value

Note: FT4, free thyroxine; TPO-Ab, thyroid peroxidase antibody; ER, estrogen receptor; PR, progesterone receptor.

ing cascades such as MAPK/ERK or PI3K/Akt, which stimulate tumor cell proliferation, inhibit apoptosis, and enhance invasion and metastasis. Consequently, even FT4 levels at the upper limit of the normal range, or slightly elevated, may adversely affect breast cancer progression, consistent with prior reports [16]. TPO-Ab is a hallmark of autoimmune thyroid diseases, such as Hashimoto's thyroiditis, and its positivity typically indicates thyroid-related immune dysregulation. In breast cancer patients, elevated TPO-Ab levels may reflect a chronic inflammatory immune state. This persistent, low-grade inflammatory microenvironment can indirectly promote tumor immune evasion and angiogenesis through the release of various cytokines and growth factors, thereby creating favorable conditions for breast cancer cell proliferation, consistent with previous studies [17-19]. Furthermore, elevated FT4 and TPO-Ab levels may coexist and interact. For instance, thyroid tissue damage induced by TPO-Ab can lead to fluctuations in thyroid function, subsequently affecting FT4 levels. Together, these factors constitute a complex endocrine-immune network that may contribute to the pathological progression of breast cancer.

Previous studies have reported a close relationship between serum FT4 and TPO-Ab levels in breast cancer patients and their pathological characteristics [20]. Consistent with these findings, our study demonstrated that FT4 levels were significantly associated with tumor size, clinical stage, and lymph node metastasis, suggesting that thyroid function may be closely related to breast cancer progression and aggressiveness. A possible explanation is that thyroid hormones (T4/T3), acting as signaling molecules that regulate cellular metabolism and proliferation, can bind to thyroid hormone receptors (TRs) on tumor cells and directly activate downstream proliferative pathways, such as the MAPK and PI3K pathways. This activation stimulates tumor cell growth and division, contributing to increased tumor size. The higher metabolic demands associated with elevated thyroid hormone levels may also promote tumor angiogenesis, supplying nutrients to support tumor expansion. As tumor volume increases and local invasiveness intensifies, the likelihood of lymph node metastasis naturally rises, providing a mechanistic explanation for the observed positive correlations between FT4 levels, higher tumor stage, and lymph node involvement. These results suggest that elevated thyroid hormone levels may create a more "permissive" microenvironment, thereby facilitating malignant progression [21, 22]. Furthermore, TPO-Ab levels were associated with additional indicators, including ER and PR expression, likely through mechanisms involving immune regulation and autoimmune background. TPO-Ab, a hallmark of autoimmune thyroid diseases such as Hashimoto's thyroiditis, reflects a systemically active autoimmune state in affected patients. This immune dysregulation and persistent activation may exert dual effects on the tumor microenvironment. On one hand, elevated TPO-Ab levels may act as a biomarker of broader imbalances. Such dysregulation could impair effective immune surveillance against tumor cells, thereby creating conditions favorable for tumor initiation and progression, which may explain the observed associations with larger tumor size, advanced stage, and lymph node metastasis [23, 24]. On the other hand, TPO-Ab levels were correlated with ER and PR expression, suggesting a potential link between autoimmune status and hormone receptor patterns. Several studies have proposed that autoimmune conditions may influence the expression or function of ER and PR through a complex immune-endocrine network, thereby modulating receptor expression patterns [25, 26]. Alternatively, patients with specific immune backgrounds, such as TPO-Ab positivity, may preferentially develop tumors of the hormone receptor-positive molecular subtype, implying an intrinsic biological connection between immune status and tumor characteristics.

Table 8. Logistic analysis of factors associated with breast cancer recurrence

Variable	B	SE	Wald χ^2	OR	95% CI	P
Breast cancer stage	1.422	0.621	5.244	4.632	1.783-9.473	0.022
Lymph node metastasis	1.228	0.493	6.205	3.466	1.485-7.265	0.012
Tumor diameter	0.584	0.245	5.682	2.690	1.308-4.551	0.017
Postoperative chemoradiotherapy	1.579	0.621	6.469	3.845	1.686-8.353	0.011
ER (+)	0.482	0.162	8.857	4.636	1.684-4.482	0.003
PR (+)	0.463	0.200	5.361	2.936	1.419-5.895	0.021
FT4	0.616	0.304	4.105	3.615	1.332-5.033	0.042
TPO-Ab	0.473	0.228	4.305	2.550	1.013-4.997	0.039

Note: FT4, free thyroxine; TPO-Ab, thyroid peroxidase antibody; ER, estrogen receptor; PR, progesterone receptor; OR, odds ratio; CI, confidence interval; SE, standard error.

Previous studies have demonstrated that breast cancer recurrence is influenced by multiple factors. In our analysis of recurrence-associated factors, tumor stage, lymph node metastasis, postoperative radiotherapy and chemotherapy, ER and PR expression, as well as FT4 and TPO-Ab levels, emerged as significant predictors. Mechanistically, tumor stage serves as a fundamental prognostic indicator; more advanced stages (e.g., stage III) reflect a higher tumor burden and a substantially increased risk of recurrence. Lymph node metastasis is another critical factor, with patients exhibiting positive axillary lymph nodes-particularly those with multiple metastases or extracapsular extension-facing a higher likelihood of regional and distant recurrence. Although postoperative adjuvant radiotherapy and chemotherapy can effectively eradicate residual tumor cells and reduce recurrence, their ultimate efficacy is constrained by the intrinsic biological behavior of the tumor. Molecular subtyping is also critically important. Tumors negative for ER and PR generally exhibit higher proliferative activity and poorer prognosis, rendering these patients more susceptible to early recurrence. Beyond tumor-intrinsic factors, the endocrine and immune environment may further influence recurrence risk. Studies have suggested that thyroid dysfunction, evidenced by alterations in FT4 and elevated TPO-Ab - a profile indicative of autoimmune activation - may be associated with impaired immune surveillance, thereby contributing to tumor recurrence and progression. This perspective aligns with previous findings.

In summary, FT4 and TPO-Ab levels are closely associated with the occurrence and progression of breast cancer and demonstrate favorable predictive performance. These thyroid hormone indicators are also significantly correlated with tumor pathological features, providing valuable information for clinical assessment and supporting their potential application in clinical practice. However, several limitations should be acknowledged. This study is a single-center, retrospective, nested case-control design, which may introduce inherent biases. In addition, the relatively small sample size underscores the need for validation in larger, multi-center studies. Finally, the collection of more comprehensive follow-up data would further strengthen the robustness and scientific validity of the study conclusions.

Disclosure of conflict of interest

None.

Address correspondence to: Yun Cai, Department of Traditional Chinese Medicine, The First Affiliated Hospital of Xi'an Jiaotong University, No. 277 Yanta West Road, Xi'an 710061, Shaanxi, China. Tel: +86-02985324801; E-mail: hjj1761669@163.com

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