ORIGINAL RESEARCH

# Correlation Analysis of Breast and Thyroid Nodules: A Cross-Sectional Study

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**Objective:** Based on physical examination, to explore the relationship between breast mass (BM) and thyroid nodule (TN) prevalence, and to further explore other related factors that affect the occurrence of BM and TN.

**Methods:** From January 1, 2018, to January 1, 2021, 12,538 female subjects received breast and thyroid ultrasound examinations at the same time in the health examination center of the Affiliated Hospital of North Sichuan Medical College. Univariate analysis and multivariate logistic analysis were used to screen the relevant factors affecting TN and BM, and propensity score matching was used to further verify the results of the relationship between breast and thyroid.

**Results:** A total of 4975 (39.7%) of the included subjects have BM and a total of 6315 (50.4%) have TN,2557 (20.4%) had both BM and TN. The logistic regression results show that patients with TN are more likely to suffer from BM [OR = 1.185, 95% CI (1.099–1.278), p<0.0001]. In addition, age, free T4, HDL, height, BMI, systolic blood pressure, diastolic blood pressure, and albumin are independent factors affecting the occurrence of BM; patients with BM are more likely to have TN [OR = 1.180, 95% CI (1.094–1.272), p<0.0001], and age, free T3, free T4, AST, ALT, albumin, height, and BMI are independent influencing factors on the occurrence of TN. The result of propensity score matching confirmed the relationship between BM and TN.

**Conclusion:** There is a bidirectional pathogenic relationship between BM and TN, women with BM are at increased risk of TN, and women with TN are more likely to have BM. Thyroid hormone is not only related to the occurrence of TN but also affects the occurrence of BM.

**Keywords:** breast, thyroid, nodule, propensity score analysis

## Introduction

Breast and thyroid diseases are becoming more and more common in the population and significantly impact women's health.[1,2] The discovery of nodules is often the first sign that attracts people's attention in the early stages of breast or thyroid disease. Previous studies have shown that some factors, such as age, thyroid function, fasting glucose, sex, and blood lipid, may affect the risk of TN and BM.[3–7]

Ultrasound is a commonly used imaging method for breast and thyroid diseases[8,9] and therefore plays an important role in health screening. Previous prospective and retrospective studies[10–14] have shown an interaction between thyroid and breast diseases, but most of them[11,13,14] have focused on the relationship between thyroid and breast cancers, and neglected the early signs of malignant diseases. In particular, the interrelationship between breast disease and thyroid hormones is still controversial at

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this stage.[15] One of the essential objectives of this study was to investigate the relationship between thyroid hormone levels and the prevalence of BM in patients through a cross-sectional study with a large sample.

Therefore, this study aimed to explore the prevalence of TN and BM in women and related factors by collecting thyroid ultrasound and breast ultrasound examination data from health checkups. This study will help to analyze the prevalence trend of TN and BMand contribute to early screening and prevention of breast and thyroid diseases.

## Materials and Methods
### Basic Information
A total of 12,538 females who received breast and thyroid ultrasound examinations in the health examination center of Affiliated Hospital of North Sichuan Medical College from January 2018 to January 2021 were selected.

### Inclusive Criteria
1) All women who received comprehensive health examination (including thyroid, breast ultrasound examinations, fasting blood glucose, liver function, thyroid function and blood lipid test at least) from January 2018 to January 2021. 2) Women aged 18 or above.

### Exclusion Criteria
1) Patients under 18 years old; 2) Male patients; 3) Patients with missing relevant data (such as age, thyroid function, thyroid or breast ultrasound report missing).

The design and purpose of this study are in line with the ethical principles of medical research in the Helsinki Declaration and approved by the Ethics Committee of the Affiliated Hospital of North Sichuan Medical College.

## Ultrasound Image Acquisition and Analyses
### Ultrasound Assessment of Thyroid
Using HI VISION Preirus (Hitachi Aloka Medical, Ltd.), L9 linear array probe, frequency 5 ~ 13mhz, with RET function and tissue diffuse quantitative analysis function, the patient took the pillow supine position, head back, fully exposed the neck examination area, routine examination of thyroid, thyroid nodules, calcification in nodules, bilateral thyroid lobe size and isthmus thickness, etc. Thyroid was classified according to Kwak Thyroid Imaging Reporting and Data System (TI-RADS) standards.[16]

### Ultrasound Assessment of Breast
PHILIPS IU22 color Doppler ultrasound system/Mindray DC-80 ultrasound system, L9-3 broadband line array probe, frequency 7.5–10 MHz, mechanical index 0.07. SonoVue (SV; Bracco, spa, Milan, Italy) was used as the contrast agent. Patients lie supine, fully expose the chest, and the high-frequency L9-3 broadband linear array probe was applied to scan the bilateral breast and axillary separately. Ultrasound was applied to check the size, number, and echo of the lesion, and color Doppler was used to observing the blood flow in the lesion. The image was analyzed and diagnosed by two experienced doctors. Breast lesions were evaluated by Breast Imaging Reporting and Data System (BI-RADS) standards.[17] BM is defined as breast lesions with three-dimensional characteristics of shape, edge and direction under ultrasound, including breast cyst, mixed or solid mass and intraductal mass,[18] and breast adenopathy for which BI-RADS classification was performed.

## Blood Sample Analysis
### Blood Routine Test
Mindray BC-6800 hematology analyzer was used;

### Liver Function Test
The liver function was measured by Roche cobas c701 analyzer.

### Blood Lipid Detection
The instrument used is Hitachi 7600 automatic biochemical analyzer, and the reagent is the matching reagent of the machine; enzyme coupling method was used for the detection of triglyceride (TG) and total cholesterol (TC), the direct method was used for the detection of high-density lipoprotein cholesterol (HDL), and low-density lipoprotein cholesterol (LDL) Selective clearance method was used for detection, and very-low-density lipoprotein cholesterol (VLDL) was calculated.

### Thyroid Function Assay
All samples were analyzed using Siemens ADVIA Centaur. The reference intervals of FT4 was 0.89–1.76 ng/dl, FT3 was 2.3–4.2 pg/mL, TSH was 0.55–4.78 IU/mL.

### Glucose Determination
Glucose oxidase method and Hitachi 7170S automated analyzer were used for glucose detection.

## Test Method

Peripheral venous blood was collected from all blood samples at least 8 hours after fasting and analyzed in the laboratory of Affiliated Hospital of North Sichuan Medical College. All operations are carried out by our professional staff in strict accordance with the instrument or reagent operation instructions.

## Statistical Analysis

Stata 15 and SPSS 23 were used for statistical analysis, with P < 0.05 as the difference was statistically significant. Kolmogorov–Smirnov (KS) test was used to test the normality of continuous variables. The measurement data in line with normal distribution was expressed by (x±s), and a *t*-test was used for comparison between groups. The measurement data in non-normal distribution was expressed by Medians (p25–p75), and the Kruskal–Wallis test was used for comparison between groups. The counting data were described by n (%), and a chi-square test was used to a comparison between groups.

After univariate analysis of all the factors and considering the statistical significance and medical significance of the relevant factors, the covariates were selected and then included in the logistic regression analysis. We used binary logistic regression to explore the relationship between TN, BM and other covariates. In addition, we used multivariate logistic regression to explore the relationship between TN with different TI-RADS grades and BM with different BI-RADS grades and other included covariates.

To further confirm the association of TN and BM, we conducted a sensitivity analysis using propensity score matching(PSM).[19] Taking TN or BM as dependent variable, age, liver function examination, blood lipid level, fasting blood glucose and thyroid function related examination results as independent variables, the propensity score was estimated by logistic regression. A 1:1 matched analysis using nearest-neighbor matching with a caliper distance of 0.02 without replacement was performed based on the estimated propensity score of each patient. Finally, paired chi-square was used to test the relationship between TN and BM.

## Results

A total of 4975 (39.7%) of the included subjects have BM, and a total of 6315 (50.4%) have TN,2557 (20.4%) had both BM and TN.

Univariate analysis showed statistically significant differences in age, height, BMI, diastolic blood pressure, systolic blood pressure, free T3, free T4, triglycerides, LDL, HDL, total cholesterol, glucose, albumin, AST, and ALT (Table 1), and the effect of different levels of thyroid function on thyroid and breast nodules was also statistically significant (Table 2).

**Table 1** Anthropometric and Biochemical Characteristics of Subjects with Different BM and TN Status by Ultrasonography

| Variable | Negative | BM | TN | Coexistence of BM and TN | P-value |
|---|---|---|---|---|---|
| Age (years) | 42 (32–50) | 41 (33–48) | 49 (42–55) | 46 (40–51) | <0.0001 |
| Height (cm) | 156 (152–159) | 156 (153–160) | 155 (151–159) | 156 (152–160) | <0.0001 |
| BMI | 22.64 (20.81–24.73) | 22.21 (20.57–24.13) | 23.53 (21.60–25.53) | 22.97 (21.19–24.90) | <0.0001 |
| SBP | 114 (105–125) | 112 (105–122) | 120 (109–134) | 117 (108–129) | <0.0001 |
| DBP | 68 (62–76.5) | 68 (62–75) | 72 (65–81) | 71 (64–79) | <0.0001 |
| HDL(mmol/L) | 1.50 (1.29–1.73) | 1.50 (1.30–1.74) | 1.46 (1.25–1.70) | 1.48 (1.26–1.73) | <0.0001 |
| LDL(mmol/L) | 2.63 (2.14–3.16) | 2.59 (2.14–3.10) | 2.81 (2.29–3.33) | 2.68 (2.20–3.21) | <0.0001 |
| TG(mmol/L) | 1.02 (0.77–1.44) | 1.00 (0.75–1.37) | 1.16 (0.86–1.62) | 1.09 (0.82–1.50) | <0.0001 |
| TC(mmol/L) | 4.75 (4.19–5.40) | 4.70 (4.17–5.30) | 4.94 (4.37–5.58) | 4.80 (4.27–5.42) | <0.0001 |
| Fasting Glucose (mmol/L) | 4.82 (4.53–5.15) | 4.82 (4.52–5.12) | 4.91 (4.59–5.29) | 4.84 (4.53–5.17) | <0.0001 |
| FT3(pg/mL) | 2.93 (2.73–3.16) | 2.91 (2.72–3.13) | 2.92 (2.73–3.12) | 2.90 (2.73–3.10) | 0.023 |
| FT4(ng/dl) | 1.24 (1.14–1.37) | 1.25 (1.14–1.37) | 1.23 (1.13–1.35) | 1.24 (1.14–1.36) | 0.024 |
| TSH(uIU/mL) | 2.60 (1.74–3.83) | 2.65 (1.77–3.85) | 2.54 (1.69–3.82) | 2.52 (1.73–3.69) | 0.081 |
| AST | 21 (18–25) | 20 (18–24) | 22 (19–26) | 21 (18–25) | <0.0001 |
| ALT | 14 (11–20) | 13 (10–19) | 15 (12–21) | 14 (11–20) | <0.0001 |
| Total bilirubin | 14.0 (11.5–17.6) | 14.2 (11.5–17.8) | 14.0 (11.4–17.3) | 14.2 (11.6–17.5) | 0.094 |
| Plasma albumin | 46.2 (44.6–47.9) | 46.1 (44.6–47.8) | 46.0 (44.4–47.6) | 45.9 (44.3–47.5) | <0.0001 |

**Abbreviations:** BM, breast mass; TN, thyroid nodule; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TG, triglycerides;TC, total cholesterol; FT3, free-T3; FT4, free-T4; TSH, thyroid-stimulating hormone; ALT, alanine aminotransferase; AST, aspartate aminotransferase; SBP, systolic blood pressure; DBP, diastolic blood pressure.

**Table 2** Effect of BM and TN by Baseline Thyroid Hormone Level

| Variable | Negative (n=3805) | BM (n=2418) | TN (n=3758) | Coexistence of BM and TN (n=2557) | | P-value |
|---|---|---|---|---|---|---|
| **FT3: n (%)** | | | | | | |
| <2.3 | 41 (1.1%) | 37 (1.5%) | 23 (0.6%) | 26 (1.0%) | | 0.005 |
| 2.3–4.2 | 3465 (91.1%) | 2275 (94.1%) | 3506 (93.3%) | 2423 (94.8%) | | <0.0001 |
| >4.2 | 299 (7.9%) | 106 (4.4%) | 229 (6.1%) | 108 (4.2%) | | <0.0001 |
| **FT4: n (%)** | | | | | | |
| <0.89 | 43 (1.1%) | 29 (1.2%) | 28 (0.7%) | 18 (0.7%) | | 0.099 |
| 0.89–1.76 | 3452 (90.7%) | 2276 (94.1%) | 3493 (92.9%) | 2434 (95.2%) | | <0.0001 |
| >1.76 | 310 (8.1%) | 113 (4.7%) | 237 (6.3%) | 105 (4.1%) | | <0.0001 |
| **TSH: n (%)** | | | | | | |
| <0.55 | 93 (2.4%) | 55 (2.3%) | 89 (2.4%) | 46 (1.8%) | | 0.355 |
| 0.55–4.78 | 3156 (82.9%) | 2029 (83.9%) | 3124 (83.1%) | 2144 (83.8%) | | 0.661 |
| >4.78 | 556 (14.6%) | 334 (13.8%) | 545 (14.5%) | 367 (14.4%) | | 0.839 |

**Notes:** The reference (normal) range of FT4: 0.89–1.76 ng/dl, FT3: 2.3–4.2 pg/mL, TSH: 0.55–4.78IU/mL.

According to the result of binary logistic regression, we can conclude that the occurrence risk of BM was higher in women with TN than those without TN [OR = 1.185, 95% CI (1.099–1.278)]. The differences in age, free T4, HDL, height, BMI, systolic blood pressure, diastolic blood pressure, and albumin also remained statistically significant (Table 3).

The results of binary logistic regression analysis with TN as the dependent variable showed that the occurrence risk of TN in women with BM was higher than that in women without BM [OR = 1.180, 95% CI (1094–1.272), p<0.0001], and the difference was still statistically significant after correcting for other covariates. Age, free T3, free T4, AST, ALT, albumin, height, and BMI remained statistically significant in the multivariate logistic regression (Table 4).

After RADS grading, the results of multivariate logistics regression showed that the strongest adjusted correlation was noted in BI-RADS category ≥4A BM (OR = 2.011), which indicated that women with high malignant possible TN had a higher probability of suffering from malignant BM. (Table 5)

The strongest adjusted correlation was noted in TI-RADS category ≥4A TN (OR = 1.338), higher than the OR between TN and BM of other grades (1.231 and 1.194, respectively), again indicating a closer relationship

**Table 3** Multivariable-Adjusted Odds Ratios for BM

| Variable | B | S.E. | Wald | P-value | Odds Ratio | 95% CI |
|---|---|---|---|---|---|---|
| Age | −0.11 | 0.002 | 23.429 | <0.0001 | 0.989 | 0.985–0.993 |
| Height | 0.019 | 0.004 | 28.259 | <0.0001 | 1.019 | 1.012–1.026 |
| BMI | −0.025 | 0.007 | 11.099 | 0.001 | 0.976 | 0.962–0.990 |
| SBP | −0.006 | 0.002 | 7.495 | 0.006 | 0.994 | 0.990–0.998 |
| DBP | 0.008 | 0.003 | 6.487 | 0.011 | 1.008 | 1.002–1.013 |
| **FT3** | | | | | | |
| <2.3 | 0.25 | 0.182 | 1.890 | 0.169 | 1.283 | 0.899–1.832 |
| 2.3–4.2 | 1 (reference) | | | | | |
| >4.2 | −0.055 | 0.259 | 0.045 | 0.832 | 0.947 | 0.570–1.573 |
| **FT4** | | | | | | |
| <0.89 | −0.028 | 0.201 | 0.019 | 0.891 | 0.973 | 0.656–1.442 |
| 0.89–1.76 | 1 (reference) | | | | | |
| >1.76 | −0.571 | 0.256 | 4.958 | 0.026 | 0.565 | 0.342–0.934 |
| TG | 0.034 | 0.030 | 1.274 | 0.259 | 1.035 | 0.975–1.098 |
| HDL | 0.191 | 0.085 | 5.089 | 0.024 | 1.211 | 1.025–1.429 |
| LDL | 0.060 | 0.061 | 0.972 | 0.324 | 1.062 | 0.942–1.197 |
| TC | −0.081 | 0.062 | 1.681 | 0.195 | 0.922 | 0.816–1.042 |
| Fasting glucose | −0.043 | 0.022 | 3.776 | 0.052 | 0.958 | 0.917–1.000 |
| AST | −0.005 | 0.003 | 2.483 | 0.115 | 0.995 | 0.988–1.001 |
| ALT | 0.003 | 0.002 | 1.291 | 0.256 | 1.003 | 0.998–1.007 |
| Plasma albumin | −0.027 | 0.008 | 11.051 | 0.001 | 0.974 | 0.958–0.989 |
| TN | 0.170 | 0.039 | 19.390 | <0.0001 | 1.185 | 1.099–1.278 |

**Table 4** Multivariable-Adjusted Odds Ratios for TN

| Variable | B | S.E. | Wald | P-value | Odds Ratio | 95% CI |
|---|---|---|---|---|---|---|
| Age | 0.052 | 0.002 | 491.225 | <0.0001 | 1.053 | 1.049–1.058 |
| Height | 0.025 | 0.004 | 46.220 | <0.0001 | 1.025 | 1.018–1.032 |
| BMI | 0.027 | 0.007 | 13.602 | <0.0001 | 1.028 | 1.013–1.043 |
| SBP | 0.004 | 0.002 | 3.828 | 0.050 | 1.004 | 1.000–1.008 |
| DBP | 0.003 | 0.003 | 0.705 | 0.401 | 1.003 | 0.997–1.008 |
| FT3 | | | | | | |
| <2.3 | −0.645 | 0.194 | 11.123 | 0.001 | 0.524 | 0.359–0.766 |
| 2.3–4.2 | 1 (reference) | | | | | |
| >4.2 | 0.346 | 0.257 | 1.811 | 0.178 | 1.413 | 0.854–2.337 |
| FT4 | | | | | | |
| <0.89 | −0.362 | 0.208 | 3.018 | 0.082 | 0.697 | 0.463–1.047 |
| 0.89–1.76 | 1 (reference) | | | | | |
| >1.76 | −0.500 | 0.253 | 3.914 | 0.048 | 0.606 | 0.369–0.995 |
| TSH | | | | | | |
| <0.55 | −0.180 | 0.129 | 1.935 | 0.164 | 0.835 | 0.648–1.076 |
| 0.55–4.78 | 1 (reference) | | | | | |
| >4.78 | −0.016 | 0.054 | 0.081 | 0.776 | 0.985 | 0.885–1.095 |
| TG | 0.048 | 0.031 | 2.285 | 0.131 | 1.049 | 0.986–1.115 |
| HDL | −0.022 | 0.085 | 0.067 | 0.796 | 0.978 | 0.827–1.156 |
| LDL | 0.007 | 0.061 | 0.012 | 0.913 | 0.993 | 0.881–1.120 |
| TC | −0.069 | 0.063 | 1.211 | 0.271 | 0.933 | 0.826–1.055 |
| Fasting Glucose | −0.008 | 0.021 | 0.140 | 0.708 | 0.992 | 0.952–1.034 |
| AST | −0.011 | 0.004 | 8.863 | 0.003 | 0.989 | 0.982–0.996 |
| ALT | 0.005 | 0.002 | 4.694 | 0.030 | 1.005 | 1.000–1.010 |
| Plasma albumin | −0.016 | 0.008 | 3.954 | 0.047 | 0.984 | 0.968–1.000 |
| BM | 0.165 | 0.038 | 18.557 | <0.0001 | 1.180 | 1.094–1.272 |

between TN and BM of higher malignant potential. (Table 6).

In addition, we pooled the incidence of TN and BM according to the TI/BI-RADS classification of breast and thyroid (Table 7).

After propensity score matching, 4664 pairs were successfully matched between TN group and non-TN groups, and 2014 women in the TN group suffered from BM. There were 1815 patients with BM in the non-TN group, and the paired chi-square results showed that patients with thyroid nodules were more likely to have breast nodules (P < 0.0001). 4966 pairs of BM-group and non-BM groups were successfully matched, 2556 patients in BM group and 2358 patients in the non-BM group had TN, and the paired chi-square results showed that patients with BM

were more likely to have TN (P < 0.0001). The result of PSM is the same as that of logistic regression, which proves that the results of this study are stable and reliable. Table 8 showed the characteristics before and after Propensity Score Matching.

## Discussion

According to our findings, BM and TN usually occur synchronously, which is consistent with the results of previous studies. Shi et al[20] found that the prevalence of TN in the normal population was 34.49%, while the prevalence of thyroid nodules in the group with benign breast disease was 43.64% and in the group with breast cancer was 56.17%, both significantly higher than the normal population group. Van Fossen et al[21] found a 0.67-fold

**Table 5** Multivariable-Adjusted Odds Ratios (95% CI) for BM with Different BI-RADS Categories

| Variable | BI-RADS 2 | BI-RADS 3 | BI-RADS≥ 4A |
|---|---|---|---|
| TI-RADS 1 | 1 (reference) | | |
| TI-RADS 2 | 1.165(0.974–1.393)* | 1.028(0.894–1.183) | 1.156(0.825–1.621) |
| TI-RADS 3 | 1.226(1.077–1.397)* | 1.191(1.079–1.315)* | 1.177(0.921–1.504) |
| TI-RADS ≥ 4A | 1.218(0.944–1.572)* | 1.348(1.116–1.627)* | 2.011(1.367–2.959)* |
| Age | 0.987(0.980–0.994)* | 0.988(0.983–0.993)* | 1.007(0.994–1.020) |
| Height | 1.017(1.006–1.028) | 1.021(1.013–1.030) | 1.011(0.991–1.032) |
| BMI | 1.004(0.983–1.027) | 0.958(0.942–0.975) | 1.005(0.965–1.046) |
| SBP | 0.995(0.989–1.001) | 0.996(0.991–1.001) | 0.978(0.966–0.989) |
| DBP | 1.006(0.997–1.015) | 1.005(0.999–1.012) | 1.035(1.017–1.052) |
| FT3 | | | |
| <2.3 | 1.776(1.098–2.870) | 1.100(0.716–1.690) | 0.876(0.266–2.882) |
| 2.3–4.2 | 1 (reference) | | |
| >4.2 | 0.640(0.303–1.351) | 1.178(0.634–2.191) | 1.061(0.212–5.319) |
| FT4 | | | |
| <0.89 | 0.932(0.519–1.676) | 1.086(0.690–1.711) | 0.257(0.034–1.935) |
| 0.89–1.76 | 1 (reference) | | |
| >1.76 | 0.989(0.478–2.047) | 0.422(0.227–0.785)* | 0.423(0.084–2.120) |
| Plasma albumin | 0.972(0.949–0.996)* | 0.978(0.960–0.996)* | 0.956(0.914–1.000) |
| TG | 1.029(0.939–1.127) | 1.032(0.961–1.108) | 1.066(0.928–1.224) |
| HDL | 1.210(0.936–1.565) | 1.233(1.014–1.499)* | 1.064(0.675–1.676) |
| LDL | 1.072(0.891–1.290) | 1.067(0.925–1.231) | 0.976(0.708–1.346) |
| TC | 0.916(0.758–1.106) | 0.914(0.790–1.057) | 1.047(0.756–1.451) |
| Fasting Glucose | 1.023(0.965–1.085) | 0.924(0.872–0.978)* | 0.889(0.771–1.025) |
| AST | 1.002(0.992–1.012) | 0.988(0.979–0.996)* | 1.010(0.995–1.024) |
| ALT | 0.996(0.989–1.004) | 1.007(1.002–1.013) | 0.994 (0.983–1.006) |

**Note:** *$P$ < 0.05.

increased risk of subsequent breast cancer in women with thyroid cancer and a 2-fold increased risk of subsequent thyroid cancer in women with breast cancer. In conclusion, an increasing number of researchers have found correlation between thyroid disease and breast disease, especially in terms of malignancy.

This suggests that there may be some common etiology between TN and BM, which may result from genetic, environmental and hormonal factors. Current studies provide some clues to explain this relationship. Some studies have found[22,23] that this may be related to mutations in PTEN, a tumor suppressor gene that predisposes women to breast, thyroid, kidney, and endometrial cancers. Similarities also exist between thyroid and breast tissues, where both thyroid follicular cells and breast cells store iodine through sodium-iodine transporter-mediated iodine uptake.[24] This suggests that iodine uptake and oxidation

may play an important role in the development of mammary nodules. It has also been shown[25] that T3 induces mammary cell proliferation by activating the same estradiol-related signaling pathway that controls cell cycle progression. Since both glands are regulated by the hypothalamic-pituitary axis, when there are abnormal thyroid hormone or estrogen levels, this may lead to the simultaneous occurrence of TN and BM in a person.

Our results showed that 39.7% of the included 12,538 women had BM, 50.4% had TN, and 20.4% had both BM and TN. The nodule incidence was higher compared to the results of previous studies, which may be related to the following:1) Only women were included in this study, and women have a higher prevalence of BM and TN relative to men;[26,27] 2) The subjects included in this study were from medical checkup centers, and generally patients are more likely

**Table 6** Multivariable-Adjusted Odds Ratios (95% CI) for TN with Different TI-RADS Categories

| Variable | TI-RADS 2 | TI-RADS 3 | TI-RADS ≥ 4A |
|---|---|---|---|
| BI-RADS 1 | 1 (reference) | | |
| BI-RADS 2 | 1.145 (0.958–1.370)* | 1.231(1.081–1.401)* | 1.212(0.939–1.564) |
| BI-RADS 3 | 1.018 (0.885–1.170) | 1.194(1.081–1.318)* | 1.338(1.108–1.617)* |
| BI-RADS ≥ 4A | 1.136 (0.810–1.592) | 1.187(0.931–1.514) | 2.020(1.373–2.971)* |
| Age | 1.030(1.023–1.037)* | 1.063(1.057–1.068)* | 1.055(1.044–1.065)* |
| Height | 1.021 (1.010–1.033) | 1.024 (1.016–1.032) | 1.039 (1.023–1.055) |
| BMI | 1.021 (0.998–1.044) | 1.031 (1.014–1.048) | 1.027 (0.996–1.059) |
| SBP | 1.002 (0.995–1.008) | 1.003 (0.999–1.008) | 1.010 (1.002–1.019) |
| DBP | 1.003 (0.994–1.012) | 1.002 (0.996–1.009) | 1.004 (0.992–1.016) |
| FT3 | | | |
| <2.3 | 0.789 (0.442–1.407) | 0.389(0.243–0.622)* | 0.922(0.429–1.985) |
| 2.3–4.2 | 1 (reference) | | |
| >4.2 | 2.426 (0.927–6.349) | 1.312(0.757–2.276) | 1.070(0.352–3.254) |
| FT4 | | | |
| <0.89 | 0.394(0.174–0.890)* | 0.865(0.552–1.354) | 0.530(0.184–1.528) |
| 0.89–1.76 | 1 (reference) | | |
| >1.76 | 0.343(0.131–0.896)* | 0.673(0.391–1.156) | 0.694(0.233–2.070) |
| TSH | | | |
| <0.55 | 0.358 (0.199–0.645)* | 0.987(0.751–1.298) | 0.935(0.551–1.586) |
| 0.55–4.78 | 1 (reference) | | |
| >4.78 | 1.043 (0.886–1.229) | 0.982(0.872–1.107) | 0.862(0.678–1.096) |
| Plasma albumin | 1.010 (0.985–1.036) | 0.973(0.956–0.991)* | 0.987(0.953–1.022) |
| TG | 1.042 (0.951–1.141) | 1.053(0.984–1.127)* | 1.049(0.913–1.206) |
| HDL | 1.040 (0.806–1.341) | 0.955(0.791–1.153) | 1.011 (0.685–1.494) |
| LDL | 0.914 (0.765–1.092) | 0.996(0.872–1.139) | 1.244 (0.936–1.655) |
| TC | 1.047 (0.871–1.258) | 0.926(0.807–1.062)* | 0.725(0.542–0.971)* |
| Fasting Glucose | 1.027 (0.968–1.090) | 0.978(0.934–1.024) | 0.994(0.914–1.080) |
| AST | 0.995 (0.984–1.006) | 0.988(0.980–0.996)* | 0.987(0.972–1.002) |
| ALT | 1.001 (0.993–1.009) | 1.006(1.001–1.011)* | 1.009(1.000–1.019) |

**Note:** *$P < 0.05$.

**Table 7** Ultrasound BI-/TI-RADS Categories of Breast and Thyroid

| Variable | Breast (n=12,538) | Thyroid (n=12,538) |
|---|---|---|
| **RADS 1** | 7563(60.3%) | 6223(49.6%) |
| **RADS 2** | 1499(11.9%) | 1467(11.7%) |
| **RADS 3** | 3099(24.7%) | 4154(33.1%) |
| **RADS ≥ 4A** | 377(3.0%) | 694(5.5%) |

**Abbreviation:** BI-/TI-RADS, Breast/Thyroid Imaging Reporting and Data System.

to go to hospitals for comprehensive health checkups after unintentionally finding out they have BM or TN; 3) Consistent with the current epidemiological trend of thyroid and breast cancers, the incidence of TN and BM is increasing year by year;[28,29] 4) Compared to previous studies, the definition of BM is not exactly the same; for example, we explicitly defined breast adenopathy with BI-RADS grading as BM.

**Table 8** Characteristics Before and After Propensity Score Matching

| Variable | Before PSM (n=12,538) | | | After PSM(n=9932) | | | Before PSM (n=12,538) | | | After PSM(n=9328) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | BM Group | Non-BM Group | P | BM Group | Non-BM Group | P | TN Group | Non-TN Group | P | TN Group | Non-TN Group | P |
| Age | 44 (36–50) | 46 (35–53) | 0.0001 | 44 (36–50) | 43 (33–51) | 0.536 | 48 (41–54) | 41 (32–49) | 0.0001 | 45 (37–50) | 45 (37–51) | 0.011 |
| Height | 156 (152–160) | 155 (152–159) | 0.0001 | 156 (152–160) | 156 (153–160) | 0.453 | 155 (152–159) | 156 (152–160) | 0.0001 | 156 (152–159) | 156 (152–159) | 0.717 |
| BMI | 22.64 (20.83–24.56) | 23.07 (21.17–25.11) | 0.0001 | 22.64 (20.83–24.56) | 22.72 (20.93–24.69) | 0.363 | 23.31 (21.4–25.24) | 22.48 (20.7–24.46) | 0.0001 | 22.86 (21.08–24.75) | 22.89 (21.09–24.88) | 0.129 |
| SBP | 114 (107–126) | 116 (107–129) | 0.0001 | 114 (107–126) | 114 (106–125) | 0.083 | 118 (109–132) | 113 (105–124) | 0.0001 | 115 (107–125) | 115 (107–127) | 0.001 |
| DBP | 69 (63–77) | 70 (63–79) | 0.0001 | 69 (63–77) | 69 (63–77) | 0.206 | 72 (64–80) | 68 (62–76) | 0.0001 | 69 (63–77) | 70 (63–78) | 0.012 |
| FT3 | 2.91 (2.73–3.12) | 2.92 (2.73–3.14) | 0.0001 | 2.91 (2.73–3.12) | 2.91 (2.72–3.11) | 0.616 | 2.91 (2.73–3.12) | 2.92 (2.72–3.15) | 0.02 | 2.91 (2.73–3.12) | 2.91 (2.71–3.12) | 0.344 |
| FT4 | 1.25 (1.14–1.37) | 1.24 (1.13–1.36) | 0.0001 | 1.25 (1.14–1.37) | 1.23 (1.13–1.35) | 0.299 | 1.24 (1.14–1.36) | 1.25 (1.14–1.37) | 0.001 | 1.24 (1.14–1.36) | 1.23 (1.12–1.36) | 0.216 |
| TSH | 2.58 (1.74–3.78) | 2.57 (1.72–3.82) | 0.095 | 2.57 (1.74–3.77) | 2.58 (1.74–3.88) | 0.713 | 2.53 (1.74–3.78) | 2.62 (1.75–3.83) | 0.003 | 2.53 (1.69–3.78) | 2.62 (1.75–3.83) | 0.967 |
| Plasma albumin | 46 (44.4–47.6) | 46.1 (44.5–47.7) | 0.101 | 46 (44.4–47.6) | 46 (44.4–47.7) | 0.531 | 46 (44.3–47.5) | 46.2 (44.6–47.8) | 0.0001 | 46 (44.4–47.6) | 46 (44.4–47.7) | 0.372 |
| TG | 1.05 (0.79–1.45) | 1.1 (0.81–1.53) | 0.0001 | 1.05 (0.79–1.45) | 1.05 (0.78–1.46) | 0.998 | 1.14 (0.84–1.57) | 1.02 (0.76–1.41) | 0.0001 | 1.07 (0.8–1.45) | 1.08 (0.8–1.49) | 0.011 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| HDL | 1.49 (1.28–1.74) | 1.48 (1.27–1.72) | 0.069 | 1.49 (1.28–1.74) | 1.49 (1.2775–1.73) | 0.729 | 1.46 (1.25–1.71) | 1.5 (1.29–1.74) | 0.0001 | 1.49 (1.27–1.73) | 1.49 (1.28–1.72) | 0.297 |
| LDL | 2.63 (2.17–3.16) | 2.72 (2.21–3.25) | 0.0001 | 2.63 (2.17–3.16) | 2.65 (2.16–3.18) | 0.854 | 2.75 (2.25–3.28) | 2.61 (2.14–3.14) | 0.0001 | 2.68 (2.21–3.2) | 2.69 (2.2–3.22) | 0.316 |
| TC | 4.75 (4.22–5.36) | 4.85 (4.27–5.5) | 0.0001 | 4.75 (4.22–5.36) | 4.77 (4.21–5.4) | 0.91 | 4.88 (4.34–5.52) | 4.73 (4.18–5.36) | 0.001 | 4.79 (4.25–5.44) | 4.81 (4.26–5.46) | 0.195 |
| Fasting Glucose | 4.83 (4.53–5.15) | 4.86 (4.55–5.22) | 0.0001 | 4.83 (4.53–5.15) | 4.81 (4.52–5.14) | 0.524 | 4.89 (4.57–5.25) | 4.82 (4.53–5.15) | 0.0001 | 4.84 (4.53–5.15) | 4.84 (4.55–5.18) | 0.274 |
| Total bilirubin | 14.2 (11.5–17.6) | 14 (11.4–17.4) | 0.017 | 14.2 (11.5–17.6) | 14.2 (11.5–17.6) | 0.576 | 14.1 (11.5–17.4) | 14.1 (11.5–17.7) | 0.108 | 14.1 (11.5–17.6) | 14.1 (11.6–17.6) | 0.722 |
| AST | 21 (18–24) | 21 (18–25) | 0.001 | 21 (18–24) | 21 (18–25) | 0.717 | 21 (18–25) | 21 (18–25) | 0.026 | 21 (18–25) | 21 (18–25) | 0.587 |
| ALT | 14 (10–20) | 15 (11–21) | 0.012 | 14 (10–20) | 14 (11–20) | 0.801 | 15 (11–21) | 14 (10–20) | 0.014 | 14 (11–20) | 15 (11–21) | 0.559 |

In our study, age was found to be an independent risk factor for the occurrence of TN, and this result is consistent with the results of previous studies.[30] The results in multivariate logistic regression indicated that age was a protective factor for BI-RADS grade 2 and 3 BM, which may be associated with the high incidence of benign breast hyperplasia in young women. As with the results of previous studies,[31,32] this paper also found that abnormal lipid levels can influence the occurrence of TN. In this paper, ALT and AST were also found to be associated with the occurrence of TN. Recently, Komori et al[33] found an epidemiological correlation between head and neck tumors and hepatitis B virus infection. So it may be that abnormal liver function due to hepatitis virus infection causes a statistical correlation between TN occurrence and liver function, and hepatitis B virus infection is a serious public health problem in China, where tens of millions of hepatitis B virus carriers.[34,35] The association between hepatitis B virus infection and TN requires our attention, and further studies are necessary to investigate the underlying mechanisms causing this phenomenon.

A large number of studies have investigated the relationship between thyroid hormone levels and breast carcinogenesis, and the role of thyroid hormones on the development of breast cancer has received widespread attention. On the one hand, Rasool et al[36] found significantly higher T3 and T4 levels in the breast cancer group than the normal population, suggesting that high levels of T 3 and T 4 are significantly associated with the risk of breast cancer. A 30-year cohort study conducted by Sogaard et al[37] in Denmark also showed that women with hyperthyroidism were at greater risk of breast cancer. Women with hypothyroidism had a slightly lower risk of breast cancer. A previous in vitro experiment similarly confirmed that thyroid hormones promote nuclear estrogen receptor alpha (ERα)-dependent cells and promote angiogenesis and breast cancer cell growth through activation of ERα-mediated pathways.[25] However, in a study by Kuijpens et al,[38] thyroid hypofunction and lower free T4 levels were associated with an increased risk of breast cancer in postmenopausal women. These studies suggest that we may have an imbalance between estrogen and thyroid hormones promoting the development and progression of breast cancer. Our study found that higher free T4 reduced the risk of developing BM. This relationship was mainly observed in BI-RADS 3 breast, as retrospective studies are susceptible to confounding by other confounding factors, especially estrogen, which, together with T4,

acts on ERα to promote breast cell proliferation. We also do not know whether any of the women examined were taking oral levothyroxine for hypothyroidism, among other factors, which may confound our conclusions. However, previous studies and our findings suggest an association between thyroid hormone levels and the development of breast disease, and more researches are required to clarify the specific mechanisms of action between thyroid function and BM.

This paper contains a large sample size and multiple covariates, as did the previous study,[6] but an important advantage of this study is the introduction of thyroid hormones that are extremely important for the occurrence of TN and BM, which makes us be able to explain the effect of thyroid hormone on thyroid and breast. Moreover, this article uses propensity score matching to verify the relationship between TN and BM, making our results more reliable. There are some shortcomings in this study: certain important covariates were not included, especially estrogen. Many previous studies[39–41] have shown that thyroxine and estradiol share a signaling pathway that regulates the growth of breast cancer cells. Because women rarely undergo sex hormone screening during health checkups, the effect of other hypothalamic-pituitary axis-related hormones on TN or BM development was not discussed in this article to ensure sample size. Further studies are needed to assess whether sex hormones affect the development of thyroid and breast disease.

In conclusion, elucidating the common pathogenesis between BM and TN will have important implications for the diagnosis and prevention of these diseases. Especially in light of current studies, both BM and TN have a high prevalence, and there is an association between the pathogenesis of both. Therefore, clinicians may consider routine imaging of the thyroid or breast at the time of physical examination, especially if a high TI-RADS-graded TN or a high BI-RADS-graded BM is found, or if other risk factors are combined, necessitating examination of the other gland. A large sample, prospective, multi-center study is needed further to explore the pathological relationship between thyroid and breast nodules.

## Ethics Approval and Consent to Participate

The Ethics Committee approved this study of the Affiliated Hospital of North Sichuan Medical College. Because of the retrospective nature of the study, patient

informed consent for inclusion was waived. All information was anonymous. The study was conducted in accordance with the Declaration of Helsinki.

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## Disclosure

The authors declare that they have no conflicts of interest in this work.

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