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Mental Health Status of Patients with Thyroid Nodules: A Cross-Sectional Study

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Purpose: This study aims to investigate the mental health status of patients with high-risk and low-risk thyroid nodules (TNs), and the potential psychological risk factors that may exist in patients with high-risk nodules.

Patients and Methods: In this cross-sectional study, a total of 7645 adults who participated in physical examinations from January 2021 to December 2023 were included. During the physical examination, they all completed thyroid ultrasound examinations and laboratory tests, and filled out self-administered questionnaires, as well as the Symptom Checklist-90 (SCL-90) and the Stress Self-Assessment Questionnaire-53 (SSQ-53). These were used to collect general information, mental health status, and stress levels of the subjects. According to the degree of malignant risk, TNs were categorized into high-risk groups (HRG) and low-risk groups (LRG). Differences between the two groups were compared in terms of general information, mental health status scores, and laboratory indicators.

Results: The overall detection rate of TNs was 34.5%, with a significantly higher rate in women. There were significant differences in age and gender between HRG and LRG; The total score of SCL-90 in the HRG was significantly higher than that in LRG (128.78 ±45.65 vs 120.59±31.68, p=0.044); HRG exhibited a higher proportion of positive rates in the somatization (P=0.033) and anxiety (P=0.048) factors of the SCL-90. Among the 10 factors of SCL-90, the scores of somatization (P=0.011), obsessive-compulsive (P=0.010), interpersonal sensitivity (P=0.032), depression (P=0.036) and additional factors (diet and sleep) (P=0.008) in HRG were significantly higher. The results of SSQ-53 suggest that the overall stress level in HRG is higher, and the cognitive stress is significantly higher than that in LRG (P=0.003). Multivariate logistic regression analysis showed that age, gender, and SCL-90 total score were risk factors for high-risk TNs.

Conclusion: High-risk TNs are more common in females and older adults. The existence of high-risk TNs is related to poor mental health status.

Keywords: thyroid nodules, thyroid cancer, mental health, psychological stress, influencing factor

Introduction

With the development of the economy and changes in people's pace of life, the prevalence of thyroid diseases is gradually increasing and receiving more attention. The thyroid gland is an important endocrine organ in the human body, closely related to metabolism, physical development, and emotions. As a common disease of the endocrine system, thyroid nodules (TNs) are mass lesions formed by the abnormal growth of thyroid cells. The prevalence of TNs is gradually increasing in the general population —up to 60% as documented by high-resolution ultrasonography.[1] The prevalence of TNs in mainland China is approximately 32%, with variations across different provinces, notably higher in Beijing.[2]

Previous studies have indicated that the occurrence of TNs is associated with gender, age, iodine, ionizing radiation and genetic factors.[3,4] Although most TNs are benign, there is a risk of malignant transformation — very few of these lesions ultimately prove to be malignant (about 10%).[5] Thyroid cancer (TC) is the most common endocrine malignancy, accounting for approximately 2.1% of all cancer diagnoses globally, with female patients making up 77% of cases.

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According to China's cancer statistics from 2023, the current incidence of TC in China is 14.65 per 100,000 individuals, ranking eighth among all malignant tumors and third among female malignant tumors.[6] Between 2005 and 2015, the incidence rate of TC in China increased at an average annual rate of 12.4%, becoming the fastest growing malignant tumor.[7] At present, the prevalence of TNs and TC is increasing worldwide, and it is showing a trend of affecting younger populations.[8] Therefore, it is essential to investigate the risk factors of TNs and their potential for cancer.

At present, it is believed that excessive psychological pressure and long-term negative emotions such as anxiety and depression may be one of the risk factors for thyroid disease. Some studies have even investigated negative emotions as an independent risk factor for TC.[9] However, the precise correlation between psychological factors and TNs (benign or malignant) remains poorly understood. Thyroid diseases have always been closely associated with mental illnesses, with symptoms accompanied by emotional disorders being more common. For instance, hyperthyroidism is prone to emotional issues such as anxiety and depression. Furthermore, studies have found that hyperthyroidism may increase the risk of bipolar disorder.[10] The prevalence of psychological negative emotions in patients with Hashimoto's thyroiditis was high.[11] Research showed that psychosocial stress appears to increase the susceptibility to chronic diseases, such as major depressive disorder (MDD) and cancer. Furthermore, chronic psychosocial stress elevates the mortality rate of multiple types of cancer.[12] Negative emotions can impair immune function,[13] leading to immune dysfunction and subsequently causing chronic inflammation. Chronic inflammation not only affects thyroid function but may also lead to abnormal proliferation of glandular cells, which can progress to the formation of TNs and even malignant transformation.[9,14] There is ample clinical and basic research evidence supporting the significant role of inflammation in tumor growth and progression. Recent research on the neurobiology of depression and the pathophysiology of cancer has revealed that there may be common biological and behavioral mechanisms between the two.[15]

To our knowledge, there are few studies exploring the association between mental health and TNs, as well as the potential impact of psychological state on the risk level of nodules. Therefore, this study collected relevant data from participants who underwent health checks at a tertiary hospital in Beijing. Self-administered questionnaires were used to collect general information, while the Symptom Checklist 90 (SCL-90) and Stress Self-Assessment Questionnaire (SSQ-53) were used to assess psychological status and stress levels, and laboratory values were used to assess physiological status. By analyzing TNs based on their imaging classification, researchers aim to explore the psychological, biochemical, and other factors that may influence the transition of TNs from low-risk to high-risk, promote the prevention of TC, and further improve thyroid health management.

Materials and Methods

Research Objects

This is a large cross-sectional study. Participants were recruited from individuals who underwent health examinations at the Health Management (Physical Examination) Center of Peking University Third Hospital between January 2021 and December 2023.

Requirements for inclusion: (1) Age 18 and above; (2) Completion of thyroid ultrasound; (3) Completion of psychological evaluation. According to the Helsinki Declaration, protocols involving human participants are reviewed and approved by the Institutional Ethics Committee of Peking University Third Hospital (Project number: M2022255). After being fully informed goals and methods of the study, all participants signed an informed consent form and consented to the use of the current health survey data, relevant physical exam results, and laboratory results.

Methods

General Information

A self-made questionnaire was used to collect general data from participants, including age, gender, marital status, etc. All participants completed the questionnaires (including psychological questionnaires).

Thyroid Ultrasonography

The thyroid ultrasound examination is conducted by two registered doctors holding professional ultrasound certificates. Ultrasound was performed using the Resona R9 color Doppler ultrasound examination system (Mindray, Shenzhen, China), equipped with an L15-3 linear array probe (frequency range 3MHz-15MHz). We classified TNs according to the C-TIRADS guidelines.[16] (The Chinese Thyroid Imaging Reporting and Data System established through a score-based methodology comprises the following classification categories: Category 1: No intervention required; Category 2: Malignancy risk 0%; Category 3: Malignancy risk <2%; Category 4A: Malignancy risk 2%-10%; Category 4B: Malignancy risk 10%-50%; Category 4C: Malignancy risk 50%-90%; Category 5: Malignancy risk >90%; Category 6: Biopsy-proven malignant nodules).

Mental Health Assessment

The Symptom Checklist 90 (SCL-90)[17] was used to assess the participant's psychosomatic status. The scale consists of 90 items, divided into 10 factors: somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, psychoticism, and additional items (mainly sleep and diet conditions). Using a 5-point scale, the higher the score, the worse the health condition. If the total score is ≥160 and/or any factor score is ≥2 (the 10 factors mentioned above, reflecting the characteristics of symptom clusters), the participant's psychological assessment result is considered positive. According to the comparison of the total score of SCL-90 with the health norm of the Chinese population, a total score range of 90–159 indicates health/sub-health, while a total score of 160 or above indicates abnormal mental health level (160–199 indicates mild, 200–249 indicates moderate, and 250 or above indicates severe). The degree of psychological stress was assessed using the Stress Self-Assessment Questionnaire-53 (SSQ-53). The scale contains 53 questions to assess the level of stress experienced by individuals in the past month, which is roughly divided into four stress factors: physical, emotional, cognitive, and behavioral (0–0.08 points for level 1, 0.09–0.19 points for level 2, 0.2–0.28 points for level 3, 0.29–0.42 points for level 4, 0.43–0.62 points for level 5, 0.63–0.91 points for level 6, 0.92–1.3 points for level 7, 1.31–1.72 points for level 8, 1.73–4 points for level 9, and 1.73–4 points for level 9 with ≥2 points for question 38 and ≥3 points for question 36 or 51 for level 10). The higher the score, the greater the stress. People with a stress level of 7 or above are considered to have a high level of stress, exhibit psychological and physiological symptoms of excessive stress, and need stress management.

Hematology Examination

Collect the elbow vein blood of participants and centrifuge it at 3000 r/min for 15 minutes at 4°C. The SYSMEX XN-2000 fully automated blood analyzer was used for whole blood cell count analysis. The Beckman Coulter AU5800 automatic biochemical analyzer was used to analyze blood biochemistry. Thyroxine, triiodothyronine, free triiodothyronine, thyroid-stimulating hormone, and other thyroid-related markers were measured using a Siemens Atellica analyzer.

Statistical Analysis

All data were analyzed using SPSS 26.0. The two-sample *t*-test is used to compare inter-group data, which were normally distributed in general data and expressed as mean ± standard deviation ($\bar{x} \pm s$). The Mann–Whitney *U*-test is used to compare data that do not follow a normal distribution, represented as M (Q1, Q3). The Chi-square test was used to compare groups, and count data were expressed as n (%). All statistical analyses were considered statistically significant when the two-sided p-value was less than 0.05.

Results

General Features and Classification of TNs

Among the participants who underwent health examinations between January 2021 and December 2023, 7645 cases were ultimately included according to the inclusion criteria and data integrity analysis. This included 4051 males (53.0%) and 3594 females (47.0%). The number of people who TNs detected was 2640 (34.5%), including 1250 males (30.9%) and 1390 females (38.7%). The prevalence of TNs in females was significantly higher than that in males (p<0.001). The number of people who underwent total or partial thyroidectomy was 104 (1.4%), including 28 males (0.7%) and 76 females (2.1%) (p<0.001) (Table 1).

Table 1 Gender Differences in the Prevalence of TNs

Variables	Males (%)	Females (%)	t-value/x2-value	P-value
Total number (7645 cases)	4051(53.0%)	3594(47.0%)		
Number of nodules detected (34.5%)	1250(30.9%)	1390(38.7%)	51.500	<0.001
Total or partial thyroidectomy (1.4%)	28(0.7%)	76(2.1%)	28.757	<0.001

According to the C-TIRADS guidelines to classify the malignant risk of TNs, participants with C-TIRADS category 4 and above were classified as a high-risk group (HRG), with a total of 129 cases (1.7%), participants with C-TIRADS category 3 and below (including normal ones) were classified as a low-risk group (LRG), with a total of 7516 cases (98.3%). There were significant differences in age, gender, and marital status between the two groups (Table 2).

The SCL-90 Results of the High-Risk Group Showed More Abnormal Psychological States

The total score and average score of SCL-90 in the high-risk group (HRG) were 128.78 ± 45.65 and 1.43 ± 0.51, respectively. These scores were significantly higher than those in the low-risk group (LRG), which had a total score of 120.59 ± 31.68 and a total average score of 1.34 ± 0.35. In the positive items, the proportion of somatization and anxiety items was significantly higher in the HRG (somatization P=0.033, anxiety P=0.048). Among the 10 factors of SCL-90, the HRG exhibited significantly higher scores in somatization (P=0.011), obsessive-compulsive symptoms (P=0.010), interpersonal sensitivity (P=0.032), depression (P=0.036), and additional items (eg diet, sleep) (P=0.008) compared to the LRG. According to the total score, the mental health level of the subjects was divided into abnormal and relatively normal states. No significant difference was found in the proportion of subjects with abnormal mental health status between the HRG and LRG (Table 3).

The High-Risk Group of TNs Showed Higher Psychological Stress

The overall stress level of the HRG was higher, and the cognitive stress score was significantly higher than that of the LRG (P=0.003). According to the stress score, levels 7 and above are considered to have excessive stress. According to this classification, no significant difference was found between the HRG and the LRG (Table 4).

Table 2 Differences in Demographic Characteristics Between High-Risk Group and Low-Risk Group of TNs

Variables	HRG (n=129)	LRG (n=7516)	t-value /x2-value	P-value
Age (years)	44.22±11.08	38.43±10.05	5.901	<0.001
18–29 years	12(0.8%)	1588(99.2%)	53.773	<0.001
30–39 years	40(1.4%)	2867(98.6%)		
40–49 years	32(1.8%)	1795(98.2%)		
50–59 years	34(2.9%)	1140(97.1%)		
≥60 years	11(8.0%)	126(92.0%)		
Gender				
Males (%)	39(30.2%)	4012(53.4%)	27.277	<0.001
Females (%)	90(69.8%)	3504(46.6%)		
Marital status				
Married (%)	111(87.4%)	5567(75.5%)	9.658	0.008
Unmarried (%)	16(12.6%)	1803(24.4%)		
Divorced (%)	0(0.0%)	5(0.1%)		

Table 3 Results of Symptom Checklist 90 (SCL-90) in Both Groups

Variables	HRG (n=129)	LRG (n=7516)	t-value /x2-value	P-value
Total score *	128.78±45.65	120.59±31.68	2.029	0.044
The total average score *	1.43±0.51	1.34±0.35	2.034	0.044
Factor points				
Somatization *	1.42±0.50	1.30±0.38	2.573	0.011
Obsessive-compulsive *	1.63±0.63	1.52±.48	2.576	0.010
Interpersonal sensitivity*	1.47±0.57	1.38±0.44	2.143	0.032
Depression *	1.47±0.60	1.36±0.44	2.113	0.036
Anxiety	1.42±0.56	1.35±0.41	1.501	0.136
Hostility	1.41±0.64	1.36±0.45	0.960	0.339
Phobic anxiety	1.19±0.44	1.14±0.28	1.381	0.170
Paranoid ideation	1.29±0.47	1.24±0.38	1.309	0.191
Psychoticism	1.32±0.46	1.24±0.34	1.835	0.069
Additional items* (eg diet, sleep)	1.67±0.67	1.50±0.54	2.696	0.008
The proportion of positive factors				
Somatization (≥2) *	14(10.9%)	470(6.3%)	4.524	0.033
Obsessive-compulsive (≥2)	24(18.6%)	1190(15.8%)	0.729	0.393
Interpersonal sensitivity (≥2)	14(10.9%)	811(10.8%)	0.001	0.982
Depression (≥2)	15(11.6%)	689(9.2%)	0.919	0.338
Anxiety (≥2) *	17(13.2%)	624(8.3%)	3.925	0.048
Hostility (≥2)	15(11.6%)	755(10.0%)	0.351	0.554
Phobic anxiety (≥2)	4(3.1%)	178(2.4%)	0.062	0.803
Paranoid ideation (≥2)	9(7.0%)	494(6.6%)	0.034	0.854
Psychoticism (≥2)	7(5.4%)	372(4.9%)	0.061	0.805
Additional items (eg diet, sleep) (≥2)	31(24.0%)	1444(19.2%)	1.891	0.169
Mental health level (abnormal)	42(32.6%)	2325(30.9%)	0.157	0.692

Notes: *p-value, significant at <0.05.

Table 4 Results of the Stress Self-Assessment Questionnaire-53 (SSQ-53) in Both Groups

Variable	HRG (n=129)	LRG (n=7516)	z-value /x2-value	P-value
Overall stress	0.27(0.09,0.51)	0.21(0.08,0.47)	−1.666	0.096
Physiology	0.30(0.10,0.69)	0.25(0.10,0.55)	−1.759	0.079
Mood	0.17(0.02,0.49)	0.11(0.00,0.44)	−1.165	0.244
Cognition*	0.50(0.06,1.00)	0.25(0.00,0.75)	−2.949	0.003
Action	0.18(0.00,0.36)	0.18(0.00,0.36)	−1.066	0.287
Overall stress level (≥7)	14(10.9%)	623(8.3%)	1.140	0.286
Physiological grade (≥7)	15(11.7%)	586(7.8%)	2.648	0.104
Emotional grade (≥7)	14(10.9%)	756(10.1%)	0.103	0.749
Cognitive grade (≥7)	15(11.7%)	575(7.7%)	2.899	0.089
Action grade (≥7)	9(7.0%)	432(5.8%)	0.374	0.541

Notes: *p-value, significant at <0.05.

Physical Examination Results of the Two Groups

By comparing the differences in physical indicators including body mass index (BMI), blood pressure, and laboratory values between HRG and LRG, it was found that compared to LRG, the levels of total cholesterol (P=0.038), thyroxine (P<0.001), and free thyroxine (P<0.001) were significantly elevated in HRG; meanwhile, the levels of thyroid-stimulating hormone (TSH) (P=0.001), triiodothyronine (T3) (P=0.014), free triiodothyronine (FT3) (P<0.001), erythrocytes (P=0.008), hemoglobin (HGB) (P<0.001), uric acid (UA) (P=0.006), and creatinine (Cr) (P=0.001) were significantly reduced (Table 5).

Analysis of Risk Factors for High-Risk Nodules

In the multivariate logistic regression analysis, age, gender, marital status, erythrocytes, hemoglobin, total cholesterol, creatinine, uric acid, and SCL-90 total score were used as independent variables, and the presence of high-risk nodules was used as the dependent variable. The results indicated that age (OR=1.060 per year, 95% CI [1.038–1.082], p<0.001), female gender (OR=3.430 vs male, 95% CI [1.738–6.771], p<0.001), and SCL-90 total score (OR=1.006, 95% CI [1.001–1.010], p=0.013) were independently associated with the risk of having high-risk nodules. The model demonstrated good fit (Hosmer-Lemeshow test p>0.05). Age was an independent risk factor for the occurrence of high-risk TNs, with a 6% increase in risk for each additional year of age. Women were significantly more likely to have high-risk nodules than men, with a risk of 3.43 times higher. The SCL-90 total score was an independent factor influencing the occurrence of high-risk TNs, with a 0.6% increase in risk for each additional score (Table 6).

Table 5 Differences in Physical Examination Results Between the Two Groups

Variables	HRG (n=129)	LRG (n=7516)	t-value/Z-value /x2-value	P-value
BMI (kg/m2)	23.61±3.67	23.88±3.66	−0.834	0.404
SBP (mm hg)	120.66±15.04	119.45±15.10	0.897	0.370
DBP (mm hg)	74.38±10.47	73.81±10.91	0.585	0.559
White blood cells	5.69±1.53	5.94±1.45	−1.936	0.053
Erythrocytes *	4.71±0.47	4.83±0.51	−2.656	0.008
Hemoglobin *	139.83±16.53	145.33±16.52	−3.679	<0.001
Platelets	252.01±59.16	249.47±55.41	0.505	0.614
FPG	5.19±0.77	5.23±1.05	−0.413	0.679
Glycated hemoglobin	5.62±0.47	5.62±0.71	−0.070	0.944
TC*	5.11±1.02	4.93±0.93	2.070	0.038
TG	1.15(0.84,1.72)	1.11(0.79,1.64)	−0.588	0.556
HDL-C	1.36±0.33	1.32±0.32	1.394	0.172
LDL-C	3.00±0.84	2.91±0.75	1.178	0.241
UA*	320.48±84.21	343.28±91.00	−2.770	0.006
Homocysteine	10.4(8.8,13.9)	11.2(9.2,14.2)	−1.684	0.092
Urea	4.70±1.09	4.83±1.17	−1.218	0.223
CR*	75.30±12.89	79.62±14.07	−3.392	0.001
AST	20.00(17.00,23.75)	20.00(17.00,25.00)	−0.949	0.342
ALT	18(13,26)	18(13,27)	−0.790	0.430
TSH*	1.60(0.59,2.94)	2.01(1.44,2.82)	−3.251	0.001
T4*	9.00±2.07	7.77±1.58	6.329	<0.001
FT4*	1.39±.26	1.27±0.20	4.821	<0.001
T3*	1.07±0.19	1.12±0.22	−2.454	0.014
FT3*	3.21±0.39	3.37±0.47	−3.562	<0.001

Notes: *p-value, significant at <0.05.

Abbreviations: BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; UA, uric acid; CR, creatinine; AST, Aspartate transaminase; ALT, alanine aminotransferase; TSH, thyroid stimulating hormone; T4, thyroxine; FT4, free thyroxine; T3, triiodothyronine; FT3, free triiodothyronine.

Table 6 Multivariate Analysis of Risk Factors for High-Risk Nodules

Factors	B	SE	Wald Test	P-value	OR	95% CI
Age	0.058	0.010	31.327	0.000	1.060	1.038–1.082
Gender (male)	1.233	0.347	12.620	0.000	3.430	1.738–6.771
Marital status (Married)	0.056	0.324	0.029	0.864	1.057	0.560–1.995
Erythrocytes	0.514	0.269	3.642	0.056	1.672	0.986–2.835
Hemoglobin	−0.009	0.009	1.104	0.293	0.991	0.974–1.008
TC	0.036	0.097	0.142	0.706	1.037	0.858–1.254
CR	0.002	0.010	0.029	0.864	1.002	0.982–1.002
UA	0.000	0.001	0.103	0.749	1.000	0.998–1.003
SCL-90 total score	0.006	0.002	6.161	0.013	1.006	1.001–1.010

Abbreviations: TC, total cholesterol; CR, creatinine; UA, uric acid.

Discussion

Current study found that the prevalence of TNs is relatively high. TNs, including potentially malignant nodules, are more common in women. Age is also a risk factor for the development of high-risk nodules. Patients with high-risk nodules tend to have poorer mental health and higher psychological stress, suggesting that poor mental health status may be associated with the deterioration of nodules. Study investigated the impact of physical indicators, including those from routine physical examinations, on TNs and found that age, being female, and poor mental health status (high SCL-90 total score) are independent risk factors for the presence of high-risk TNs.

In recent years, the prevalence of TNs has significantly increased. This survey was conducted at a large comprehensive hospital in Beijing among people over 18 years old who underwent health check-ups. Research shows that the prevalence of TNs in this population is 34.5%, which is consistent with previous survey results.[18] According to the literature, the prevalence rate varies in different regions, showing a regional-specific manner in China. The differences may be caused by factors such as age, gender, genetics, living environment, dietary habits, and iodine nutrition status.[2,18]

In this study, the prevalence of TNs in women was 38.7%, significantly higher than that in men (30.9%). Multivariate analysis results indicated that the probability of high-risk nodules in women was 3.4 times higher than that in men. This is consistent with previous research findings.[19,20] Sex hormones play a significant role in this process. Evidence suggests that estrogen receptors are expressed in both normal and malignant thyroid tissues, indicating that estrogen may directly regulate the proliferation and function of human thyroid cells. Furthermore, it can regulate genes involved in the progression of the thyroid cell cycle, potentially contributing to the pathogenesis of TC or the thyroid hyperplasia.[21] Meanwhile, research suggests that women are also at a higher risk of developing anxiety, depression, and stress-related disorders, with a likelihood twice that of men.[22] This can also partially explain the high comorbidity phenomenon between emotional issues, stress-related diseases, and TNs, as well as the potential common pathological pathways among these diseases.

Current study revealed that the average age of the high-risk TNs patients is higher than that of the low-risk TNs population, indicating that age plays a significant role in regulating the incidence rate of potential malignant TNs. Furthermore, age is an independent risk factor for the emergence of high-risk TNs, with the risk increasing by 6% for every additional year of age. This is consistent with previous research findings.[23] The mechanism may be that as age increases, thyroid tissue undergoes degenerative changes, leading to diffuse compensatory hyperplasia of the thyroid gland.[24] Recent studies suggest that the age-specific incidence rate curve for malignant nodules is now changing, reaching a peak around the age of 40 or 50, rather than increasing with age.[25]

Previous studies have indicated that the occurrence of TNs is associated with negative emotions, and negative emotions are also considered as an independent risk factor for TC. Consistent with previous research, current study reveals that subjects in the high-risk nodule group have a higher total score on the SCL-90, indicating a poorer overall mental health status. Furthermore, they exhibit higher scores in factors such as somatization, interpersonal sensitivity, anxiety, depression, obsession-compulsion, and diet and sleep, suggesting that subjects with high-risk nodules experience maladjustment in various aspects of their lives, including emotional, somatic sensations, and social interactions. This includes negative emotional experiences such as depressive symptoms and anxiety spectrum symptoms (including

obsession), subjective physical discomfort (somatization), poor diet, poor sleep conditions, and other adverse physical experiences, as well as negative experiences in social life such as discomfort and inferiority in interpersonal relationships (interpersonal sensitivity). Maladjustment is accompanied by increased psychological stress, leading to a decline in overall mental health status. Multivariate analysis reveals that poor mental health status (increased total score on the SCL-90) is an independent risk factor for the presence of high-risk nodules. For every 1-point increase in the total SCL-90 score, the risk increases by 0.6%. Therefore, it is speculated that poor mental health status may be a triggering and exacerbating factor in the development of malignant TNs.

Long term research has found a bidirectional causal relationship between mental health problems and thyroid diseases, such as a positive correlation between anxiety and hypothyroidism, and a positive correlation between autoimmune thyroiditis, hypothyroidism, and recurrent or chronic depression.[26] Emotional disorders and thyroid diseases are regulated by the neuroendocrine axis. Chronic stress (including depression and anxiety-related disorders) affects thyroid dysfunction through the cross-action of the hypothalamic-pituitary-adrenal (HPA) and hypothalamic-pituitary-thyroid (HPT) axes. Overactivation of the HPA axis leads to excessive cortisol release, which could inhibit the activity of the HPT axis. This, in turn, can increase susceptibility to anxiety and depression.[27] The prolonged secretion of glucocorticoids caused by chronic stress can interfere with the immune system's response by altering cytokines, inducing low-grade chronic inflammation, and inhibiting the function of immune protective cells. Continuous exposure to specific endocrine-disrupting chemicals (EDCs) has an impact on thyroid development, function, and proliferation, leading to thyroid diseases and potential cancers.[28] In summary, thyroid hormone imbalance, chronic inflammation, and endocrine disruptors are all potential risk factors for oxidative stress. Oxidative stress can cause DNA damage, leading to mutations in TC-related genes.[29] Studies on cancer subjects have also found that stress appears to affect every stage of tumor progression.[30]

On the other hand, the mere presence of malignant nodules can easily trigger negative emotions and exert significant psychological pressure. Cancer related concerns persist for several years after the patient's diagnosis and treatment.[31] A survey found that within 2–4 years after diagnosis, 41.0% of patients expressed concerns about death, 43.5% of patients were concerned about the harm of treatment, 54.7% of patients were concerned about their quality of life being compromised, 58.0% of patients were concerned about family risks, and 63.2% were concerned about recurrence.[32] 20–40% of women express high levels of concern, with younger patients being more concerned about disease recurrence.[33] In a study targeting women with cancer, it was found that TC patients are more prone to anxiety and fatigue.[34] A survey conducted one year after diagnosis of differentiated TC showed that among 235 patients, 75% expressed concerns about recurrence, and 23% expressed negative views about life.[35] Therefore, the symptoms of cancer itself and the emotional issues it triggers could also increase the psychological burden on patients.

To our knowledge, there is limited research on the relationship between mental health status and TNs, whether benign or malignant. This study compares the mental health status of patients with low-risk and high-risk TNs, clearly indicating a significant correlation between high-risk TNs and poor mental health. However, there are still some limitations to this study. Current research is a cross-sectional study, which can only demonstrate the correlation between poor mental health and high-risk TNs, but cannot explore the causal relationship. Next, we will further establish a cohort to explore its deeper association.

Conclusion

This large cross-sectional study found that the prevalence of TNs is relatively high. Both benign and potentially malignant nodules are more common in women. Compared to benign nodules, potentially malignant nodules occur at a higher age. Through the detection of mental health status and psychological stress, it was found that patients with high-risk nodules have poorer mental health and greater psychological stress, manifested as more negative emotions, physical discomfort, and interpersonal tension. This suggests that poor mental health status may be an important factor in the development of malignant nodules. This indicates that we need to pay attention to the mental health status of patients with TNs, so as to make strategic adjustments in preventing the occurrence of malignant nodules and reducing the adverse consequences caused by malignant nodules.

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Disclosure

The authors report no conflicts of interest in this work.

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