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ORIGINAL RESEARCH

Nomogram Prediction Model of Thyroid Nodule in Healthcare Professionals: Based on Physical and Psychological Risk Factors

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Background: Thyroid nodules are a common condition with a 7–15% likelihood of developing thyroid cancer. The prevalence of thyroid nodules in healthcare professionals is poorly understood, and how psychosomatic factors affect the occurrence of thyroid nodules is an interesting question. Therefore, the aims of this study are to explore the physiological and psychological aspects associated of thyroid nodules in healthcare professionals and establish a prediction model to provide a supportive basis for the primary prevention of thyroid nodules.

Methods: A total of 738 healthcare professionals in a tertiary general hospital were selected by convenience sampling to complete an online psychological questionnaire and physical examination (biochemical indicators, ultrasound, etc.) from February to May 2023. Logistic regression was used to analyze risk factors, and the prediction model was established by nomogram.

Results: A total of 406 of 738 healthcare professionals had thyroid nodules, the detection rate was 55.0%, among those detected, 24.1% were male and 75.9% were female. Multivariate logistic regression analysis showed: compared with ≤40 years old, aged 41–50 years old, or >50 years old were risk factors for thyroid nodules (OR=2.071/8.034); female (OR=1.873) was also risk factor for thyroid nodules relative to male; in addition, anxiety (OR=1.105), perceived stress (OR=1.045), fatty liver (OR=2.716), TSH abnormality (OR=1.944), and ALT abnormality (OR=2.252) were also risk factors. Based on the above seven influencing factors, a nomogram was drawn and verified internally. The results showed that the area AUC under the ROC curve of the model was 0.713, and the calibration curve indicated that the model consistency was acceptable.

Conclusion: The detection rate of thyroid nodules is higher in healthcare professionals. A combination of psychological and physiological factors in TNs has a significant impact on thyroid nodules. Identifying risk factors for thyroid nodules and managing them promptly is important for the complete health of healthcare professionals.

Keywords: thyroid nodules, anxiety, perceived pressure, psychosomatic risk factors, risk prediction model, nomogram

Introduction

Thyroid nodules (TNs) are sporadic lesions caused by local abnormal growth of thyroid cells.[1] Depending on the method of detection (eg, palpation, ultrasound, and autopsy), the prevalence of TNs ranges from 2% to 65% in different countries, and a pooled analysis of studies in China showed a prevalence rate of 30.2% of TNs.[2] Thyroid nodules can be detected in 19–68% of randomly selected by high-resolution ultrasound (US), with a higher prevalence in women and the elderly.[3] Currently, thyroid nodules are becoming more common in physical examination. A few studies have shown that the highest detection rate of TNs among different professions is found among healthcare professionals, reaching 48.5–65.8%.[4–6] Although the majority of thyroid nodules are benign, 10–15% are found to be malignant on follow-up examinations.[7] When thyroid nodules are detected, patients are followed up for long periods with regular checkups, which can be a heavy financial burden if they are over-screened.[8] Moreover, TNs are almost asymptomatic in the early stages, and when clinical symptoms appear they are usually treated with surgery, which is often accompanied by complications such as hypothyroidism and laryngeal nerve damage, affecting patients' quality of life.[9] Early

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identification of risk factors for the development of TNs and the high-risk groups is an important means of achieving primary prevention, and early intervention can prevent the normal thyroid gland from changing to a sub-healthy state.

Thyroid nodules result from an interaction of genetic, environmental, and endocrine factors.[10] Risk factors have been shown to include exposure to radiation or chemicals, a family history of thyroid nodules or cancer; demographic characteristics such as gender and age; and other testing data such as thyroid stimulating hormone, BMI, total cholesterol, and fasting blood glucose.[11] Several studies have re-validated that females, advanced age, central obesity, overweight obesity, hypertension, hyperglycemia, and hyperlipidemia are independent risk factors for thyroid nodules.[11–14] However, there is no consensus on which physiologic measures should be closely monitored by the public, and further confirmation is needed, psychological factors (eg, anxiety, psychological stress, etc.) affecting thyroid nodules have received little attention.[15]

In addition to the metabolic indicators mentioned above had been confirmed as risk factors, occupational stress, bad mood, and anxiety may also lead to the occurrence of TNs. Thyroid dysfunction has long been recognized to be associated with altered mood and cognition.[16] Thyroid disorders and autoimmune thyroid diseases are strongly linked to negative emotions.[17] Psychological stress is one of the non-genetic risk factors for common thyroid disorders.[18,19] Studies have also demonstrated a strong correlation between thyroid disease and anxiety and depression.[20] There is a positive causal relationship between borderline personality disorder and a single non-toxic thyroid nodule.[21] Doubtfully, although it has been hypothesized that the effects of emotional factors, mood disorders, and mental stress may be associated with thyroid disease, there have been no studies exploring these as risk factors for the development of TNs.

Implementing early health management strategies may help reduce the incidence of thyroid cancer, making it essential to manage risk factors for thyroid nodules. Currently, there are still unmet research needs in the basic study of thyroid nodules.[15] Few studies, both domestically and internationally, have established nomogram prediction models for thyroid nodules, and psychological factors have not been comprehensively considered in the analysis of risk factors. In this study, we aim to further explore the risk factors associated with thyroid nodules (TNs) from the perspective of psychology. Additionally, we analyze the psychosomatic factors contributing to the development of thyroid nodules by integrating physiological and psychological indicators, and construct a risk prediction model to provide a practical basis for managing the risk factors of thyroid nodules.

Methods

Participants and Procedures

A cross-sectional, self-reported study was conducted from February to May 2023. The convenience sampling method was employed to select 800 workers from a tertiary general hospital in China for all online questionnaires and the collection of clinical characteristics. Through the completeness of the questionnaire and the exclusion criteria, the final valid number was 738. The inclusion criteria: (1) age ≥18 years old; (2) work experience ≥1 year; (3) engaged in medical, medical technology, nursing, or other related positions; (4) undergoing thyroid ultrasound and related physical examination. The exclusion criteria: (1) responsible for transport, logistics and other support personnel; (2) after thyroidectomy or total thyroidectomy; (3) receiving drugs (such as amiodarone and iodine) or hormones (such as glucocorticoids and somatostatin) that affect thyroid function; (4) pregnant women or taking estrogen. The investigators were uniformly trained. The test data and questionnaires can only be used with the informed consent of the participants. The study was approved by the Ethics Committee of the First Affiliated Hospital of Army Medical University ((B)KY2023088).

Measurements

Physical Examination Indicators

1. Physical measurements: height, weight and body mass index (BMI) were measured automatically by professional nursing staff using a health analyzer (SK-X80); blood pressure was measured by an OMRON electronic sphygmomanometer (HBP-9021, Japan); and waist circumference and hip circumference were operated and recorded following internationally standardized methods.

2. Biochemical detection: venous blood was collected early in the morning on an empty stomach after 8 hours of fasting, and the indexes included white blood cell count (WBC), neutrophil count (NEU), neutrophil percentage (NEU%), lymphocyte count (LYMPH), lymphocyte percentage (LYMPH%), red blood cell count (RBC), mean corpuscular volume (MCV), platelet count (PLT), mean platelet volume (MPV), hemoglobin content (HGB), total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), albumin (Alb), blood urea (UN), blood uric acid (UA), fasting blood glucose (FBG), serum creatinine (Cr), alanine transferase (ALT), thyrotropin (TSH), triiodothyronine (T3), free triiodothyronine (FT3), free thyroxine (FT4), thyroxine (T4), etc. All samples are uniformly tested by the laboratory of the center and relevant departments of the hospital, using methods such as hematology analyzers, oxidase, enzyme chemistry, chemiluminescence, immunoassay, and others, respectively.
3. Inflammatory markers: neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and systemic immunoinflammatory index (SII), calculated from serum sampling data.
4. Ultrasound examination: (i) thyroid ultrasound: Philips Color Ultrasound EPIQ 7 (probe frequency 7–10 MHz/50mm) was used, and the thyroid gland was swept in multiple views by a professional ultrasound doctor, who recorded in detail the location, size, shape, boundary, internal structure, echo, and blood flow status of thyroid nodules, and carefully described the possibility of malignant nodules and the status of regional lymph nodes.[22] (ii) abdominal ultrasound: Philips Color Ultrasound EPIQ 7 (probe frequency 3.5–5MHz/50 mm) is used to observe the degree of hepatic steatosis and give a diagnosis by a professional ultrasound doctor.

Diagnostic Criteria

1. Thyroid nodules follow the Thyroid Imaging Reporting and Data System (TI-RADS) diagnostic criteria.[23] In this study, TI-RADS grade 0 was defined as the absence of thyroid nodules, and TI-RADS grades 1–5 were defined as the presence of thyroid nodules.
2. Biochemical criterion: A. BMI: <18.5kg/m^2 is low body mass, 18.5–23.9kg/m^2 is normal body mass, 24.0–27.9kg/m^2 is overweight, ≥28.0kg/m^2 is obese; B. Central obesity: male waist ≥90cm, female waist ≥85cm; C. RBC: 3.8×10^{12}/L~5.1×10^{12}/L; D. HGB: 115~150g/L; E. Hypertension: systolic blood pressure ≥140mmHg or diastolic blood pressure ≥90mmHg; F. Dyslipidemia: TC ≥5.7mmol was hypercholesterolemia (high TG), TG ≥1.73mmol/L was hypertriglyceridemia (high TC), LDL-C ≥3.1mmol/L was high LDL-C, HDL-C <0.9mmol/L was low HDL-C; G. Glucose abnormality: 6.1mmol/L≤FPG<7.0mmol/L for impaired fasting blood glucose (IFG), FPG ≥7.0mmol/L for diabetes; H. Abnormal serum creatinine: 45–84 μmol/L; I. Hyperuricemia: male UA >420μmol/L, female UA >350μmol/L; J. Thyroid function test 5 items: T3 (1.3–3.1 nmol/L), T4 (66–181 nmol/L), TSH (0.27–4.20 μIU/mL), FT3 (3.1–6.8 pmol/L), FT4 (12–22 pmol/L); K. Alanine transferase: 4–50 IU/L.

Questionnaire Survey

1. Hospital Anxiety and Depression Scale (HADS): The scale was developed in 1983 and written by Zigmond and Snaith as a screening tool to measure anxiety and depressive symptoms.[24] The scale consists of 14 items, with 7 items dedicated to assessing depression and 7 items focused on anxiety. Each item is rated using a Likert scale of 4 (0–3), with higher scores indicating higher levels of anxiety or depression. The scores of both anxiety and depression subscales were divided into 0–7 for normal, 8–10 for mild anxiety and depression, 11–14 for moderate anxiety and depression, and 15–21 for severe anxiety and depression, of which any scale ≥8 points was considered as anxiety and depression. The internal consistency reliabilities of the anxiety and depression subscales were 0.83 and 0.81, respectively.[25]
2. Perceived Stress Scale (PSS): The questionnaire, compiled by American psychologist Dr. Cohen in 1983 and translated into Chinese by Yang Tingzhong in 2003, is used to measure individuals' perception of life pressure.[26] This study used a version of 14 items, including two dimensions of tension and loss of control, with five options for each item: never, rarely, sometimes, often, and always, corresponding to 0–4 points. The total score is 0–56 points. The higher the score, the greater the stress. Cronbach's α of the scale was 0.954.[27]

3. Insomnia Severity Index (ISI): This scale was designed by Bastien to assess the severity of an individual's subjective insomnia, with higher scores indicating greater insomnia.[28] The scale consists of 7 entries, each rated on a scale of 0–4, with a total score ranging from 0 to 28, and a score greater than 7 is considered to be the presence of insomnia, which is categorized as no significant insomnia (0–7), sub insomnia (8–14), clinical insomnia (15–21), and severe insomnia (>21). The Cronbach's α for this scale was 0.93.[29]

Statistical Methods

Data were analyzed using the SPSS 25.0 software. The normality was tested by applying the Kolmogorov–Smirnov test. Except the normal distribution of neutrophil percentage and lymphocyte percentage, which were described by $\bar{x} \pm s$, the rest of the data presented a skewed distribution, which was described by M (P25, P75), and the count data were expressed by percentage (%). Comparison between groups was performed by *t*-test, Mann–Whitney U rank sum test, or χ^2 test. Indicators that were statistically significant in the one-way analysis were included in the multifactorial logistic regression analysis and independent risk factors were identified. Based on the results of the multi-factor analysis, R Studio software was further used to construct a nomogram model for predicting the risk of thyroid nodules. The AUC was used to assess the model differentiation and draw a calibration curve to validate the accuracy of the model.

Results

Basic Physical and Mental Conditions of Healthcare Professionals

This study effectively investigated 738 people, the response rate was 92.3%. The average age of the 738 medical personnel was 30 (28, 34) years, of which 216 were male (29.3%) and 522 female (70.7%). Thyroid nodules were detected in 406 patients with a detection rate of 55.0%, of which 24.1% were male and 75.9% were female. Other laboratory indicators and psychological conditions are shown in Table 1.

Table 1 The Physical and Mental Conditions of Healthcare Professionals

Variables	Total	TN (-) group	TN (+) group	F/Z/χ^2	*P*
Age (years old)	30 (28, 34)	30 (28, 33)	31 (28, 35)	−1.800	0.072
Gender				11.474	<0.001
Male	216 (29.3%)	118 (54.6%)	98 (45.4%)		
Female	522 (70.7%)	214 (41.0%)	308 (59.0%)		
Height (cm)	162 (158, 167)	162 (159, 167)	162 (158, 167)	−0.568	0.570
Weight (kg)	59.5 (52.0, 66.5)	58.8 (52.0, 65.1)	60.5 (53.0, 67.0)	−2.176	0.030
BMI (Kg/m^2)	22.1 (20.0, 24.7)	21.7 (19.6, 24.4)	22.6 (20.4, 24.8)	−2.992	0.003
Systolic pressure (mmHg)	118 (110, 126)	118 (110, 125)	118 (110, 126)	−0.752	0.452
Diastolic pressure (mmHg)	75 (68, 82)	74 (68, 81)	75 (68, 82)	−1.073	0.283
Waistline (cm)	73.0 (68.0, 81.0)	72.0 (66.0, 79.0)	74.0 (69.0, 82.0)	−3.559	<0.001
Hipline (cm)	93.0 (89.0, 97.0)	93.0 (89.0, 96.0)	93.8 (89.0, 98.0)	−1.989	0.047
WBC (×10^9/L)	5.38 (4.57, 6.32)	5.41 (4.63, 6.30)	5.31 (4.51, 6.35)	−0.582	0.561
NEU (×10^9/L)	3.14 (2.52, 3.85)	3.16 (2.49, 3.85)	3.14 (2.57, 3.88)	−0.320	0.749
NEU% (%)	59.28±8.03	59.35±7.87	59.30±8.19	1.093	0.296
LYMPH (×10^9/L)	1.68 (1.43, 2.02)	1.70 (1.43, 2.00)	1.67 (1.43, 2.03)	−0.096	0.923
LYMPH% (%)	32.3±7.4	32.32±7.33	32.21±7.52	0.532	0.466
RBC (×10^{12}/L)	4.59 (4.31, 4.96)	4.55 (4.27, 4.90)	4.63 (4.33, 5.04)	−2.104	0.035
MCV (fL)	90.2 (87.5, 94.0)	90.2 (87.5, 94.0)	90.1 (86.9, 93.1)	−1.362	0.173
PLT (×10^9/L)	220 (189, 254)	219 (188, 253)	220 (191, 256)	−0.627	0.531
MPV (fL)	10.1 (9.4, 10.9)	10.1 (9.4, 10.9)	10.1 (9.4, 10.9)	−0.575	0.565
HGB (g/L)	139 (132, 150)	140 (131, 149)	139 (132, 151)	−0.571	0.568
TC (mmol/L)	4.71 (4.18, 5.36)	4.71 (4.16, 5.36)	4.70 (4.19, 5.36)	−0.419	0.675

(*Continued*)

Table 1 (Continued).

Variables	Total	TN (-) group	TN (+) group	F/Z/χ^2	*P*
TG (mmol/L)	0.86 (0.64, 1.26)	0.81 (0.60, 1.12)	0.92 (0.68, 1.35)	−3.870	<0.001
LDL-C (mmol/L)	2.86 (2.49, 3.31)	2.85 (2.47, 3.29)	2.87 (2.51, 3.31)	−0.762	0.446
HDL-C (mmol/L)	1.47 (1.26, 1.65)	1.48 (1.27, 1.68)	1.44 (1.25, 1.63)	−1.578	0.115
Alb (g/L)	45.1 (43.5, 46.5)	45.2 (43.5, 46.5)	44.9 (43.5, 46.5)	−0.283	0.777
UN (mmol/L)	4.46 (3.80, 5.30)	4.50 (3.81, 5.41)	4.41 (3.73, 5.21)	−0.961	0.337
UA (mmol/L)	317.2 (269.9, 386.2)	312.8 (265.4, 374.2)	318.8 (271.3, 391.9)	−1.270	0.204
FBG (mmol/L)	5.17 (4.92, 5.48)	5.16 (4.92, 5.41)	5.19 (4.93, 5.52)	−1. 617	0.106
Cr (mmol/L)	61.4 (54.4, 72.6)	60.7 (54.1, 72.4)	62.3 (54.6, 73.2)	−0.973	0.331
ALT (IU/L)	15.9 (11.7, 24.0)	14.9 (11.3, 21.8)	16.6 (11.9, 25.1)	−2.393	0.017
TSH (uIU/mL)	2.20 (1.42, 3.27)	2.02 (1.35, 3.03)	2.28 (1.50, 3.46)	−2.076	0.038
T3 (nmol/L)	2.10 (1.81, 2.39)	2.12 (1.82, 2.42)	2.07 (1.79, 2.38)	−1.149	0.250
FT3 (pmol/L)	5.05 (4.47, 5.66)	5.05 (4.51, 5.68)	5.05 (4.43, 5.65)	−0.653	0.514
FT4 (pmol/L)	17.31 (15.64, 19.40)	17.4 (15.5, 19.4)	17.2 (15.8, 19.4)	−0.434	0.664
T4 (nmol/L)	103.7 (89.2, 119.7)	102.8 (88.3, 119.3)	104.6 (90.0, 120.5)	−0.747	0.455
Fatty liver				13.531	<0.001
Yes	84 (11.4%)	22 (26.2%)	62 (73.8%)		
No	654 (88.6%)	310 (47.4%)	344 (52.6%)		
Anxiety	4 (2, 7)	3 (1, 6)	5 (3, 8)	−7.124	<0.001
Depression	4 (2, 7)	4 (2, 7)	5 (3, 7)	−3.772	<0.001
Perceived pressure	23 (17, 28)	21 (15, 28)	25 (19, 28)	−6.038	<0.001
Insomnia	6 (2, 11)	7 (3, 11)	6 (2, 11)	−0.993	0.321

Univariate Analysis of Thyroid Nodules

Based on the results of the inter-group comparison, literature review, and clinically significant indicators, risk factors were included for univariate analysis.[11–14,22] Mann–Whitney U rank sum test or χ^2 test was used. The results were shown in Table 2: among healthcare professionals, there were statistical differences in age, gender, hypercholesterolemia, abnormal ALT, fatty liver, abnormal TSH, anxiety, depression, and perceived pressure ($P < 0.05$).

Table 2 Univariate Analysis of Thyroid Nodules in Healthcare Professionals

Variables	TN (-) group	TN (+) group	Z/χ^2	*P*
Age (years old)			17.551	<0.001
≤30	187 (56.3%)	202 (49.8%)		
31~40	126 (38.0%)	146 (36.0%)		
41~50	17 (5.1%)	38 (9.4%)		
>50	2 (0.6%)	20 (4.9%)		
Gender			11.474	<0.001
Male	118 (35.5%)	98 (24.1%)		
Female	214 (64.5%)	308 (75.9%)		
BMI			7.506	0.057
Low body mass	38 (11.4%)	28 (6.9%)		
Normal body mass	197 (59.3%)	231 (56.9%)		
Overweight	81 (24.4%)	118 (29.1%)		
Obese	16 (4.8%)	29 (7.1%)		
Central obesity			3.592	0.058
No	306 (92.2%)	357 (87.9%)		
Yes	26 (7.8%)	49 (12.1%)		

(*Continued*)

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Table 2 (Continued).

Variables	TN (-) group	TN (+) group	Z/χ^2	*P*
Hypertension			0.023	0.880
No	302 (91.0%)	368 (90.6%)		
Yes	30 (9.0%)	38 (9.4%)		
Blood glucose			0.444	0.801
Normal	319 (96.1%)	386 (95.1%)		
Impaired glucose tolerance	8 (2.4%)	12 (3.0%)		
Diabetes	5 (1.5%)	8 (2.0%)		
High TC			1.656	0.198
No	287 (86.4%)	337 (83.0%)		
Yes	45 (13.6%)	69 (17.0%)		
High TG			6.946	0.008
No	300 (90.4%)	340 (83.7%)		
Yes	32 (9.6%)	66 (16.3%)		
High LDL-C			0.056	0.813
No	209 (63.0%)	259 (63.8%)		
Yes	123 (37.0%)	147 (36.2%)		
Low HDL-C			0.840	0.359
No	327 (98.5%)	396 (97.5%)		
Yes	5 (1.5%)	10 (2.5%)		
Hyperuricemia			0.489	0.484
No	248 (74.7%)	294 (72.4%)		
Yes	84 (25.3%)	112 (27.6%)		
Abnormal serum creatinine			2.024	0.155
No	291 (87.7%)	369 (90.9%)		
Yes	41 (12.3%)	37 (9.1%)		
ALT abnormality			4.849	0.028
No	320 (96.4%)	376 (92.6%)		
Yes	12 (3.6%)	30 (7.4%)		
Fatty liver			13.531	<0.001
No	310 (93.4%)	344 (84.7%)		
Yes	22 (6.6%)	62 (15.3%)		
NLR	1.90 (1.47, 2.30)	1.86 (1.47, 2.43)	−0.034	0.973
PLR	129.5 (105.8, 156.3)	128.0 (105.6, 158.0)	−0.056	0.955
SII ($\times 10^9$)	407.3 (302.0, 529.2)	408.3 (304.4, 559.4)	−0.344	0.731
RBC abnormality			2.682	0.101
No	270 (81.3%)	310 (76.4%)		
Yes	62 (18.7%)	96 (23.6%)		
TSH abnormality			4.581	0.032
No	307 (92.5%)	356 (87.7%)		
Yes	25 (7.5%)	50 (12.3%)		
Anxiety	3 (1, 6)	5 (3, 8)	−7.124	<0.001
Depression	4 (2, 7)	5 (3, 7)	−3.772	<0.001
Perceived pressure	21 (15, 28)	25 (19, 28)	−6.038	<0.001
Insomnia	7 (3, 11)	6 (2, 11)	−0.993	0.321

Multivariate Analysis of Thyroid Nodules

The presence of thyroid nodules was used as the dependent variable (yes=1, no=0), and variables that were included in the one-way analysis of statistical differences were used as independent variables. Multi-factor logistic regression analysis was carried out by stepwise forward method. Since there was no statistical difference between the 30–40-year-olds for the ≤30-year-olds suffering from thyroid nodules, the two groups were combined and then analyzed. As shown in

Table 3 Multivariate Analysis of Thyroid Nodules in Healthcare Professionals

Variables	*β*	SE	Walds	*P*	OR	95% CI
Constant	−1.993	0.294	46.055	<0.001	0.136	
Age (years old, ≤40 as reference)			11.774	0.003		
41~50	0.728	0.325	5.005	0.025	2.071	1.094~3.918
>50	2.084	0.779	7.150	0.007	8.034	1.744~37.000
Gender (male as reference)	0.628	0.179	12.259	<0.001	1.873	1.318~2.661
Anxiety	0.100	0.028	12.592	<0.001	1.105	1.046~1.168
Perceived pressure	0.044	0.013	11.506	<0.001	1.045	1.019~1.072
Fatty liver (no as reference)	0.999	0.288	12.068	<0.001	2.716	1.546~4.773
TSH abnormality (no as reference)	0.690	0.275	6.284	0.012	1.994	1.162~3.421
ALT abnormality (no as reference)	0.812	0.401	4.097	0.043	2.252	1.026~4.942

Notes: R^2=0.189, P<0.001.

Table 3: that compared with ≤40 years old, aged 41–50-year-old or >50-year-old were risk factors for thyroid nodules (OR=2.071/8.034); females (OR=1.873) were also risk factor for thyroid nodules relative to males; in addition, anxiety (OR=1.105), perceived stress (OR=1.045), fatty liver (OR=2.716), TSH abnormality (OR=1.944), and ALT abnormality (OR=2.252) were also risk factors.

Prediction Model of Physical and Mental Risk Factors for Thyroid Nodule

Based on the above logistic regression risk factors, a nomogram model for thyroid nodule risk prediction of healthcare professionals was constructed. The total score was calculated according to the sum of scores corresponding to various factors in the nomogram model. A vertical line with the score intersecting the points on the risk axis below is the risk value of thyroid nodules, as shown in Figure 1. The internal validation results indicated that the AUC of the area under

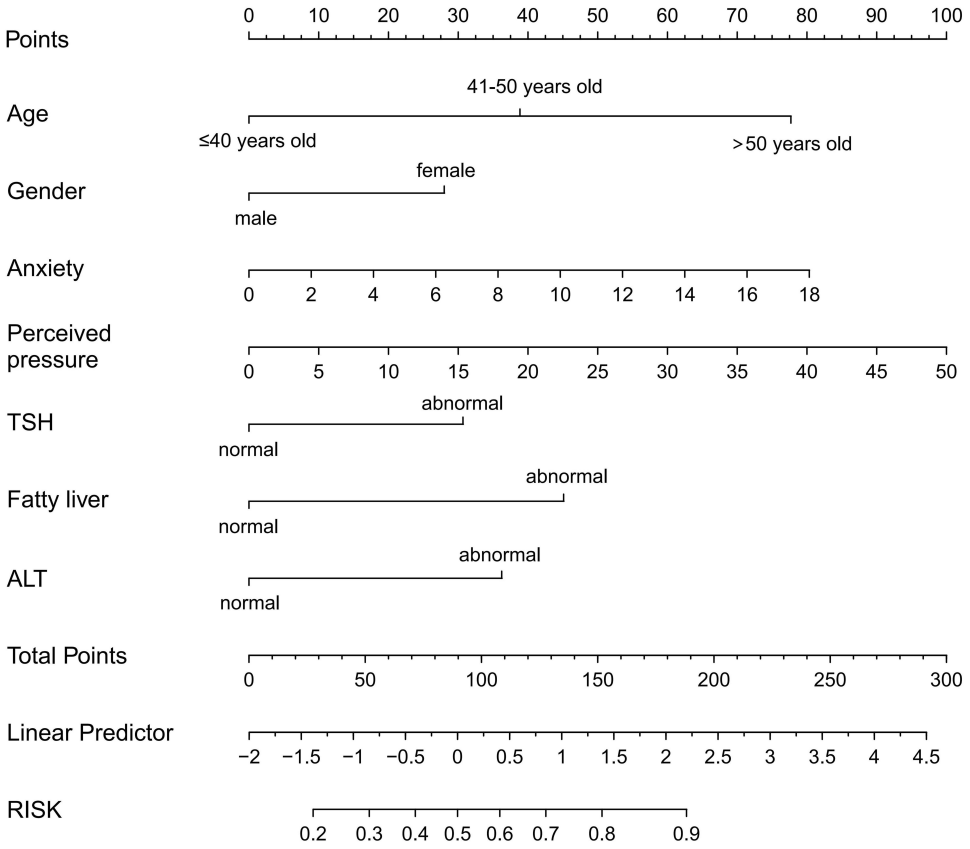

Figure 1 The nomogram model of thyroid nodule risk prediction.

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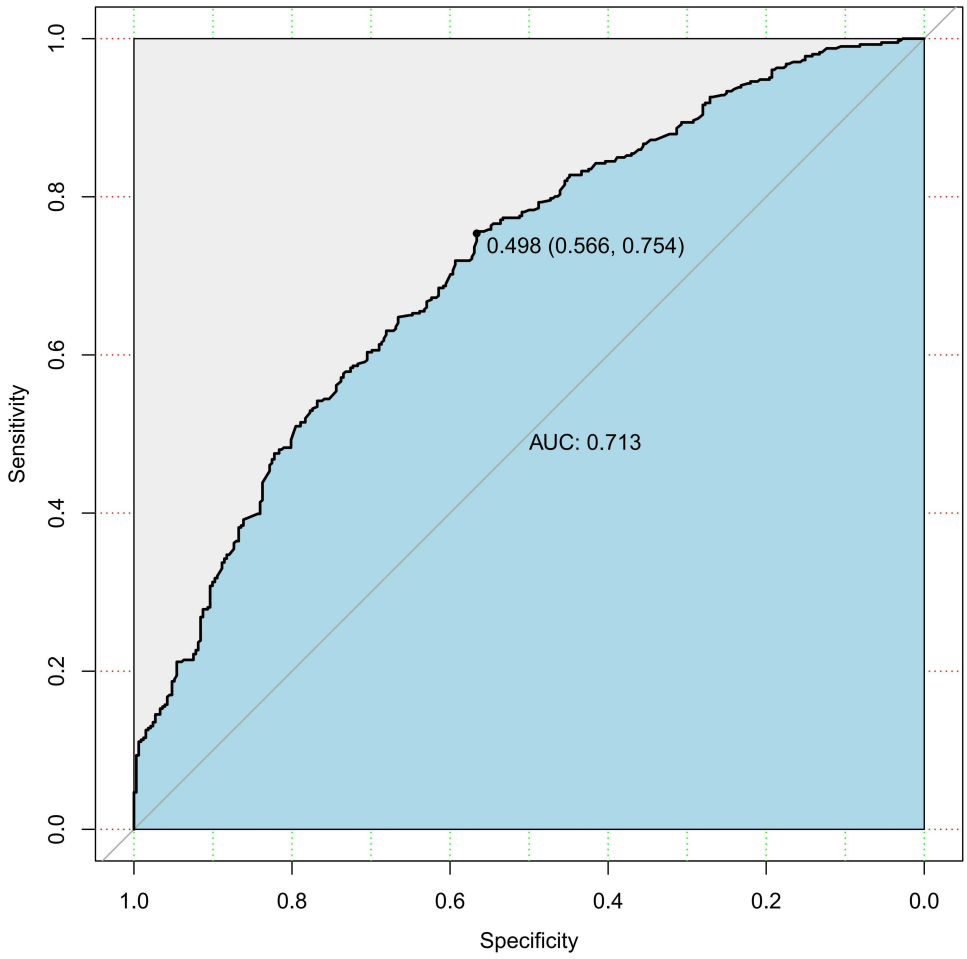

Figure 2 ROC analysis of thyroid nodule risk prediction.

the ROC curve was 0.713, suggesting that the model predicted a certain degree of differentiation with a sensitivity of about 80% (see Figure 2). As shown in Figure 3, the fitted calibration curve aligns more closely with the 45° diagonal line, suggesting a better agreement between the model's predicted risks and actual outcomes.

Discussion

The global increase in thyroid nodules (TNs) presents new public health concerns, with TNs becoming more prevalent in 2012–2022 compared to 2000–2011.[2] There are country differences in nodule detection globally, with South Africa and Denmark having high nodule detection rates of 79% and 54%, respectively, while the United States and Canada have similar and much lower rates of nodule diagnosis, at about 30%.[30] The prevalence of thyroid nodules in China is 10.12%–46.56%,[31] which brings a certain disease burden. The detection rate of thyroid nodules among the healthcare professionals in this study was high at 55.0%, higher than that of the general medical examination population (36.9%)[32] and slightly higher than the results of other studies in healthcare professionals (48.5%).[6] The reason for higher morbidity than the general physical examination population is, on the one hand, the stressful nature of the healthcare professionals' work and exposure to risk factor, on the other hand, compared with the general population, the annual physical examination of healthcare professionals may increase the detection rate to a certain extent. The higher detection rate than other healthcare professionals may be due to the fact that the other study was conducted in 2021, while the present study tested in 2023, because the prevalence of thyroid nodules is increasing every year.[4] Long-term mental stress, frequent overtime and overtime work, high pressure in the work society, and exposure to risk factors in the work

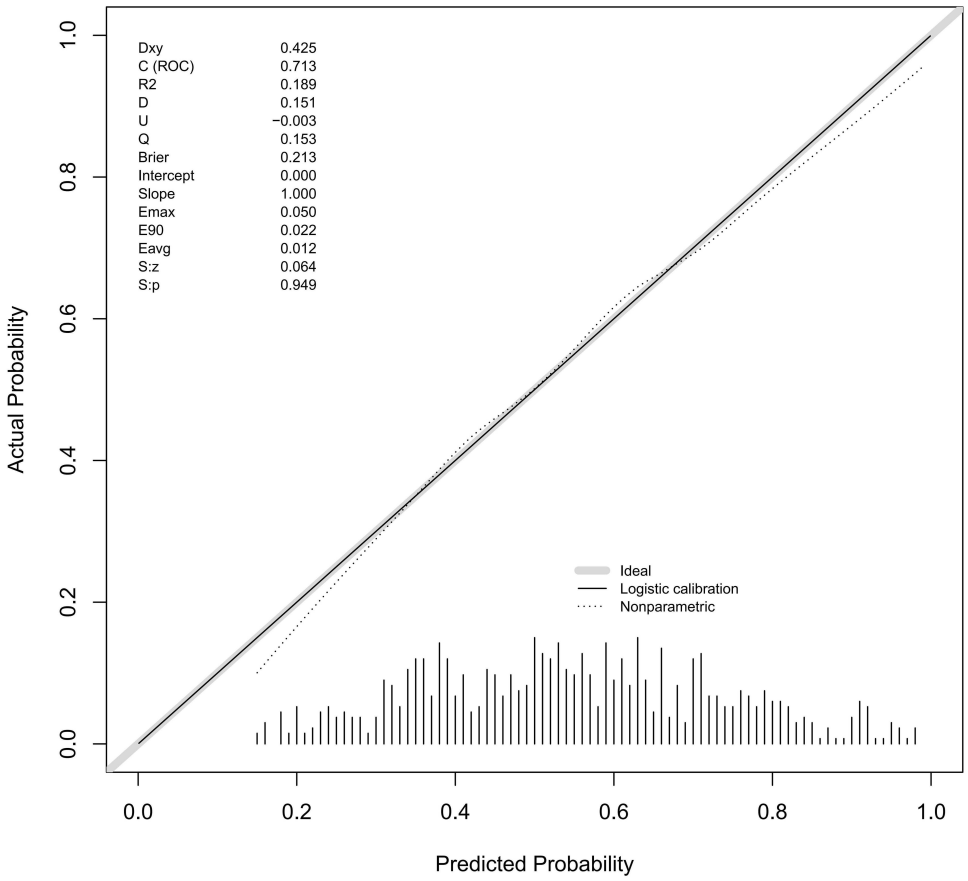

Figure 3 Calibration curve for internal verification of thyroid nodule risk prediction.

environment of medical workers puts the organism in a state of stress for a long period of time and limits the regulation of the immune system, which can lead to endocrine disorders, resulting in the occurrence of diseases.[33,34] As a result, the condition of thyroid nodules in healthcare professionals should be looked into, focusing on the analysis of the factors due to the nature of their profession and psycho-social stress.

This study presented that age and female were well-known independent risk factors for thyroid nodules, which was highly consistent with other studies.[8,32,35] In this study, multi-factor analysis showed that the older the age, the greater the incidence of thyroid nodules, especially the healthcare professionals over 50 years old. The function of human organs begins to decline with age, reactive oxygen species will precipitate, thyroid tissue changes, atrophy occurs, adenocyte fibrosis occurs, and nodules gradually form.[36] In addition, environmental hazards to the human body over time and increasingly accumulated, coupled with a decline in the body's immune system, the thyroid cells stressed and damaged, resulting in fibrous connective tissue proliferation and inflammatory infiltration, and ultimately the appearance of nodules.[37] This also suggests the need for increased thyroid ultrasound screening for healthcare professionals over 50 years of age. Same as previous studies,[8,38] logistic regression results showed that female healthcare professionals were 1.873 times more likely to develop thyroid nodules than men. The higher susceptibility of women to thyroid nodules may be attributed to estrogen exposure, progesterone, and pregnancy.[39] Estrogen induces proliferation of thyroid follicular cells via classical genomic and non-genomic pathways, thereby promoting nodule growth.[13,40] It had also been shown that 17βestradiol can stimulate normal thyroid cells via the estrogen receptor.[41] In summary, the focus of thyroid nodule screening for healthcare professionals is on the female population over 50 years of age.

The logistic regression analysis, nomogram and ROC curves of this study also have proved that TSH abnormality, ALT abnormality, and fatty liver were risk factors for the development of thyroid nodules, which was consistent with

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other studies.[10,13,42] In this study, TSH abnormalities (TSH may be elevated or decreased) in the thyroid nodule group were significantly different from those in the non-nodule group. A study supported that TSH levels are significantly lower in male patients with thyroid nodules,[43] and elevated TSH levels had also been shown to be an influential factor in thyroid nodules.[10] TSH plays a key role in the formation of thyroid nodules. It not only promotes the synthesis of nucleic acids and proteins in thyroid follicular epithelial cells, stimulates the proliferation of thyroid cells, and increases the size of the gland but also acts as an influencing factor for the survival of thyroid cells, and protects them from apoptosis.[43] However, the use of TSH as an initial screening strategy for thyroid nodules needs to be approached with caution from an economic point of view.[44] ALT is one of the most commonly used and sensitive indicators of liver function and can influence the development of thyroid nodules.[42] Abnormal ALT suggests abnormal liver function, and some studies have explored the correlation between head and neck tumors and viral hepatitis,[45] which provides support for the results of this study, but the mechanism still needs to be further explored. The emergence of fatty liver as a risk factor for thyroid nodules may be due to the mediating role of insulin resistance. One study found that insulin resistance (IR) can lead to the accumulation of excess fatty acids in the liver and the formation of fatty liver.[46] Also, insulin resistance can cause thyroid cells to proliferate and promote nodule formation.[47] So IR may be moderated in TN by fatty liver. This also alerts us to be on the lookout for thyroid nodules in TSH abnormalities, ALT abnormalities, and fatty liver in healthcare professionals.

This study also found that anxiety and perceived stress were independent risk factors for thyroid nodules. For the first time, psychological factors and physiological indicators were integrated to build a thyroid nodule prediction model, and the model was verified, which was the highlight of this study. Other studies have also demonstrated a correlation between thyroid nodules and negative emotions (anxiety, depression, etc.).[48] Psychological stress is also one of the frequently cited non-genetic risk factors for thyroid disease.[16,20] Experiencing negative emotions over a long period of time can lead to a buildup of chronic stress, which is a nonspecific systemic response that occurs. Psychological stress may lead to dysregulation of the hypothalamic–pituitary–adrenal (HPA) and hypothalamic-pituitary-thyroid (HPT) axes, which may result in thyroid hormone imbalance, thus affecting thyroid function, but the mechanism of which is not clear yet.[49,50] Psychological status is a long-term dynamic process that is influenced by when and where it is measured. Although the current study showed that psychological status is a predictive risk factor for thyroid nodules, prospective studies are needed to dynamically monitor the relationship between psychological status and the occurrence of thyroid nodules to repeatedly validate and explore the mechanisms of their occurrence.

In this study, we applied the nomogram model to sub-clinical status thyroid nodules, which can be used to personalize the prediction of subjects and achieve the first step of primary prevention of chronic disease risk - assessment, which comprehensively determined the contribution of different types of factors to the risk of developing thyroid nodules, and thus provided a more comprehensive and accurate prediction.[51] In addition, the nomogram model further quantified and visualized the risk factors of the logistic regression results precisely, connecting the seven predictor variables of age, gender, anxiety, stress, TSH, fatty liver, and ALT with the predicted results through simple lines, which can be used to find the corresponding points on the axes according to the patient's actual situation, and then quickly obtain a comprehensive risk prediction value by connecting lines or by projection. This intuitive presentation allowed physicians or researchers to read the predictions directly without complex calculations, while the data could all be collected during the subject's physical examination, especially through simple measures of anxiety and other psychological questionnaires, which were simple to administer, zero-cost, and low-risk, and which can easily assess and predict the occurrence of thyroid nodules. The internal validation of this model with an AUC of 0.713 for the ROC curve and a calibration curve close to the 45°diagonal indicated that the consistency and differentiation between its predicted and actual risks are acceptable and that it has a good predictive performance for the occurrence of thyroid nodules. The nomogram graphs still had reference value, which was helpful to visually identify the healthcare professionals at high risk of thyroid nodules, to control the risk factors and propose corresponding preventive measures. In the practical implications of the model, doctors in health management centers and primary care Settings can use Nomogram to quickly screen clients for the risk of TNs and give professional advice according to the degree of risk. Furthermore, the model can be applied to the physical examination report to facilitate the client to have a more intuitive feeling of the quantified risk information.

This study still has the following shortcomings. Firstly, the questionnaire reflected the mental status of the participants at the time of the study, but the development of thyroid nodules may be affected by long-term stress. A long-term cohort study should be conducted in the future to select different time points for measurement. Secondly, this study was conducted in one hospital in China, and the cohort was predominantly young, with 75% of participants below 34 years old, which may limit its generalization to other regions or populations. Finally, this study only established a preliminary model based on physiological and psychological factors, and in the future, lifestyle, environment, genetics and other factors can be included to improve the prediction. Healthcare professionals can be classified by workplace, which will help to understand the underlying psychological factors or occupational exposures that affect participants.

Conclusion

This study focused on the combined effects of psychological and physiological factors on the development of thyroid nodules (TNs) in healthcare professionals, and found that the detection rate of thyroid nodules in them is at a high level. Given the high prevalence of TNs and the possibility of their transformation into malignant tumors, it is crucial to understand the factors that contribute to their development. At the same time, it is of great significance to explore the factors associated with TNs to guide early prevention in clinical practice. Attention should be paid to healthcare professionals who are at high risk of developing TNs, such as the elderly, females, and those with anxiety, stress, TSH abnormal, fatty liver, and ALT abnormal, to manage the risk factors at an early stage, and to provide a solid foundation for early screening and prevention of the development of thyroid nodules.

Data Sharing Statement

The dataset for this study was provided by the corresponding author upon reasonable request.

Ethics Statement

All processes of this study followed the Declaration of Helsinki and were approved by the Ethics Committee of the First Affiliated Hospital of Army Medical University ((B)KY2023088).

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no competing interests in this work.

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