



Research of correlation between personality traits and hormones with the nature of pulmonary nodules

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ABSTRACT

Background: Rising rates of lung cancer screening have contributed to an increase in pulmonary nodule diagnosis rates. Studies have shown that psychosocial factors and hormones have an impact on the development of the oncological diseases. Therefore, we conducted this study to explore the potential relationship between pulmonary nodules pathology and patient personality traits and hormone levels.

Methods: This study enrolled 245 individuals who had first been diagnosed with pulmonary nodules in Tangdu Hospital and admitted for surgery. The personality profile of these patients was analyzed on admission using the C-Type Behavioral Scale and hormone levels were measured in preoperative serum samples. Associations between nodule pathology, personality scores, and hormone levels, were then assessed through Statistical methods analysis.

Results: Behavioral scale analyses revealed significant differences four items, including depression, anger outward, optimism, and social support ($P < 0.05$). Specifically, patients with higher depression scores were more likely to harbor malignant pulmonary nodules, as were patients with lower levels of anger outward, social support, and optimism. Univariate analyses indicated that nodule pathology was associated with significant differences in nodule imaging density, CT value, testosterone levels, and T₄ levels ($P < 0.05$), and logistic regression analyses revealed pulmonary nodule imaging density and T₄ levels to be significant differences of nodule pathology.

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Conclusion: The results showed a significant association between nodules pathology and the personality characteristics of the patients (depression, anger outward, optimism, social support), the patients' T₄ levels and the imaging density of the nodules.

1. Introduction

Cancer is one of the most prominent causes of global mortality, lowering the life expectancy of individuals throughout the world [1]. Lung cancer is a very common type of cancer and the deadliest such malignancy [2], with 10 million lung cancer deaths globally in 2020 accounting for 18 % of all cancer-associated death, with new lung cancer diagnoses (11.4 %) being only second to breast cancer with respect to prevalence [3]. While there have been many recent advances in diagnosing and treating lung cancer, many patients continue to experience poor outcomes in part due to the fact that many patients are only diagnosed when tumors are already very advanced and have metastasized [4]. The National Lung Screening Trial (NLST) revealed that annual low-dose chest computed tomography (CT) screen efforts can decrease rates of lung cancer-associated mortality by 20 % relative to annual chest X-rays [5], and the European Lung Cancer Screening Trial further emphasized the benefits of this low-dose CT screening strategy [6]. The rise of lung cancer screening has led to a concomitant increase in the diagnosis of pulmonary nodules, which are defined as small (<3cm) focal areas of distinctive radiographic density surrounded by lung tissue [7]. These nodules are classified as being either solid or subsolid, with subsolid nodules being additionally separated into ground-glass nodules without any solid component and part-solid (both ground-glass and solid components), based on the CT appearance [8]. Given that the majority of nodules identified upon screening are benign in nature, it is vital that nodules likely to be malignant be identified as reliably as possible in order to maximize the benefits of such screening programs [9]. However, analyzing potentially malignant nodules remains a pressing clinical problem. Ensuring that patients receive timely and professional advice can positively impact tension and anxiety in patients while making them more likely to undergo regular follow-up monitoring.

Analyses of newly identified pulmonary nodules necessitate a comprehensive review of prior imaging findings to determine whether the identified nodules have undergone any changes in size or other characteristics [7,10]. A variety of CT radiomics features are taken into consideration when evaluating these nodules including their shape, margins, density, internal characteristics (calcification, fat attenuation/cavitation), and other complex characteristics (pleural retraction, air bronchogram, bubble-like lucencies, cystic airspace, vascular convergence) [11]. The identification of additional risk factors linked to pulmonary nodule characteristics can thus aid in the diagnosis and follow-up monitoring of affected patients.

Some research suggests that the incidence of cancer can be influenced by psychosocial factors, including depression, personality traits, or major life events [12]. While many studies have explored this possibility, the results have been inconsistent, and detected relationships between personality and cancer, have either not been significant [13–16] or have been only significant to a limited degree, suggesting this relationship to be somewhat mild [17–19]. In addition, many studies have outlined the important role that hormones can play in disease, particularly hormone-sensitive organs. Estrogen is a known lung cancer-related risk factor [20], and it can promote the development of the tumor microenvironment [21]. In vitro work has revealed that both non-small cell and small cell lung cancer tissues, as well as normal lung tissue, express androgen receptors [22–24]. The thyroid hormones T₃ and T₄ can additionally promote proliferating cell nuclear antigen (PCNA) accumulation within NSCLC cells in a dose-dependent fashion at T₃ concentrations above the normal range or at T₄ doses within the normal physiological range, thus promoting the proliferation of tumor cells [25,26]. We know that malignant pulmonary nodules are lung cancer, and benign nodules may be lung inflammation, hamartomas, granulomas, lymph nodes in the lungs and so on [27]. Therefore, given the existing findings, we hypothesize that there is a correlation between personality traits and hormones that influence the nature of small lung nodules.

Currently, there have not been any studies exploring the relationship between personality characteristics, hormones, and pulmonary nodules findings in patient populations. This research was thus designed to explore the correlative associations between the pathology for pulmonary nodules and both personality characteristics and serum hormone levels in a prospective manner, and ultimately test our hypothesis.

2. Materials and methods

2.1. Research objects

The medical ethics committee of Tangdu Hospital approved this research, which enrolled patients diagnosed with pulmonary nodules at this hospital between January 2021 and June 2022 who were admitted for surgery. Eligible patients were: (1) individuals diagnosed for the first time with one or more small pulmonary nodules that were ≤3 cm in diameter as measured by computed tomography (CT) who were admitted for surgery and whose pathological results were available; (2) postmenopausal women; (3) individuals that agreed to participate in this research by completing a questionnaire and providing serum samples for hormone level analyses after admission. Patients were excluded if: (1) they exhibited metastases or tumors in other organs; (2) they suffered from severe heart, lung, liver, or kidney diseases; (3) they had been diagnosed with mental illnesses or were unable to complete the survey; (4) they exhibited severe limitations to intelligence or cognition; or (5) they refused to complete the questionnaire and/or to undergo analyses of serum hormone levels.

2.2. Estimation of sample size

Most studies are based on the rules of thumb to determine sample size, so the calculation of sample size in this study uses a rule of thumb to determine sample size, i.e., 15 times the number of independent variables according to the minimum sample size requirement. In this study, the sample size is calculated according to the number of observed variables, and it was that 16 variables would eventually be included in the analysis, and in order to ensure the reliability of the end results, the sample size estimate should be no less than 15 times the rule of thumb, and the sample size should be at least 240 (that is, 16variables*15 times).

2.3. Personality trait analyses

The personality traits of pulmonary nodule patients were evaluated with Temoshok's "cancer-prone personality" [28], i.e. "C-Type Behavioral". The C-Type Behavioral Scale and related scoring methods were based on medical psychology of Shandong University Version of the department. The reliability and validity of this scale have been demonstrated in prior studies, and it consists of 9 items focused on depression, anxiety, anger, anger outward, anger inward, rationality, control, optimistic and social support. Scale scoring details see [Table 1](#).

2.4. Serum hormone levels

Following hospital admission, 5 mL samples of venous blood were obtained from each patient, centrifuged (20 min, 2500 rpm, 5 °C), and the serum fraction was stored at -80 °C. Levels of androgens (testosterone), estrogens (estradiol, estriol), and thyroid hormones (T₃, T₄) were measured with commercial ELISA kits (Jiangsu Meimian industrial Co., Ltd, China).

2.5. Statistical analysis

Continuous variables are given as means ± standard deviations (SD). For categorical variables males and females were respectively scored as 1 and 0. With respect to imaging density, pure ground-glass nodules, mixed ground-glass nodules, and solid nodules were respectively scored with values 1, 2, and 3. Smoker and non-smoker status were respectively scored with values of 1 and 0. A history of tumors and no history of tumors were respectively scored as 1 and 0. Normally distributed continuous data were analyzed with t-tests, whereas nonparametric tests were otherwise used. Chi-square tests were used for categorical variables. Multivariate analyses were performed using a logistic regression approach. All analyses were performed using SPSS 26.0.

3. Results

In total, 245 patients participated in this research, all of whom completed personality questionnaires and serum samples for hormone analyses. Postoperative pathological results from these patients revealed 28 cases of benign nodules and 217 cases of malignant nodules. For further details regarding participant characteristics, see [Table 2](#).

Personality questionnaire results are shown in [Table 3](#), [4](#). Scores for anxiety, depression, anger, anger outward, optimism, and

Table 1
Scale scoring criteria and reference values.

Items	Scoring questions	Normal person		Cancer patients
		Man	Woman	
Anxiety	1R, 4, 10R, 13, 24, 28R, 32R, 39, 46, 50R, 54, 58, 62R, 67R, 71R, 77R, 81, 86, 90R, 94	40.06 ± 5.89	40.35 ± 5.71	Higher
Depression	2, 7R, 11, 15, 20R, 22R, 25, 30, 36, 40, 43R, 51R, 55, 61R, 70, 75R, 82, 87R, 92, 96R	36.76 ± 4.90	38.06 ± 5.14	Higher
Anger	9, 19, 33, 44, 52, 64, 74, 85, 89, 95	22.40 ± 5.97	22.76 ± 11.46	Higher
Anger inward	3, 8, 27, 45, 69, 72	13.48 ± 2.09	13.88 ± 2.52	Higher
Anger outward	14, 17, 31, 34, 49, 56	17.48 ± 3.18	17.29 ± 3.60	Lower
Rational	6, 12, 18, 29, 35, 41, 47R, 53, 59, 63, 68, 73, 79, 84, 91R	40.26 ± 5.63	40.04 ± 4.58	Higher
Controlling	21, 23, 38, 42, 60, 65	17.12 ± 4.51	17.06 ± 5.42	Higher
Optimistic	5, 16R, 26, 37, 48, 57, 66, 78	24.12 ± 3.46	23.77 ± 3.33	Lower
Social support	76, 80, 83, 88, 93, 97	18.52 ± 2.57	18.65 ± 4.62	Lower

Note: Numbers in the table refer to the sequence number of the questions in the scale, and 'R' is the reverse scoring of the question. Each question was scored on a 4-point scale (none 1, occasionally 2, often 3, always 4).

social support in male patients diagnosed with malignant nodules were significantly different from the scale norm, while scores for depression, anger, anger outward, optimism, and social support in postmenopausal female patients with malignant nodules differed significantly from the scale norm. Based on the scale evaluation criteria anger outward, optimism, and social support scores should be lower than the norm in cancer patients and other items in cancer patients should be higher than the norm, so the significant anxiety and anger observed in male patients as well as the significant anger results in postmenopausal female patients were excluded. Depression, anger outward, optimism, and social support thus differed significantly in patients diagnosed with malignant pulmonary nodules, suggesting that these characteristics are associated with tumor development and progressions, potentially as a consequence of the long-term manifestation of the suppression of anger, negative attitudes, insufficient support, and lack of recognition from surrounding individuals. No linear or non-linear relationships were detected between any of these personality trait scores and hormone levels.

Univariate analyses were next conducted based on patient details and hormone test results, revealing that there were significant differences between patients with benign and malignant lesions with respect to pulmonary nodule imaging density, CT values, T₄ levels ($P < 0.05$; Table 5). This suggested that these three variables were risk factors associated with malignant pulmonary nodules. Subsequent multivariate analysis only showed that imaging density and T₄ levels was significant independent predictors of malignant pulmonary nodules (Table 6). Specifically, each unit increase in T₄ levels was associated with a 1.5 % rise in the odds of patient's pulmonary nodules being malignant. Relative to pure ground glass nodules, the odds of partially-solid nodules being malignant rose by 38 %, and these odds rose by 10.9 % for solid nodules.

4. Discussion

The results from this study suggest that the personality traits and T₄ levels observed in patient are significantly associated with malignant pulmonary nodules. Specifically, patients with malignant lesions were likely to exhibit higher depression scores as well as lower anger outward, optimism, and social support scores. Given the increasingly common nature of pulmonary nodule screening, most patients have at least some familiarity with pulmonary nodule. Even so, the diagnosis of a pulmonary nodule may lead to the exacerbation of feelings of depression and anxiety, particularly in patients scheduled to undergo surgical interventions and individuals with a history of long-term depression and limited social support. These factors, in turn, may adversely impact efforts to treat these patients and may contribute to the development of malignant nodules. Factors such as optimism, social support, and other positive characteristics are predictive of longer survival in individuals with malignant diseases [29,30]. It is thus important that clinicians provide patients with detailed information while they undergo clinical follow-up so that they are better able to maintain a positive attitude conducive to their ability better face their disease from a psychosocial perspective.

The rapid pace of modern society leaves many individuals facing high levels of stress, which has been linked to the suppression of immune function in both healthy individuals and in patients already dealing with psychological stress associated with a cancer diagnosis [31]. Such stress can contribute to persistent activation of the hypothalamic-pituitary-adrenal (HPA), and the resultant impairment of normal immune surveillance mechanisms may contribute to the onset and/or progression of certain forms of cancer [32]. Both environmental and psychosocial stressors can activate a cascade of information processes in the peripheral and central nervous systems, in turn triggering the fight-or-flight stress responses mediated by the autonomic nervous system (ANS) or defeat/-withdrawal responses governed via the HPA [33]. Thyroid hormone secretion is also regulated through this HPA axis. These prior findings align with the present results. While estrogen and androgens have previously been reported to impact lung cancer cells, no significant relationship between these hormones and pulmonary nodule pathological status was observed in this study. This may be a

Table 2
Patient characteristics.

Items	Sex(%)		t/ χ^2	P
	Male	Postmenopausal female		
N	128	117		
Age	60.2 ± 10.6	61.2 ± 7.1	-0.87	0.388
Smoking				
Yes	74(57.8)	1(0.9)	93.36	0.000*
No	54(42.2)	116(99.1)		
Tumour history				
Yes	15(11.7)	12(10.3)	0.13	0.715
No	113(88.3)	105(89.7)		
Nodule diameter	1.6 ± 0.6	1.4 ± 0.5	2.74	0.007*
CT value	-266.0 ± 258.9	-307.3 ± 242.1	1.29	0.199
Imaging density				
Ground-glass	22(17.2)	20(17.1)	4.17	0.125
Part-solid	62(48.4)	70(59.8)		
Solid	44(34.4)	27(23.1)		
Pathology				
Malignant	109(85.2)	108(92.3)	3.09	0.079
Benign	19(14.8)	9(7.7)		

Note: Tumor history includes the tumor history of both the patient and their immediate family members (parents). * indicates significant between-group differences, $P < 0.05$.

Table 3

Comparison of normative scores on type C behavioral scale in men with lung cancer ($\bar{X} \pm SD$).

Items	Lung cancer group	normal reference values	t	P
N	119			
Anxiety	37.70 ± 7.76	40.06 ± 5.89	-3.177	0.002
Depression	39.69 ± 6.80	36.76 ± 4.90	4.496	0.000
Anger	18.23 ± 5.09	22.40 ± 5.97	-8.550	0.000
Anger inward	13.80 ± 2.59	13.48 ± 2.09	1.283	0.202
Anger outward	13.00 ± 3.54	17.48 ± 3.18	-13.210	0.000
Rational	39.43 ± 5.87	40.26 ± 5.63	-1.475	0.143
Controlling	17.12 ± 3.71	17.12 ± 4.51	-0.002	0.998
Optimistic	22.83 ± 3.85	24.12 ± 3.46	-3.507	0.001
Social support	16.01 ± 3.26	18.52 ± 2.57	-8.030	0.00

NOTE: * indicates significant between-group differences, $P < 0.05$.

Table 4

Comparison of normative scores on type C behavioral scale in women with lung cancer ($\bar{X} \pm SD$).

Items	Lung cancer group	normal reference values	t	P
N	108			
Anxiety	39.52 ± 9.27	40.35 ± 5.71	-0.932	0.353
Depression	41.66 ± 8.09	38.06 ± 5.14	4.621	0.000*
Anger	19.05 ± 5.57	22.76 ± 11.46	-6.926	0.000*
Anger inward	13.78 ± 2.64	13.88 ± 2.52	-0.402	0.688
Anger outward	14.05 ± 3.31	17.29 ± 3.60	-10.182	0.000*
Rational	39.48 ± 6.42	40.04 ± 4.58	-0.904	0.368
Controlling	16.66 ± 4.05	17.06 ± 5.42	-1.034	0.303
Optimistic	22.49 ± 4.21	23.77 ± 3.33	-3.159	0.002*
Social support	16.80 ± 3.14	18.65 ± 4.62	-6.139	0.000*

NOTE: * indicates significant between-group differences, $P < 0.05$.

Table 5

Univariate analysis of risk factors associated with pulmonary nodule pathology.

Group	Malignant	Benign	t/χ^2	P
N	217	28		
Age	59.11 ± 9.68	60.89 ± 9.07	-0.971	0.332
Sex				
Male	109	19	3.088	0.079
Female	108	9		
Diameter	1.46 ± 0.57	1.50 ± 0.66	-0.354	0.723
Imaging density				
Ground glass	40	2	28.302	0.000*
Part-solid	127	5		
solid	50	21		
CT value	-303.02 ± 16.95	-151.89 ± 42.78	-3.044	0.003*
Smoking				
YES	62	12	2.401	0.121
NO	155	16		
Tumor history				
YES	25	2	0.485	0.749
NO	192	26		
Testosterone	Male 4.65 ± 2.10	5.58 ± 1.44	-1.487	0.067
	Female 4.63 ± 1.72	4.74 ± 1.09	-0.177	0.860
Estradiol	Male 347.11 ± 93.31	315.71 ± 103.94	1.330	0.186
	Female 344.76 ± 110.62	325.55 ± 108.05	0.501	0.617
Estriol	Male 596.45 ± 137.41	549.74 ± 124.71	1.385	0.168
	Female 558.06 ± 153.15	626.87 ± 191.41	-1.270	0.206
T ₃	4.59 ± 1.35	4.83 ± 1.21	-0.882	0.379
T ₄	184.89 ± 44.43	160.56 ± 52.33	2.671	0.008*

NOTE: * indicates significant between-group differences, $P < 0.05$.

The female in the table represent postmenopausal woman in the study subjects.

consequence of the effects of these hormones on lung disease at the cellular level, or the result of differences in the concentrations of these hormones among organs [23,34]. Furthermore, under physiological conditions, the changes in these hormones in the lungs are largely negligible, therefore the chances of them influencing the pathogenesis of lung cancer may be limited. Although the chances of

Table 6
Multivariate logistic regression analysis of risk factors associated with pulmonary nodule pathology.

	OR(95%CI)	95%CI	P
T ₄	1.015	1.005–1.025	<0.01
Imaging density			
Ground glass	1	1	
Part-solid	1.38	0.253–7.523	<0.01
solid	0.109	0.023–0.506	<0.01

NOTE: * indicates significant between-group differences, $P < 0.05$.

them influencing lung cancer pathogenesis may be limited, further research on this topic is warranted. In the current study, no correlation was observed between patients' personality traits and hormone levels, which is somewhat at odds with our hypothesis that there is a correlation between hormones and personality traits, possibly as a result of the complex physiological regulatory mechanisms that control these relationships.

In summary, patient personality traits and T₄ levels were herein found to be associated with the malignant pulmonary nodules, indicating that psychological and behavioral factors, including personality and hormonal status, should be taken into consideration when assessing individuals with potentially malignant pulmonary nodules in an effort to continue improving efforts to distinguish between malignant and benign nodules.

Ethnical statement

The research was approved by IEC of Institution for National Drug Clinical Trials, Tangdu Hospital, Fourth Military Medical University (NO. 202204-01). All research subjects signed an informed consent form.

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Data availability statement

Data will be made available on request.

CRedit authorship contribution statement

Yonggang Teng: Writing – original draft, Project administration, Investigation, Formal analysis, Conceptualization. **Chaoli Wang:** Investigation, Conceptualization. **Yabo Zhao:** Investigation. **Yongyu Teng:** Investigation. **Chaoren Yan:** Data curation. **Yongkai Lu:** Formal analysis. **Shijun Duan:** Resources. **Jian Wang:** Writing – review & editing, Visualization, Funding acquisition. **Xiaofei Li:** Writing – review & editing, Visualization, Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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