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Low triiodothyronine syndrome and depression: a cross-sectional study in the elderly based on comprehensive geriatric assessment

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Abstract

Introduction: Thyroid diseases such as low triiodothyronine syndrome (LT3S) are more common in the elderly population. Comprehensive geriatric assessment (CGA) has been proposed as a supplementary tool for evaluating medical, functional, psychological, and frailty status and various geriatric syndromes. This study aimed to evaluate the impact of thyroid diseases on overall health status using a novel CGA strategy.

Material and methods: 477 patients were enrolled between January 2019 and December 2022. A structured CGA was conducted by a multidisciplinary team to identify older high-risk patients. Multivariate regression was performed to assess independent factors associated with thyroid status and CGA.

Results: The prevalence of abnormal thyroid hormone levels in the elderly was 34.2%. LT3S and anti-thyroglobulin antibody (anti-TgAb)-positivity or anti-thyroid peroxidase antibody (anti-TPOAb)-positivity were the main manifestations of thyroid diseases in elderly patients. The patients with LT3S had a higher prevalence of diabetes ($p = 0.023$), were older ($p = 0.000$), more often female ($p = 0.014$), with higher C-reactive protein ($p = 0.001$), and with lower body mass index (BMI) ($p = 0.002$), albumin (Alb) ($p = 0.000$), and haemoglobin (Hb) ($p = 0.000$) than patients with normal thyroid function. The CGA results showed higher rates of malnutrition and depression in patients with LT3S. Further multivariate logistic regression analysis showed that Hb [odds ratio (OR): 0.975; 95% confidence interval (CI): 0.959–0.990; $p = 0.002$] and LT3S (OR: 2.213; 95% CI: 1.048–4.672; $p = 0.037$) were independently associated with depression. Female (OR: 0.393; 95% CI: 0.160–0.968; $p = 0.042$), Alb (OR: 0.892; 95% CI: 0.811–0.981; $p = 0.018$), Hb (OR, 0.964; 95% CI: 0.939–0.989; $p = 0.006$), and LT3S (OR: 3.749; 95% CI: 1.474–9.536; $p = 0.006$) were independently associated with malnutrition.

Conclusions: LT3S was closely related to depression and malnutrition. Physicians should be more concerned about elderly patients with LT3S for their physical and mental status. Regular thyroid function checks might help to detect depression earlier. **(Endokrynol Pol 2024; 75 (1): 42–50)**

Key words: *LT3S; GCA; depression; malnutrition*

Introduction

Comprehensive geriatric assessment (CGA) is a holistic evaluation of the physiological, psychological, and frailty status and social functioning [1]. Its objective is to identify health problems that might impair an older adult's overall well-being and independence and to develop a care plan tailored to their specific needs. Thyroid function is an essential part of the overall physiological functioning, and changes in thyroid function can affect the ability of older adults to function independently. Thyroid dysfunction, particularly hypothyroidism, can lead to symptoms of fatigue, weakness, depression, and cognitive impairment that overlap with the symptoms of aging and other comorbidities. Thyroid disease is common among the elderly, with an overall prevalence of 50.96% in China [2]. However, physiological changes in the hypothalamus-pituitary-thyroid axis, symptoms of thyroid disease overlapping with aging manifestations, the presence of concomitant diseases or geriatric syndromes, and multiple organ dysfunction increase the complexity of diagnosis and treatment of thyroid disease in the elderly.

Considering the multisystemic effects of thyroid hormones in the elderly, this study aimed to evaluate the impact of thyroid diseases on their overall health status using a novel CGA strategy. We hope to achieve early detection and proper management of thyroid dysfunction, which could improve the quality of life of the elderly and prevent further decline in physiological function.

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Material and methods

Subjects

This was an observational, descriptive, analytical study with a cross-sectional design. The participants were recruited from January 2019 to December 2022 using a consecutive sampling method for elderly patients in the Department of Gerontology at Peking University People's Hospital in Beijing, China. All subjects were ≥ 60 years old. They were evaluated for medical history, ongoing diseases, physical examination, comprehensive metabolic panel, and comprehensive geriatric assessment. The exclusion criteria were as follows: severe infection, respiratory failure, heart failure, dialysis, and inability to cooperate in completing comprehensive geriatric assessment.

Clinical and laboratory evaluations

We collected demographic and clinical characteristics including age, sex, body mass index (BMI), hypertension, cardiovascular disease, and diabetes. Complete blood count, blood biochemistry, blood glucose metabolism, and other patient indicators were collected retrospectively. Alanine aminotransferase (ALT), aspartate aminotransferase (AST), serum albumin (Alb), total protein (TP), serum uric acid (UA), fasting plasma glucose (FPG), total cholesterol (TC), triglyceride (TG), and low-density lipoprotein cholesterol (LDL-C) were measured using an automatic biochemical analyser (AU5832). Haemoglobin (Hb) and C-reactive protein (CRP) levels were measured using a blood cell analyser (DxH800), and glycosylated haemoglobin (HbA_{1c}) levels were measured using a HbA_{1c} analyser (Primus9210). Thyroid function examination included serum triiodothyronine (TT3), free triiodothyronine (FT3), serum total thyroxine (TT4), serum free thyroxine (FT4), thyroid stimulating hormone (TSH), anti-thyroglobulin antibody (anti-TgAb), and anti-thyroid peroxidase antibody (anti-TPOAb), which were measured on a ADVIA Centaur XP Electrochemiluminescence Immunoassay Analyser (Siemens).

Comprehensive Geriatric Assessment

CGA is a multifaceted diagnostic and treatment process that identifies the nutritional risk screening (NRS 2002), anxiety (generalized anxiety disorder 7-item, GAD-7), depression (patient health questionnaire, PHG-9), sleep quality (the Pittsburgh sleep quality index, PSQI), osteoporosis [international osteoporosis foundation (IOF); osteoporosis self-assessment tool for Asians (OSTA)], frailty (FRAIL scale and fried frailty index), cognitive function (mini-mental state examination, MMSE), and physical activity [short physical performance battery (SPPB); activities of daily living (ADL); Morse fall scale] in elderly individuals. Assessment tools, including questionnaires and measurements, were completed at the hospital.

Data analysis

Continuous variables are presented as the mean ± standard deviation (SD), and they were analysed with the independent sample t-test. Categorical variables are presented as percentages, and they were analysed using the chi-square test. Multivariate logistic regression analysis was used to analyse the association between thyroid hormone levels and different CGA domains. A probability (p) value < 0.05 was considered statistically significant. All statistical analyses were performed using SPSS software (version 24.0; SPSS Inc., Chicago, IL, USA).

Results

A total of 477 patients were enrolled in the study, with ages ranging from 60 to 97 years, with a mean of 76.4 years (SD: 9.176), and 46.3% were female. The mean TSH level in the whole population was 2.76 uIU/ml ± 7.71 uIU/mL, and the 75th percentile of TSH level was 2.86 uIU/mL. The prevalence of abnormal thyroid hormone levels in the elderly was 34.2% (163/477), 5 with hypothyroidism (1.05%), 36 with subclinical hypothyroidism (7.55%), one with hyperthyroidism (0.21%), 14 with subclinical hyperthyroidism (2.94%), 51 with low triiodothyronine syndrome(10.7%), and 56 with pure anti-TgAb- or anti-TPOAb-positivity (11.7%). Low triiodothyronine syndrome (LT3S), and pure anti-TgAb- or anti-TPOAb-positivity were the main manifestations of thyroid diseases in elderly patients.

Demographic and clinical characteristics

Distributions of age, sex, BMI, and complications are shown in Table 1. The normal and LT3S groups had similar complications including hypertension and cardiovascular disease ($p > 0.05$). The LT3S group had a higher rate of diabetes (51.0% *vs*. 34.4%, $p = 0.023$). The LT3S group were older than the normal thyroid group (82.24 ± 8.39 *vs*. 75.58 ± 8.98, $p = 0.000$), with more females (58.8% *vs*. 40.4%, $p = 0.014$) and lower BMI (22.98 ± 3.68 *vs*. 24.59 ± 3.36, $p = 0.002$). Table 2 describes the biochemical and glucose metabolism.

Table 1. *Demographic and clinical characteristics of the low triiodothyronine syndrome group and the normal group*

Characteristic	Thyroid diseases		χ^2(t) value	p-value
	Normal (n = 314)	LT3S (n = 51)		
Age	75.58 ± 8.98	82.24 ± 8.39	–4.954	0.000
Gender, female	127 (40.4%)	30 (58.8%)	6.045	0.014
BMI	24.59 ± 3.36	22.98 ± 3.68	3.128	0.002
Hypertension	203 (64.6%)	33 (64.7%)	0.000	0.994
Cardiovascular	93 (29.6%)	19 (37.3%)	1.203	0.273
Diabetes	108 (34.4%)	26 (51.0%)	5.194	0.023

Data are presented as mean ± standard deviation and counts (percentages). LT3S — low triiodothyronine syndrome; BMI — body mass index

Table 2. *Biochemical and metabolic indicators of the low triiodothyronine syndrome (LT3S) group and the normal group*

Characteristic	Thyroid diseases		χ^2(t) value	p-value
	Normal (n = 314)	LT3S (n = 51)		
Hb [g/L]	132.06 ± 14.41	116.69 ± 19.45	6.70	0.000
FPG [mmol/L]	5.60 ± 1.85	6.47 ± 2.94	–2.79	0.005
HbA_{1c} (%)	6.43 ± 1.31	6.81 ± 1.77	–1.81	0.071
ALT [U/L]	18.82 ± 12.22	17.57 ± 12.61	0.677	0.498
AST [U/L]	20.46 ± 6.94	22.47 ± 12.36	–1.687	0.092
TC [mmol/L]	4.11 ± 1.00	4.23 ± 1.07	–0.760	0.447
TG [mmol/L]	1.43 ± 0.75	1.45 ± 0.83	–0.190	0.848
LDL-C [mmol/L]	2.47 ± 0.76	2.54 ± 0.89	-0.602	0.547
TP [g/L]	65.28 ± 5.47	64.31 ± 7.19	1.118	0.263
Alb [g/L]	38.39 ± 3.66	35.33 ± 5.29	5.169	0.000
UA [μmol/L]	347.25 ± 90.61	329.51 ± 111.86	1.076	0.285
CRP [mg/L]	2.63 ± 5.87	11.09 ± 15.62	-3.595	0.001

Data are presented in mean ± standard deviation and counts (percentages). Hb — haemoglobin; FPG — fasting plasma glucose; HbA_{1c} — glycosylated haemoglobin; ALT — alanine aminotransferase; AST — aspartate aminotransferase; TC — total cholesterol; TG — triacylglycerol; LDL-C — low-density lipoprotein cholesterol; TP — total protein; Alb — albumin; UA — uric acid; CRP — C-reactive protein

Subjects with LT3S had lower Hb (116.69 ± 19.45 *vs*. 132.06 ± 14.41 g/L, p = 0.000) and Alb (35.33 ± 5.29 *vs*. 38.39 ± 3.66 g/L, p = 0.000), and higher CRP (11.09 ± 15.62 *vs*. 2.63 ± 5.87 g/L, p = 0.001) and FPG (6.47 ± 2.94 *vs*. 5.60 ± 1.85 mmol/L, p = 0.005) than subjects in the normal group. There were no significant differences in ALT, AST, HbA_{1c}, TC, TG, LDL-C, TP, and UA levels (p > 0.05).

Physical health

As shown in Table 3, the NRS 2002 scale screening results showed that the LT3S group had a higher risk of malnutrition than the normal group (43.14% *vs*. 8.5%, p = 0.000). The frailty situation was evaluated by the FRAIL scale and Fried frailty index, which divided the subjects into robust, pre-frail, and frail groups. The results showed that there was no significant difference between the LT3S and normal groups (p > 0.05).

Regarding strength, the LT3S group showed a trend toward weaker grip strength than those with normal thyroid function, but the results showed no statistical difference (23.97 ± 8.87 *vs*. 24.32 ± 9.67 kg, p = 0.853). Notably, the LT3S group had more females, which might be part of the reason for their lower grip strength. The SPPB was used to measure physical function in the elderly, and the results showed no significant difference in SPPB scores between the 2 groups of patients. Six-metre walking speed, fall risk, and level of independence were similar between the 2 groups (p > 0.05).

Mental health

The impact of LT3S on mental health is summarized in Table 3. The PHG-9 score measuring depression showed a significantly higher frequency in the LT3S group (p = 0.006), especially in the mild and severe depression groups (31.4% *vs*. 19.4% and 13.7% *vs*. 2.9%, respectively). According to the GAD7 score, which measures anxiety levels, there was a high incidence of moderate anxiety in the LT3S group (13.7% *vs*. 4.1%); however, there was no statistically significant difference between the 2 groups. The incidence of sleep disorders measured by PSQI was similar in both groups (p = 0.857). The MMSE was used to assess cognitive impairment, and the results showed that the incidence of cognitive decline was higher in those with LT3S; however, there was no statistically significant difference between the 2 groups.

Multivariable logistic regression models predicting depression and malnutrition

To construct a multivariate logistic regression model with depression and malnutrition as dependent variables, respectively, 8 potential risk factors (age, sex, BMI, diabetes, CRP, Alb, Hb, and LT3S) were used as independent variables. Multivariate analysis showed that Hb [odds ratio (OR): 0.975; 95% confidence interval (CI): 0.959–0.990; p = 0.002) and LT3S (OR: 2.213; 95% CI: 1.048–4.672; p = 0.037) were independently associated with depression (Tab. 4), and female (OR: 0.393; 95% CI: 0.160–0.968; p = 0.042), Alb (OR: 0.892; 95% CI: 0.811–0.981; p = 0.018), Hb (OR: 0.964; 95% CI: 0.939–0.989; p = 0.006), and LT3S (OR: 3.749; 95% CI:

Table 3. *Low triiodothyronine syndrome (LT3S) and comprehensive geriatric assessment*

Characteristic	Thyroid Diseases		χ^2(t) value	p-value
	Normal (n = 314)	LT3S (n = 51)		
Physical health				
Nutritional risk (NRS 2002)	27(8.5%)	22(43.14%)	37.228	0.000
Frail				
The FRAIL scale			2.857	0.240
Robust	82(26.1%)	18 (35.3%)		
Pre-frail	130 (41.4%)	23(45.1%)		
Frail	102 (32.5%)	10 (19.6%)		
Fried frailty index			0.129	0.937
Robust	130 (41.4%)	22 (43.1%)		
Pre-frail	132 (42.0%)	21 (41.2%)		
Frail	52 (16.6%)	8 (15.7%)		
Physical activity				
Grip strength, max [kg]	25.69 ± 9.92	25.60 ± 9.29	0.051	0.960
Grip strength, average [kg]	24.32 ± 9.67	23.97 ± 8.87	0.186	0.853
SPPB score	9.23 ± 2.97	9.80 ± 2.56	–0.937	0.349
6 meters walk speed [m/s]	6.86 ± 3.53	7.42 ± 3.53	–0.790	0.430
Fall risk assessment			0.138	0.933
Low risk	28 (8.9%)	5 (9.8%)		
Moderate risk	120 (38.2%)	21(41.2%)		
High risk	166 (52.9%)	25 (49.0%)		
ADL score			2.992	0.393
No dependency	138 (43.9%)	24 (47.1%)		
Mild dependency	151 (48.1%)	20 (39.2%)		
Moderate dependency	18 (5.7%)	4 (7.8%)		
Severe dependency	7 (2.2%)	3 (5.9%)		
Osteoporosis				
IOF risk, Positive	218 (69.4%)	42(82.4%)	2.675	0.102
OSTA	–1.69 ± 3.77	–2.45 ± 4.12	1.178	0.240
Mental health				
Anxiety (GAD7 score)			3.554	0.059
Normal	246 (78.3%)	33 (64.7%)		
Mild	48 (15.3%)	8 (15.7%)		
Moderate	13 (4.1%)	7 (13.7%)		
Severe	7 (2.2%)	3 (5.9%)		
Depression (PHG-9 score)			12.602	0.006
Normal	220 (70.1%)	24 (47.1%)		
Mild	61 (19.4%)	16 (31.4%)		
Moderate	24 (7.6%)	4 (7.8%)		
Severe	9 (2.9%)	7 (13.7%)		
Sleep quality (PSQI)			0.033	0.857
Positive	167 (53.2%)	26 (51.0%)		
Cognitive impairment (MMSE)			1.115	0.291
Positive	79 (25.2%)	17 (33.3%)		

Data are presented in mean ± standard deviation and counts (percentages). ADL — activities of daily living; GAD7 — generalized anxiety disorder 7-item; IOF — International Osteoporosis Foundation; MMSE — Mini-Mental State Examination; NRS — nutritional risk screening; OSTA — osteoporosis self-assessment tool for Asians; PHG-9 — Patient Health Questionnaire; PSQI — Pittsburgh Sleep Quality Index; SPPB — Short Physical Performance Battery

Table 4. *Multivariable logistic regression models between low triiodothyronine syndrome (LT3S) and depression*

Assessment	Regression coefficient	SE	OR (95% CI)	p-value
MODEL 1[a]				
Sex, female	0.235	0.246	1.264 (0.781–2.048)	0.340
Age	0.012	0.013	1.012 (0.986–1.039)	0.377
BMI	-0.017	0.036	0.983 (0.917– 1.055)	0.642
LT3S	0.901	0.332	2.461 (1.284–4.718)	0.007
MODEL 2[b]				
Sex, female	0.240	0.246	2.017 (0.784–2.059)	0.330
Age	0.012	0.013	1.012 (0.986–1.039)	0.377
BMI	-0.017	0.036	0.983 (0.917– 1.055)	0.642
Diabetes	0.107	0.254	1.113 (0.677–1.830)	0.673
LT3S	0.901	0.332	2.461 (1.284–4.718)	0.007
MODEL 3[c]				
Sex, female	-0.011	0.276	0.989 (0.576–1.698)	0.967
Age	0.005	0.015	1.005 (0.977–1.034)	0.744
BMI	0.002	0.038	1.002 (0.930–1.080)	0.958
Diabetes	0.117	0.270	1.124 (0.662–1.909)	0.665
CRP	–0.012	0.010	0.986 (0.967–1.006)	0.172
Alb	–0.033	0.034	0.968 (0.905–1.035)	0.337
Hb	–0.026	0.008	0.975 (0.959–0.990)	0.002
LT3S	0.794	0.381	2.213 (1.048–4.672)	0.037

[a]Model 1 adjusted by age, sex, BMI; [b]Model 2 adjusted by age, sex, BMI, diabetes; [c]Model 3 adjusted by age, sex, BMI, diabetes, CRP, Alb, Hb. SE — standard error; OR — odds ratio; CI — confidence interval; BMI — body mass index; Alb — albumin; CRP — C-reactive protein; Hb — haemoglobin

Table 5. *Multivariable logistic regression models between low triiodothyronine syndrome (LT3S) and nutritional risk*

Assessment	Regression coefficient	SE	OR (95% CI)	p-value
MODEL 1[a]				
Sex, female	–0.596	0.423	0.551 (0.241–1.262)	0.159
Age	0.056	0.022	1.058 (1.013–1.104)	0.010
BMI	–0.250	0.061	0.779 (0.691–0.879)	0.000
LT3S	1.621	0.419	5.060 (2.225–11.511)	0.000
MODEL 2[b]				
Sex, female	–0.596	0.423	0.551 (0.241–1.262)	0.159
Age	0.056	0.022	1.058 (1.013–1.104)	0.010
BMI	–0.250	0.061	0.779 (0.691–0.879)	0.000
Diabetes	–0.294	0.422	0.746 (0.326–1.706)	0.487
LT3S	1.621	0.419	5.060 (2.225–11.511)	0.000
MODEL 3[c]				
Sex, female	–0.933	0.459	0.393 (0.160–0.968)	0.042
Age	0.030	0.024	1.031 (0.983–1.080)	0.204
BMI	–0.236	0.070	0.790 (0.688–0.906)	0.001
Diabetes	–0.190	0.460	0.827 (0.336–2.038)	0.680
CRP	–0.002	0.012	0.998 (0.975–1.012)	0.855
Alb	–0.115	0.048	0.892 (0.811–0.981)	0.018
Hgb	–0.036	0.013	0.964 (0.939–0.989)	0.006
LT3S	1.322	0.476	3.749 (1.474–9.536)	0.006

[a]Model 1 adjusted by age, sex, BMI; [b]Model 2 adjusted by age, sex, BMI, diabetes; [c]Model 3 adjusted by age, sex, BMI, diabetes, CRP, Alb, Hb. SE — standard error; OR — odds ratio; CI — confidence interval; BMI — body mass index; Alb — albumin; CRP — C-reactive protein; Hb — haemoglobin

Table 6. *Demographic and clinical characteristics of the thyroid autoantibodies positive (TAP) group and the normal group*

Characteristic	Thyroid diseases		χ^2(t) value	p-value
	Normal (n = 314)	TAP (n = 56)		
Age	75.58 ± 8.98	76.63 ± 9.65	-0.795	0.427
Sex, female	127 (40.4%)	38 (67.9%)	14.452	0.000
BMI	24.59 ± 3.36	24.44 ± 3.10	0.309	0.757
Hypertension	203 (64.6%)	33 (58.9%)	0.673	0.412
Cardiovascular	93 (29.6%)	221 (37.5%)	1.385	0.239
Diabetes	108 (34.4%)	26 (46.4%)	2.979	0.084

Data are presented in mean ± standard deviation and counts (percentages). BMI — body mass index

Table 7. *Biochemical and metabolic indicators of the thyroid autoantibodies positive (TAP) group and the normal group*

Characteristic	Thyroid diseases		χ^2(t) value	p-value
	Normal (n = 314)	TAP (n = 56)		
Hb [g/L]	132.06 ± 14.41	126.58 ± 12.38	2.673	0.008
FPG [mmol/L]	5.60 ± 1.85	5.60 ± 0.97	0.025	0.980
HbA_{1c} (%)	6.43 ± 1.31	6.42 ± 0.91	0.039	0.969
ALT [U/L]	18.82 ± 12.22	20.57 ± 10.48	–1.005	0.315
AST [U/L]	20.46 ± 6.94	22.86 ± 8.79	–2.286	0.056
TC [mmol/L]	4.11 ± 1.00	4.32 ± 0.95	–1.433	0.153
TG [mmol/L]	1.43 ± 0.75	1.48 ± 0.88	–0.487	0.626
LDL-C [mmol/L]	2.47 ± 0.76	2.57 ± 0.74	–1.001	0.317
TP [g/L]	65.28 ± 5.47	66.79 ± 5.95	–1.883	0.060
Alb [g/L]	38.39 ± 3.66	38.95 ± 3.78	–1.045	0.297
UA [μmol/L]	347.25 ± 90.61	343.85 ± 84.83	0.261	0.794
CRP [mg/L]	2.63 ± 5.87	2.86 ± 4.57	0.297	0.766

Data are presented in mean ± standard deviation and counts (percentages). Hb — haemoglobin; FPG — fasting plasma glucose; HbA_{1c} — glycosylated haemoglobin; ALT — alanine aminotransferase; AST — aspartate aminotransferase; TC — total cholesterol; TG — triacylglycerol; LDL-C — low-density lipoprotein cholesterol; TP — total protein; Alb — albumin; UA — uric acid; CRP — C-reactive protein

1.474–9.536; p = 0.006) were independently associated with malnutrition (Tab. 5).

Comprehensive geriatric assessment in thyroid autoantibody-positive (TAP) patients

Thyroid autoantibody-positivity without thyroid dysfunction was also common in elderly patients. We further conducted subgroup analysis between thyroid autoantibody-positive patients and the normal group. Distributions of age, sex, BMI, and complications are shown in Table 6. There were more women in the TAP group compared to the normal group (67.9% *vs.* 40.4%, p = 0.000). There was no significant difference in BMI and age between the 2 groups (p > 0.05). The normal and TAP groups had similar complications including hypertension, cardiovascular disease, and diabetes (p > 0.05). Table 7 describes the biochemical and glucose metabolism. Subjects with TAP had lower haemoglobin (126.58 ± 12.38 *vs.* 132.06 ± 14.41, p = 0.008). There were no significant differences in FPG, ALT, AST, HbA_{1c}, TC, TG, LDL-C, TP, ALB, CRP, and UA levels (p > 0.05). The risk of malnutrition, anxiety, depression, sleep disorders, osteoporosis, frailty, cognitive function impairment, and decreased physical activity were similar between the thyroid autoantibody-positive group and the normal group (Tab. 8).

Discussion

Low T3 levels have been interpreted as a physiological response aimed at reducing energy expenditure and minimizing protein catabolism, and often goes unrecognized, especially in elderly patients. In this study, we investigated the association of low T3 levels with clinical characteristics, metabolic panels, and GCA scale scores in older adults. The results showed that older adults with LT3S may have a higher risk of depression and malnutrition. These findings offer a new

Table 8. *Thyroid autoantibody positivity (TAP) and comprehensive geriatric assessment*

Characteristic	Thyroid diseases		χ^2(t) value	p-value
	Normal (n = 314)	TAP (n = 56)		
Physical health				
Nutritional risk (NRS 2002)	27(8.5%)	6(10.7%)	0.194	0.660
Frail				
The FRAIL scale			0.499	0.779
Robust	82(26.1%)	16 (28.6%)		
Pre-frail	130 (41.4%)	24(42.8%)		
Frail	102 (32.5%)	16 (28.6%)		
Fried frailty index			1.498	0.473
Robust	130 (41.4%)	19 (33.9%)		
Pre-frail	132 (42.0%)	30 (53.6%)		
Frail	52 (16.6%)	7 (12.5%)		
Physical activity				
Grip strength, max [kg]	25.69 ± 9.92	26.48 ± 9.49	–0.410	0.682
Grip strength, average [kg]	24.32 ± 9.67	24.66 ± 9.87	–0.184	0.854
SPPB score	9.23 ± 2.97	9.30 ± 3.076	–0.104	0.917
6 meters walk speed [m/s]	6.86 ± 3.53	7.26 ± 3.71	–0.579	0.563
Fall risk assessment			0.832	0.400
Low risk	28 (8.9%)	8 (14.3%)		
Moderate risk	120 (38.2%)	18(32.1%)		
High risk	166 (52.9%)	30 (53.6%)		
ADL score			0.960	0.811
No dependency	138 (43.9%)	28 (50.0%)		
Mild dependency	151 (48.1%)	25 (44.6%)		
Moderate dependency	18 (5.7%)	2 (3.6%)		
Severe dependency	7 (2.2%)	1 (1.8%)		
Osteoporosis				
IOF risk, Positive	218 (69.4%)	44(78.6%)	1.450	0.229
OSTA	-1.69 ± 3.77	-2.57 ± 2.94	1.577	0.116
Mental health				
Anxiety (GAD7 score)			0.426	0.514
Normal	246 (78.3%)	40 (71.4%)		
Mild	48 (15.3%)	6 (10.7%)		
Moderate	13 (4.1%)	9 (16.1%)		
Severe	7 (2.2%)	1 (1.8%)		
Depression (PHG-9 score)			3.694	0.296
Normal	220 (70.1%)	33 (58.9%)		
Mild	61 (19.4%)	17 (30.3%)		
Moderate	24 (7.6%)	3(5.4%)		
Severe	9 (2.9%)	3 (5.4%)		
Sleep quality (PSQI)			0.085	0.771
Positive	167(53.2%)	31(55.4%)		
Cognitive impairment (MMSE)			0.030	0.862
Positive	79 (25.2%)	13 (23.2%)		

Data are presented in mean ± standard deviation and counts (percentages). ADL — activities of daily living; GAD7 — generalized anxiety disorder 7-item; IOF — International Osteoporosis Foundation; MMSE — Mini-Mental State Examination; NRS — nutritional risk screening; OSTA — osteoporosis self-assessment tool for Asians; PHG-9 — Patient Health Questionnaire; PSQI — Pittsburgh Sleep Quality Index; SPPB — Short Physical Performance Batter

perspective on the management of elderly patients with LT3S.

With increasing aging of the population, thyroid disease has become common in the elderly. Previous studies have shown that the prevalence of thyroid disease is higher in the elderly than in the overall population [2, 3]. In our study, the incidence of thyroid dysfunction was high in the elderly (34.2%). LT3S and thyroid antibody positivity were the main manifestations of thyroid abnormality in elderly patients (65.6%). The prevalence of hyperthyroidism was notably lower in the elderly (0.21%). The mean TSH level in the elderly was 2.76 uIU/mL, showing an increasing trend compared to that in younger adults. Changes in TSH may be a protective mechanism to slow catabolism in the elderly, who have a slower metabolism, less conversion of T4 to T3, weaker feedback inhibition of TSH, and higher TSH levels [4–6].

LT3S has been described in critically ill patients without prior history of thyroid disease. Typically, it manifests with low serum T3, average or low TSH, and increased reverse triiodothyronine (rT3) [7]. However, the impact of LT3S on physical function and prognostic analysis in non-acute and non-severe elderly patients was still unclear. Therefore, we focus further on the effects of LT3S on physical function in elderly patients. In our study, patients in the LT3S group had a higher rate of diabetes, were older, and were more commonly women. The BMI, and levels of haemoglobin and albumin were lower in LT3S patients, with higher levels of CRP. The pathogenesis of LT3S caused by age and hypoalbuminaemia may be due to decreased FT4 synthesis, decreased enzyme activity that promotes T3 synthesis, abnormalities in thyroid binding proteins, increased T3 clearance, drug effects, and the influence of inflammatory factors as age increases [8].

Various other chronic diseases and geriatric syndromes that often coexist with thyroid diseases in elderly patients can affect their health status [9]. To fully reflect the changes in functional, psychological, and social adjustment in older adults, the CGA approach has been used in clinical and research studies to comprehensively assess the impact of thyroid disease and its intervention methods on the overall health status of older adults, which may help reformulate or adjust treatment plans [10]. We evaluated nutritional risk, anxiety, depression, sleep quality, osteoporosis, frailty, cognitive function, and physical activity using CGA tools. Our study found a higher rate of depression and malnutrition in the patients with LT3S.

The group with LT3S function showed lower albumin levels, BMI, and haemoglobin, which may explain the increased risk of malnutrition [11]. However, even after controlling for these factors, our analysis revealed a persistent relationship between LT3S and malnutrition. At the same time, poor nutrition may also affect thyroid function and thyroid hormone levels. Low dietary calories may lower the body's metabolic rate and reduce thyroid hormone levels. Dietary deficiencies in iodine and protein can also lead to lower thyroid hormone levels, which can affect metabolism and normal functioning of the nervous system [12, 13].

Research findings suggest that the incidence of depression is higher in patients with LT3S, particularly in those with mild and severe depression. Further multivariate logistic regression analysis showed that depression was independently associated with LT3S (OR: 2.213; 95% CI: 1.048–4.672; p = 0.037). The presence of LT3S increased the odds of depression by 2.213 times. Thyroid hormones have profound effects on behaviour and appear to modulate the phenotypic expression of major mood disorders. Lower FT3 is associated with more severe depressive symptoms in anorexia patients [14]. Indeed, there is evidence that triiodothyronine may accelerate the response to antidepressants, and studies have shown that LT3 may augment the response to antidepressants in patients with refractory depression [15]. Additionally, thyroid hormone supplements appear to accelerate and enhance the clinical response to antidepressant drugs [16]. The administration of supraphysiological thyroid hormones improves depressive symptoms in patients with bipolar disorder by modulating the function of components of the anterior limbic network [17]. The absence of nocturnal TSH surges has been noted in depressed patients, and lower basal TSH levels have been reported more in patients with major depression than in those without major depression [18]. Genetically, a strong coherence was observed between thyroid disease and both major depressive disorders, and this genetic correlation was particularly strong at the major histocompatibility complex locus on chromosome 6 [19]. However, an observational study suggested that depressive symptoms should not be attributed to minor variations in thyroid function [20]. Another meta-analysis demonstrated that hypothyroidism was not associated with depression. Furthermore, levothyroxine (L-T4) supplementation for hypothyroidism has no effect on depression [21].

Thyroid autoantibody positivity was also common in elderly patients. This study further conducted subgroup analysis on thyroid autoantibody-positive patients without thyroid dysfunction. The results showed that the risk of malnutrition, anxiety, depression, sleep disorders, osteoporosis, frailty, cognitive function impairment, and decreased physical activity

were similar between the thyroid autoantibody-positive group and the normal group. The effect size for the association between thyroid autoantibodies and clinical depression was very low, and this modest association was possibly restricted to overt thyroid dysfunction [22].

This study had several limitations. First, the number of patients was relatively small, which may have caused a statistical bias. Second, this was a single-centre cross-sectional study and could not explain the causal relationship between abnormal thyroid function and diseases such as malnutrition and depression.

Conclusions

Our study suggests that LT3S is closely related to depression and malnutrition. Physicians should be more concerned about elderly patients with LT3S, not only for their apparent clinical diseases, but also for their physical and mental status. Regular thyroid function checks might help early detection of depression. CGA is an effective tool for identifying clinical issues such as malnutrition and depression in elderly patients with thyroid dysfunction. In the future, we should individualize and stratify the management of thyroid dysfunction in older adults, including treatment options and life interventions that distinguish them from younger adults.

Conflict of interests

The authors declare no conflict of interest.

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Ethics Committee approval

The study was approved by the Ethics Committee of Peking University People's Hospital.

Data availability

All data are available.

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Authors' Contributions

Q.X. and J.W. contributed to conception and design of the study. Q.X., X.L., and L.D. organized the database. Q.X. and Y.M. performed the statistical analysis. Q.X. wrote the first draft of the manuscript. J.W. finally revised the manuscript. All authors read and approved the final manuscript.

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