Original Article

Association between thyroid hormone levels and frailty in an older inpatient cohort: a cross-sectional study

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Background: Frailty is a common biological syndrome in elderly people, and the aging process regulates thyroid function. The present study aimed to determine the prevalence of frailty in an older inpatient cohort using the FRAIL scale and to evaluate the association of frailty with thyroid hormone levels.

Methods: This cross-sectional study was performed in the Department of Geriatrics, Sichuan Provincial People's Hospital, University of Electronic Science and Technology of China. From November 2019 to April 2020, 146 inpatients aged ≥65 years were recruited for the study and demographic data, frailty, geriatric assessment, and thyroid hormone levels were evaluated. Frailty was determined by the FRAIL scale, and geriatric assessment was based on activities of daily living (ADL) and instrumental activities of daily living (IADL). The data were analyzed using appropriate parametric and nonparametric statistical tests.

Results: At enrollment, 31 (21.23%) of the total participants were robust, 31 (21.23%) were pre-frail, and 84 (57.53%) were frail. The frail patients were significantly older than the robust patients and pre-frail patients (P<0.001 for both). The percentages of ADL disability differed significantly among the patients for frail versus robust, frail versus pre-frail, and pre-frail versus robust, as did the percentages of IADL disability among patients for frail versus robust and frail versus pre-frail (P<0.01 for all). In binary logistic regression analyses adjusted for age, sex, body mass index, HbA1c (%), and smoking, frailty was significantly associated with serum thyroid stimulating hormone (TSH) concentration [odds ratio (OR): 1.704], T3 concentration (OR: 0.102), ADL score (OR: 0.793), and IADL score (OR: 0.413).

Conclusions: In our study population, the prevalence of frailty was higher in older geriatric inpatients in China than other studies. Inpatients with high TSH levels were at increased risk of frailty. Conduction of future longitudinal studies is warranted to determine the relationship between thyroid hormone levels and frailty.

Keywords: Frailty; thyroid hormone levels; activities of daily living (ADL); instrumental activities of daily living (IADL); cross-sectional study

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Introduction

The global population is aging. According to data released by the Chinese National Bureau of Statistics in 2018, people aged >60 years accounted for 17.3% of the total population in China in 2017, and it is estimated that by 2050, the proportion of elderly people in China will exceed 30% of the general population. Major challenges for this aging population are likely to include an increased prevalence of conditions such as frailty, hypertension, dementia, type 2 diabetes mellitus, chronic kidney disease, and cardiac

disease. Frailty is a common biological syndrome in elderly people and is defined as a clinical state characterized by increased vulnerability to stressors and decreased physiologic reserves in multiple organ systems (1). The major negative health-related events associated with frailty include disability, hospitalization, and mortality. This type of geriatric syndrome was reported to affect 10–15% of adults aged >65 years, and to increase with aging (2-4).

The aging process regulates the function of the thyroid. In general, the activity of the thyroid hormone axis appears to decline with age, manifested by increasing thyroid-stimulating hormone (TSH) concentrations and decreasing free triiodothyronine (T3) concentrations. As a consequence, thyroid dysfunction, especially hypothyroidism or subclinical hypothyroidism, is relatively common among elderly people. Variations in thyroid hormone levels have been linked with nervous system alterations, oncogenesis, cardiac function, and metabolic changes (5). Several studies have demonstrated that alterations in thyroid hormones were associated with dementia, diabetes, dyslipidemia, atrial fibrillation, osteoporosis, and fracture development (6-9), leading to a decline in physiological capacity and stress resistance that are related to frailty. A pilot study conducted in older diabetic inpatients has demonstrated that frailty is an independent risk factor for adverse outcomes (9). Another study indicated that frailty was positively associated with chronic inflammation and down-regulation of multiple endocrine factors (10). These biomarkers included blood levels of insulin-like growth factor-1, thyroid hormones, C-reactive protein, insulin, blood glucose level, and hemoglobin. Therefore, we hypothesized that changes in thyroid hormone levels are associated with frailty. However, only a few representative studies have assessed the potential relationship between thyroid function and frailty (3,4,11), and as these studies used differing indexes of thyroid hormone levels and different frailty assessments, they produced inconsistent results. Therefore, we investigated the cross-sectional associations between thyroid hormone levels and frailty in an older hospital-based cohort. The main aims of the study were to use the FRAIL scale to survey the prevalence of frailty among older inpatients and to explore the relationship between thyroid hormone levels and frailty. We present the following article in accordance with the STROBE reporting checklist (available at https://dx.doi.org/10.21037/apm-21-1102).

Methods

This cross-sectional study recruited 146 inpatients from the Department of Geriatrics, Sichuan Provincial People's Hospital, University of Electronic Science and Technology of China, between November 2019 and April 2020. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). The research protocol was approved by the Research Ethics Committee of Sichuan Provincial People's Hospital (No.2019-331) and a signed informed consent form was obtained from each patient.

The inclusion criteria were inpatients aged ≥65 years in the Department of Geriatrics. The exclusion criteria were severe senile dementia, inability to communicate, and presence of serious illness, including serious infection, acute massive gastrointestinal hemorrhage, cerebral hemorrhage, acute stroke, acute myocardial infarction, acute heart failure, and other severe diseases.

All recruited inpatients were asked to complete a self-assessment questionnaire that included demographic data, height, weight, history of smoking, and geriatric assessment (FRAIL scale, ADL, and IADL, as described later in this text). Data for thyroid hormone levels [FT3, free thyroxine (FT4), total triiodothyronine (TT3), total thyroxine (TT4), TSH], thyroid autoantibodies were collected from the electronic medical record information system at Sichuan Provincial People's Hospital. Data of glycosylated hemoglobin (HbA1c) was also collected to eliminate the effect of blood glucose on the research.

Laboratory methods

Thyroperoxidase autoantibody (TPOAb), thyroglobulin autoantibody (TgAb), TSH, FT4, FT3, TT4, TT3, and HbA1c were measured in all participants. According to previous studies (12,13), TSH levels were significantly positively correlated with age in both females and males. So our laboratory develop the TSH reference range in accordance with NACB guidelines (14), which applies to the elderly people in this study. Thyroid hormone levels and thyroid autoantibodies were assessed using chemiluminescence immunoassay kits and the intra-assay and inter-assay coefficients of variation were all <5%. The laboratory reference values were 0.35–4.94 mIU/L for TSH, 9.01–19.05 pmol/L for FT4, 2.63–5.70 pmol/L for

FT3, 0.88–2.44 nmol/L for TT3, 62.88–150.80 nmol/L for TT4, <30 IU/mL for TPOAb, and <75 IU/mL for TgAb.

Frailty was measured by the FRAIL scale, proposed by The International Association of Nutrition and Aging (15). The FRAIL scale is a simple five-point domain scale comprising fatigue, resistance (ability to climb a single flight of stairs), ambulation (ability to walk 100 m), number of illnesses (>5), and loss of weight exceeding 5%. Scores for the scale range from 0 to 5 and participants are considered frail if they score 3–5, pre-frail if they score 1–2, and robust if they score 0. The complete descriptions of the FRAIL scale scoring criteria were in accordance with a previous study (1). The FRAIL scale has been validated as a robust predictor of subsequent mortality and disability (16).

Functional assessment was based on activities of daily living (ADL) and instrumental activities of daily living (IADL). The Barthel index is commonly used to assess ADL in health systems (17) and is composed of ten items scored according to the degree of assistance required by patients to complete the activities. The lower the score, the higher dependence of the patient. The ten items include bathing, personal hygiene, feeding, dressing, bowel control, bladder control, going to the toilet, stair climbing, bed-to-chair transfer, and ambulation. The scores for each item are computed to a total Barthel index score, with a score of 0 indicating total dependence for performing ADL and a score of 100 indicating full independence for performing ADL. ADL disability was defined as an ADL score <100. The IADL score included eight items: shopping, housekeeping, money management, food preparation, ability to use telephone, laundry, mode of transportation, and responsibility for own medications (18). The score can vary from 0 to 8 and the higher the value, the more independent the patient. IADL disability was defined as an IADL score <8.

Statistical analysis

Continuous data were presented as mean ± SD or median and range as appropriate. For comparisons of population characteristics according to the FRAIL scale classification (robust, pre-frail, frail), analysis of variance (ANOVA) and the Kruskal-Wallis test were used for continuous variables depending on the variable distribution, as appropriate. The Pearson chi-square test was used for categorical variables and binary logistic regression was used to investigate the risk factors for frailty. We conducted simple linear regression analysis between functional assessment and thyroid hormone levels. The odds ratio (OR) and 95% confidence interval (CI) were determined for the logistic regression analysis and values of P<0.05 were considered statistically significant. All analyses were carried out using IBM SPSS, version 23.0 (IBM Corp., Armonk, NY, USA).

Results

Patent characteristics

A total of 146 patients were enrolled in the study. The patients had a mean age of 85.04±8.20 years (range, 65–104 years), mean body mass index (BMI) of 22.59±3.84 kg/m2, and mean HbA1c of 6.16%±1.24%. Among the patients, 90 (61.64%) were men with a mean age of 86.32±7.97 years and 56 (38.36%) were women with a mean age of 82.98±8.19 years. The prevalence of ADL disability and IADL disability among the total patients were 79.45% and 93.84%, respectively.

At enrollment, 31 (21.23%) of the total participants were robust, 31 (21.23%) were pre-frail, and 84 (57.53%) were frail. The baseline characteristics of the study population in the different FRAIL scale categories are shown in *Table 1*. The patients in the frail group were significantly older than those in the robust group and the pre-frail group, respectively (P<0.001 for both). The frail group had a significantly lower ADL score than the robust group and the pre-frail group (P<0.001 for both). Similarly, the frail group had a significantly lower IADL score than the pre-frail group and the robust group (P<0.001 for both). The percentages of ADL disability differed significantly among the patients for frail versus robust, frail versus pre-frail, and pre-frail versus robust, as did the percentages of IADL disability among the patients for frail versus robust and frail versus pre-frail (P<0.001 for all). There were no significant differences in sex, smoking, BMI, and HbA1c according to the FRAIL score categories.

The distributions of thyroid hormone levels among the FRAIL score categories are shown in *Table 2*. The serum TSH concentration in the frail group was higher than those in the robust group and the pre-frail group (P<0.05 for both). The T4 concentration in the frail group was lower than those in the robust group and the pre-frail group (P<0.05 for both), with similar findings for the T3 concentration. However, the prevalence of positive TPOAb and TgAb showed no significant differences according to the FRAIL score groups (P>0.05 for all).

The parameters estimated from the logistic regression

Table 1 Baseline characteristics of the study population according to the FRAIL score categories

Characteristics	Robust, N=31	Pre-frail, N=31	Frail, N=84	Total, N=146	P
Male (%)	18 (58.06)	20 (64.52)	52 (61.90)	90 (61.64)	0.87
Female (%)	13 (41.94)	11 (35.48)	32 (38.09)	56 (38.36)	
Smoking (%)	15 (48.39)	14 (45.16)	37 (44.05)	66 (45.21)	0.918
Age (yr)[a]	77.00 [66–95]	83.00 [65–97]	89.50 [67–104]†₸	87.00 [65–104]	<0.001
BMI (kg/m^2)	23.27±4.31	22.56±3.31	22.34±3.85	22.59±3.84	0.52
HbA1c (%)	6.09±1.29	5.89±0.71	6.29±1.36	6.16±1.24	0.3
Score of ADL[a]	100 [80–100]	90 [60–100]	50 [0–95]†₸	70 [0–100]	<0.001
Score of IADL[a]	6 [1–8]	5 [1–8]	1 [0–7]†₸	3 [0–8]	<0.001
ADL disability (%)[b]	8 (25.81)	24 (77.42)§	84 (100.00)†₸	116 (79.45)	<0.001
IADL disability (%)[b]	24 (77.42)	29 (93.55)	84 (100.00)†₸	137 (93.84)	<0.001

P values were obtained by analysis of variance, the Kruskal-Wallis test, or the chi-square test, as appropriate. [a], the Kruskal-Wallis test, Dun-Bonferroni method was used to compare between the groups; [b], the chi-square test, Bonferroni method (adjust P values) was used to compare between the groups; significant differences were found for †frail versus robust, ₸frail versus pre-frail, and §pre-frail versus robust. BMI, body mass index; HbA1c, glycosylated hemoglobin; ADL, activities of daily living; IADL, instrumental activities of daily living.

Table 2 Analysis of the relationships between frailty and thyroid hormones levels

Variable	Robust	Pre-frail	Frail	Total	P
TSH (mIU/L)	2.47±2.11	2.57±1.95	3.82±2.64†₸	3.26±2.47	0.009[a]
FT4 (pmol/L)	13.12±1.77	12.97±1.85	12.46±1.68	12.71±1.75	0.128
FT3 (pmol/L)	4.07±0.72	3.70±0.74§	3.41±0.71†	3.61±0.76	<0.001
T4 (nom/L)	104.10±20.08	101.01±23.17	90.50±19.12†₸	95.62±20.98	0.002
T3 (nom/L)	1.36±0.25	1.21±0.23§	1.09±0.24†₸	1.17±0.26	<0.001
TPOAb (%)					0.167*
+	0 (0.00%)	3 (9.68%)	9 (10.71%)	12 (8.22%)	
–	31 (100%)	28 (90.32%)	75 (89.29)	134 (91.78%)	
TgAb (%)					0.137*
+	0 (0.00)	1 (3.23)	8 (9.52)	9 (6.16)	
–	31 (100)	30 (96.77)	76 (90.48)	137 (93.84%)	

P values were obtained by ANOVA or the chi-square test, as appropriate. [a]Log-transformed ANOVA; S-N-K method was used to compare between the groups, and significant differences were found for †frail versus robust, ₸frail versus pre-frail, and §pre-frail versus robust. *The theoretical frequency of two cells (33.33%) was less than 5, using Fisher's exact test. TPOAb(+): TPOAb-positive; TPOAb(–): TPOAb-negative; TgAb(+): TgAb-positive; TgAb(–); TgAb-negative. TSH, thyroid stimulating hormone; FT4, free thyroxine; TPOAb, thyroperoxidase autoantibody; TgAb, thyroglobulin autoantibody.

analysis between frailty and variables that might influence frailty are shown in *Table 3*. In the univariate model, concentrations of TSH, FT3, and T3, and scores for ADL and IADL were risk factors for frailty (P<0.05 for all), while in the adjusted model, concentrations of TSH and T3, and scores for ADL and IADL remained correlated with frailty (P<0.05 for all). For every 1-point increase in ADL, the possibility of frailty reduced by 81.6% in the unadjusted model and 79.3% in the adjusted model. Lastly, because only a small number of patients had positive autoantibodies,

Table 3 Logistic regression analyses for risk of frailty using the robust and pre-frail groups as reference groups, adjusted for sex, age, BMI, HbA1c (%), and smoking

Variable	Univariate model		Adjusted model[a]	
	OR (95% CI)	P	OR (95% CI)	P
TSH (mIU/L)	1.290 (1.092–1.524)	0.003	1.258 (1.040–1.522)	0.018
FT4* (pom/L)	0.821 (0.675–0.998)	0.048	0.836 (0.654–1.068)	0.151
FT3 (pom/L)	0.387 (0.228–0.655)	<0.001	0.531 (0.284–0.993)	0.048
T3 (nom/L)	0.035 (0.007–0.173)	<0.001	0.102 (0.014–0.740)	0.024
Score of ADL	0.816 (0.755–0.881)	<0.001	0.793 (0.708–0.889)	<0.001
Score of IADL	0.385 (0.291–0.510)	<0.001	0.413 (0.298–0.574)	<0.001

*, collinearity diagnostics: there is multicollinearity in FT4 and T4; [a], adjusted for sex, age, BMI, HbA1c (%), and smoking. BMI, body mass index; HbA1c, glycosylated hemoglobin; OR, odds ratio; CI, confidence interval; TSH, thyroid stimulating hormone; FT4, free thyroxine; ADL, activities of daily living; IADL, instrumental activities of daily living.

Table 4 Simple linear regression analysis between ADL/IADL and thyroid function, adjusted for age, sex, BMI, HbA1c (%), and smoking

Variable	Univariate model		Adjusted model[a]	
	B (95% CI)	P	B (95% CI)	P
ADL				
TSH (mIU/L)	−0.237 (−4.562 to −0.880)	0.004	−0.128 (−3.079 to 0.134)	0.072
FT4* (pom/L)	0.090 (−1.205 to 4.121)	0.281	0.016 (−2.016 to 2.545)	0.819
FT3 (pom/L)	0.338 (6.828 to 18.372)	<0.001	0.161 (0.565 to 11.416)	0.031
T3 (nom/L)	0.359 (22.468 to 56.088)	<0.001	0.149 (0.039 to 32.657)	0.049
IADL				
TSH (mIU/L)	−0.185 (−0.371 to −0.025)	0.025	−0.067 (−0.209 to 0.065)	0.301
FT4* (pom/L)	0.164 (0.003 to 0.494)	0.047	0.082 (−0.068 to 0.315)	0.206
FT3 (pom/L)	0.351 (0.684 to 1.753)	<0.001	0.149 (0.059 to 0.975)	0.027
T3 (nom/L)	0.380 (2.315 to 5.418)	<0.001	0.130 (−0.053 to 2.705)	0.059

*, collinearity diagnostics: there is multicollinearity in FT4 and T4; [a], adjusted for sex, age, BMI, HbA1c (%), and smoking. ADL, activities of daily living; IADL, instrumental activities of daily living; BMI, body mass index; HbA1c, glycosylated hemoglobin; TSH, thyroid stimulating hormone; FT4, free thyroxine.

the presence of thyroid autoantibodies was not included in the logistic regression.

The parameters estimated from the simple linear regression analyses between thyroid hormone levels and scores for ADL and IADL are shown in *Table 4*, respectively. After adjustment for age, sex, BMI, smoking, and HbA1c (%), the concentration of FT3 was positively associated with ADL (P<0.05) and similar findings were obtained for IADL (P<0.05 for both).

Discussion

In the present study, the prevalence of frailty measured by the FRAIL scale was 57.53% in older Chinese inpatients in the Department of Geriatrics of our hospital, which was higher than the findings of previous studies (3,4,11). This discrepancy may be explained by several reasons. First, the present study enrolled inpatients in a hospital setting, while previous studies enrolled community-dwelling older

participants. Second, the mean age in the present study was 85 years, which was 10 years older than the mean age in the previous studies. Finally, the present study included male and female participants, while two of the previous studies only included male participants (3,4).

Our results showed a complex relationship between thyroid hormone levels and frailty. After adjustment for age, sex, BMI, smoking, and HbA1c, we found a positive association between frailty and TSH concentration, but negative associations between frailty and T3 concentration, ADL score, and IADL score. The negative association between the presence of frailty and T3 concentration might be confounded by the presence of non-thyroidal illness syndrome (NTIS), which is defined as the typical changes in serum thyroid-related hormone concentrations (reduced TT3, increased reverse T3) following any acute or severe illness not arising from an intrinsic abnormality in thyroid function (19). In the present study, we did not assay reverse T3, but as described earlier, we excluded critically unwell patients from participating. Therefore, it is less likely that our results were confounded by this factor.

Our study produced the interesting finding that a high TSH concentration was associated with frailty in both sexes, which were consistent with the results of the Progetto Veneto Anziani study (11). According to the Progetto Veneto Anziani study, a high TSH concentration was associated with frailty in both men and women in cross-sectional analyses, while a low TSH concentration in women only was associated with an increased risk of frailty in longitudinal analyses. There were several possible interpretations to clarify the result. First, the presence of high TSH levels, such as those found in subclinical hypothyroidism, was associated with mild inflammation (20). There are two studies observed a correlation between TSH and CRP, patients with subclinical hypothyroidism have higher CRP concentrations, which suggests for mild inflammation (20,21). Both hyper-and hypothyroid states are associated with heart failure. Thyroid hormone, in particular the T3 metabolite is essential for normal myocyte and peripheral cardio-vascular function. The high triiodothyronine can increase resting heart rate, left ventricular ejection fraction, blood volume, and tissue metabolism, which can cause progressive left ventricular dysfunction and heart failure. About the hypothyroidism, the effects include reduced chronotropy and inotropy as well as an increase in afterload and a consequent overall reduction in stroke volume and cardiac output (22). These studies showed that high TSH levels could increase triglyceride levels and lead to increased cardiovascular disease, a condition correlated with frailty. Second, it is known that both subclinical and clinical hypothyroidism can give rise to overall metabolic reduction, and cause symptoms such as tiredness, depression, and fatigability, which are typical characteristics of frailty. Hypothyroidism is a frequent disease among the elderly, its severity depending on the degree of thyroid insufficiency. Subclinical hypothyroidism could generate hypercholesterolemia and increase the risk for coronary heart disease and cardiac mortality (23). Subclinical thyroid dysfunction has been associated with different adverse outcomes, such as cardiovascular disease, cognitive disturbances, neuromuscular impairments, and falls (4). Symptoms and signs of hypothyroidism might be mild or even absent in the elderly. Therefore, the diagnosis of thyroid dysfunction is based primarily on biochemical abnormalities. Hypothyroidism is defined as serum TSH concentrations above the reference range with low free T4 levels, and Subclinical hypothyroidism defined as elevated TSH levels with normal free T4 levels. Subclinical hypothyroidism can be divided into two categories according to TSH level: mild subclinical hypothyroidism, TSH <10 m IU/L; Severe subclinical hypothyroidism, TSH >10 m IU/L (24). The serum TSH levels increased with age in older people, thus, very mild TSH elevations in older individuals may not reflect subclinical thyroid dysfunction but rather be a normal consequence of aging. Re-evaluation of TSH in conjunction with biomarkers of autoimmunity, the degree to which TSH hormone concentrations have deviated, the patient's health condition, the potential presence of dyslipidemia and other metabolic derangements should be considered (25). Finally, neuromuscular abnormalities and low exercise tolerance are frequently observed in subjects with high TSH levels, and these abnormalities and signs have negative impacts on quality of life and overlap with frailty (26,27). Of course, because ours is an observational study, the finding of a relationship between TSH and frailty does not necessarily indicate causation. It is possible that TSH and frailty are not cause and effect, but an interaction effect.

To the best of our knowledge, several other studies (3,4,28) did not find a significant association between serum TSH concentration and frailty. The following reasons may account for this contradiction. First, the previous studies enrolled community-dwelling participants, while the present study enrolled inpatients. Second, either women or men only were included in the previous studies, not both, which cannot represent the total population. Furthermore,

the prevalence of thyroid dysfunction and frailty differ between men and women. Finally, the different evaluation tools used to assess frailty could play a role in the different findings. Compared with other methods, the FRAIL scale used in the present study is simple to use and can be easily accommodated as part of a comprehensive geriatric assessment in clinical settings. Woo *et al.* (29) confirmed that the FRAIL scale proposed for use in clinical settings was comparable to other existing screening tools. The FRAIL scale was also validated as a powerful predictor of subsequent mortality and disability (16). On this basis we consider our cross-sectional study provided representative research to investigate the relationship between thyroid hormone levels and frailty at inpatients in our Department of Geriatrics.

A relationship between serum FT4 and frailty was absent in the present study. Based on the thyroid-pituitary-hypothalamus feedback regulation system, a negative log-linear relationship was found between serum FT4 and TSH levels (30). This means that very small changes in FT4 levels can induce very large reciprocal changes in TSH levels, thus TSH is a very sensitive index for reflecting thyroid function. Kundsen *et al.* (31) found a positive association between BMI and serum TSH and a negative association between BMI and serum FT4. In another study, cigarette smoking was associated with higher serum FT4 and lower serum TSH (32). However, in other studies, clinical events were reported to be significantly associated with TSH, but not FT4. For example, metformin treatment significantly lowered serum TSH, but did not change serum FT4 (33), and Chiaravalloti *et al.* (34) found a significant positive correlation between serum TSH and cortical F-18 FDG uptake in patients with Alzheimer's disease, but no significant relationship between cortical F-18 FDG uptake and serum FT4. As serum TSH tends to become higher with increasing age (35), we suppose that pituitary sensitivity to FT4 is enhanced in aging persons. However, further studies are needed to test this hypothesis.

In the present study, the scores for ADL and IADL were negatively associated with frailty, meaning that as ADL and IADL increased, the incidence of frailty decreased. These findings were consistent with the results of two studies on community-dwelling participants (36,37), which demonstrated that frailty was associated with significantly higher risks of incident ADL and IADL disability compared with non-frailty. Disabilities in ADL and IADL are adverse outcomes of frailty and can place a large burden on frail persons. ADL and IADL are also essential activities that people need to perform to be able to live independently. Therefore, we should look for effective interventions that can prevent these disabilities to diminish the burden caused by frailty in future studies.

There are several limitations to the present study. First, it was a cross-sectional observational study, which limits the ability to research causal relationships. Second, it was a single-center study with a small sample size, which limits the power to demonstrate a relationship between thyroid hormone levels and frailty. A multi-center study with large sample study should be added for verification in future. Finally, because of the small number of cases, we were unable to explore the potential relationships between thyroid function or thyroid status and individual components of the FRAIL scale. The study researched by Yeap.et.al found that neither subclinical hyperthyroidism nor subclinical hypothyroidism was significantly associated with frailty (3). However, another study among community-dwelling older men, demonstrated that subclinical hyperthyroidism, but not subclinical hypothyroidism, is associated with increased odds of prevalent frailty (4). Further studies would be needed to test the relationship between thyroid function or function status and frailty. Despite these limitations, the superiority of the study includes its assessment of complete thyroid hormone levels (TSH, FT4, FT3, TT3, TT4, TPOAb, and TgAb), and that it provided a unique opportunity to examine the relationship between thyroid hormone levels and frailty in older inpatients at the greatest risk of being frail. Consequently, our study cohort can be regarded as being more representative of inpatients in geriatric departments than the cohorts in previous studies.

Conclusions

In conclusion, inpatients in our Department of Geriatrics with higher TSH levels were found to be at increased risk of frailty. The prevalence of frailty increases with aging, and preventing the development of frailty in older persons preserves individual health and independence, and is an important community health measure. However, the potential contribution of thyroid hormone levels to frailty in older persons remains poorly understood. Elevated circulating TSH may be an independent and significant predictor of frailty among older persons, but future longitudinal studies are needed to confirm this.

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). This research protocol was approved by the institutional ethics board of Sichuan Provincial People's Hospital (No.2019-331). Informed consent was taken as written form from all the patients.

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