Article

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A Horizontal and Longitudinal Study on the Changes of Aging Thyroid Function in Elderly Male Population

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Objectives: There are few follow-up studies on thyroid function in the same group for many years. Therefore, the purpose of this study was to retrospectively analyze the changes of thyroid function in a group of people for 8 years and to explore the changes of thyroid function in elderly men with normal thyroid function with age.

Methods: Reviewing the records of elderly men who underwent physical examination in the Beijing Hospital physical examination center from 2013 to 2020, 354 subjects were included in the study. According to age, they are divided into 4 groups. The differences in thyrotropin (TSH), anti-triiodothyronine (rT3), free triiodothyronine (FT3), and free thyroid hormone (FT4) among different age groups in initial time (2013) were compared. Longitudinal comparison of changes of thyroid function in the same age group for 8 years was compared too.

Results: At the initial time, age was negatively correlated with FT3 (r = 0.349, $p < 0.001$), positively correlated with rT3 and TSH (r = 0.182, $p < 0.001$, r = 0.212, $p < 0.001$), but not correlated with FT4. The results of eight years of analysis show that, for TSH, during the whole follow-up period, the TSH of the >80 years group was higher than that of the <60 years and 60–69 years groups, and the difference was statistically significant. The 70–79 age group was higher than the <60 years group at different time points, except for the age group <60 years. The other three groups showed an increasing trend with age, especially in the group of ≥80 years. For FT3, in 2013, the age ≥80 years group was significantly lower than that of the 70–79 years, 60–69 years, and <60 years old groups ($p < 0.05$). The analysis results at different time points in each age group showed a downward trend and then an upward trend. For FT4, there was no significant difference in FT4 among different age groups in 2013. Still, during the follow-up period, the age group ≥80 was lower than other age groups in 2019 and lower than the <60 years groups in 2014, 2015, 2019, and 2020, and the difference was statistically significant. The change rule of FT4 with the increase of age was not clear. For rT3, during the whole follow-up period, the rT3 of the >80 years group was higher than that of the <60 years and 60–69 years groups, and the difference was statistically significant. The analysis results at different time points in each age group showed a trend of rising first, then falling, and finally rising. After 2017, the rT3 of the 70–79 years and ≥80 years groups increased with age.

Conclusions: The thyroid function index of elderly men changes with age. In transverse analysis, the value of TSH is the highest, and FT3 is the lowest in the group ≥80 years old. There are differences between the changes in the longitudinal analysis and the results of the horizontal analysis. Therefore, the law of thyroid function changing with age in different individuals is not the same as that of the same individual with age, which should be paid more attention in medical research and clinical diagnosis and treatment.

Keywords: thyroid function; male; increase in age

Introduction

The thyroid gland plays an important role in the process of human aging. Significant changes in histology, biochemistry, and function have been observed in the thyroid gland of elderly individuals [1]. The results of epidemiological investigation of 78,470 cases in 31 provinces and cities of China showed that the overall prevalence rate of thyroid disease was 50.96%, and the prevalence rate of thyroid disease in the elderly was higher than that in the general population [2]. Thyroid disease is common with metabolic syndrome, diabetes, hypertension, dyslipidemia and other common diseases in the elderly [3]. Therefore, it is particularly important to study the relationship between thyroid function and age. There have been numerous studies on the relationship between thyroid hormone and age, but they have produced conflicting results, at present, most studies compare thyroid function among different age groups, but

few studies exist evaluating longitudinal thyroid function with age [1]. In the present study, a retrospective analysis was conducted to assess changes in thyroid function in the male population over the past 8 years. Additionally, a horizontal comparison of different age groups in the same year and a vertical comparison were performed. These data will provide information that accurately reflects the changes in thyroid function with age.

Materials and Methods

We extracted the thyroid function data from the male physical examination population of Beijing Hospital from 2013 to 2020 through the electronic medical record system and made a cross-sectional analysis of the thyroid function data of the population at the initial time (2013). The annual thyroid function data from 2013 to 2020 were longitudinally analyzed. To reduce confounding factors, the following entry and discharge standards were adopted, and the admission criteria were as follows: (1) age $\geq$40 years old; (2) male; (3) thyroid function tests every year; (4) negative thyroid autoantibodies (thyroid peroxidase antibody (TPOAb) $<$70 IU/mL, anti-thyroglobulin antibody (TgAb) $<$70 IU/mL). Exclusion criteria: (1) thyroid system diseases were diagnosed during follow-up; (2) drugs affecting the results of thyroid hormone determination were used during or within one month during the determination of thyroid function; (3) those in critical condition and in the late stage of the disease, including patients with severe cardiovascular, respiratory, renal, nervous system diseases and expected survival of less than 1 year. The inclusion and exclusion of all subjects were completed by the same attending endocrinologist. The thyroid function data of 919 men $\geq$40 years old were screened initially (2013). Finally, after excluding participants with evidence of thyroid disease, positive thyroid antibodies, missing data, and those who breached other exclusion criteria, we derived a reference group of 354 subjects. Fig. 1 shows participant disposition. The initial time age of this group is 45–97 years, with an average age of 70.9 years. The subjects were divided into four groups according to their initial age: $<$60 years, 60–69 years old, 70–79 years, and $\geq$80 years. A study has shown that the level of thyroid-binding globulin decreases with age, so the change of free thyroid hormone is more sensitive [4]. Due to the limited space, this article does not show the statistical results of total-triiodothyronine (TT3) and total thyroxine (TT4). This study has passed the ethical review of the Beijing Hospital Ethics Committee.

The indexes of thyroid function were detected by the ADVIACentaurCP chemiluminescence immunoanalyzer of Siemens and enzyme-labeled chemiluminescence reagents provided by Siemens (Berlin, Germany). rT3 was detected by FTG- 630 automatic radioimmunoassay produced by the Beijing 261 factory, and the experimental reagent was an rT3 kit provided by the China Atomic Energy Technology Research Institute. Normal reference range: free triiodothyronine (FT3) 2.3~4.2 pg/mL ($\geq$80 y 1.9~3.5 pg/mL), free thyroid hormone (FT4) 0.89~1.76 ng/dL, differences in thyrotropin (TSH) 0.35~5.5 µIU/mL, TGAb 0~70 IU/mL, TPOAb 0~70 IU/mL, rT3 32.5~66.4 ng/dL [1]. At present, there is no clear normal range of TSH and rT3 levels in the elderly over 80 years old, such as TSH and rT3 beyond the normal range [1]. Subjects not diagnosed with thyroid disease or treated with related drugs were included.

Statistical Analysis

The data were analyzed using R version 4.3.2. Basic characteristic data is presented as mean $\pm$ standard deviation if the continuous quantitative data conforms to the normal distribution. One-way analysis of variance (ANOVA) was used to compare multiple groups, Least Significant Difference (LSD) method was used for comparison after the event. For data that does not accord with the normal distribution, the median is used for statistical description, and the rank sum test is used for the comparison between groups; for the counting data, the number of cases (%) is used to describe, and the chi-square test or Fisher exact probability method is used for comparison between groups. Spearman correlation analysis carried out the correlation analysis between age and initial time, FT3, FT4, rT3, or TSH, and the scatter plot was drawn for visualization. The generalized estimation equation (GEE) was used for the comparative analysis of FT3, FT4, rT3, TSH, and other indexes in different age groups at different times to account for the longitudinal repeated measurement data are not independent and may be missing. The homework correlation matrix is set exchangeable, considering the possible impact of uneven distribution of covariables in different age groups on the results. When carrying out the GEE, we corrected body mass index (BMI), smoking, diabetes, hypertension, and endocrine system diseases in the model and drew a line chart and bar chart based on the estimated mean for visualization. In the post-comparison, we used the false discovery rate (FDR) method to correct p values and the significant letter marking method to mark results. All the tests were bilateral, and the difference was considered statistically significant at $p < 0.05$.

Results

Study Subjects

The general characteristics of subjects at study initiation and group distributions are summarized in Table 1. A total of 354 male subjects were enrolled, with an average age of 70.97 $\pm$ 10.60 years. Statistical analysis of the basic data of different age groups showed that there were significant differences in smoking, diabetes, hypertension, and endocrine system diseases among the four groups. Still, there was no significant difference in BMI and malignant tumors.

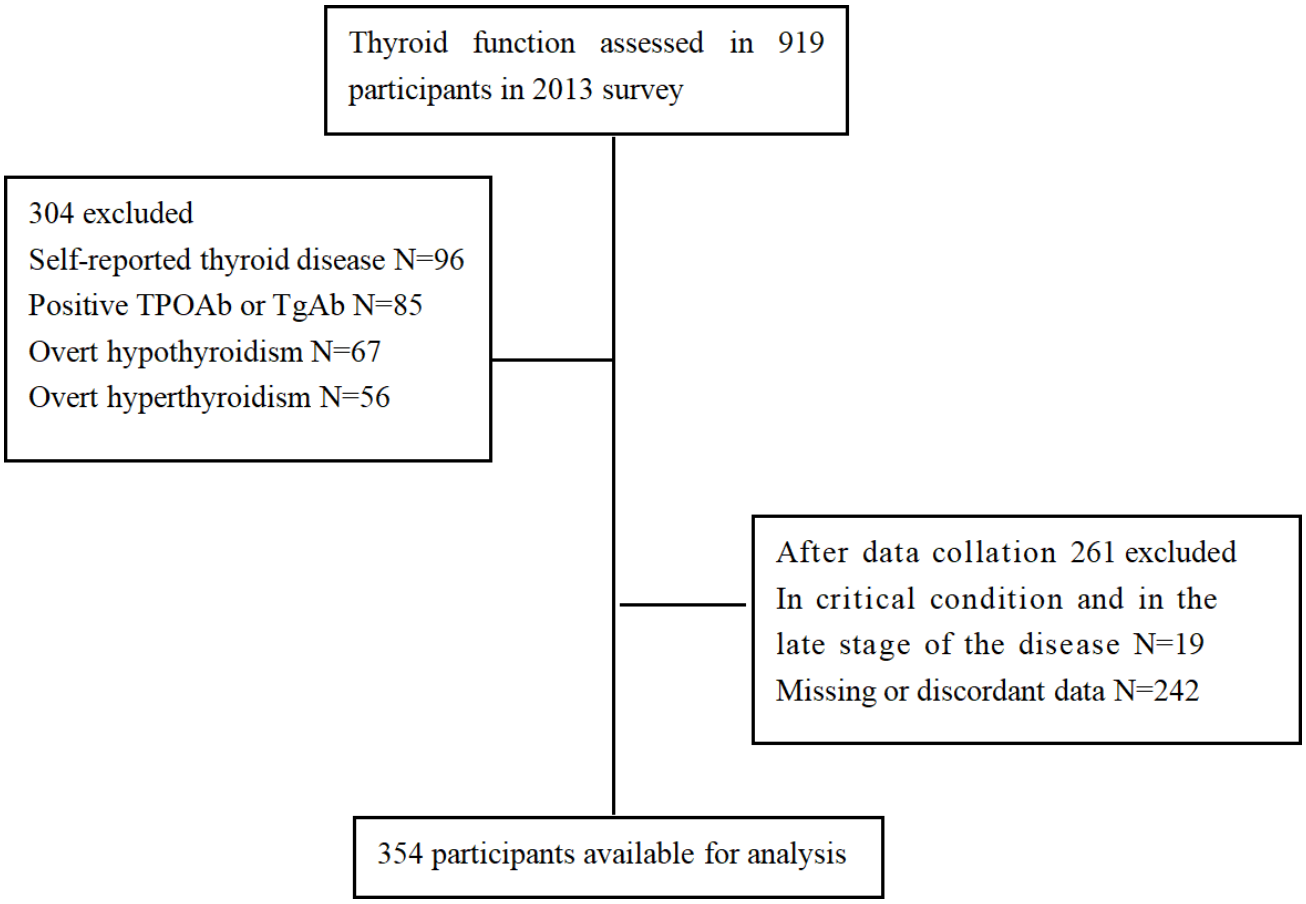

Fig. 1. Participant disposition.

Correlation Analysis between Thyroid Function Indexes and Age at Initial Time

Spearman correlation analysis was used to analyze the correlation between age and initial time (2013) FT3, FT4, rT3, and TSH. The results showed that age was negatively correlated with FT3 ($r = 0.349$, $p < 0.001$, Fig. 2A), positively correlated with rT3 ($r = 0.182$, $p < 0.001$, Fig. 2C), positively correlated with TSH ($r = 0.212$, $p < 0.001$, Fig. 2D), but not significantly correlated with FT4 ($r = 0.034$, $p < 0.524$, Fig. 2B), as shown in Fig. 2.

Cross-Sectional Analysis and Longitudinal Analysis

The same group of elderly men was stratified by age, and the changes in thyroid function in the 8 years from 2013 to 2020 were compared. Data are summarized in Table 2 and visualized in Figs. 3,4.

For TSH, the results of the GEE showed a significant difference in TSH among different age groups (Group: $p < 0.001$) and time (Time: $p < 0.001$), but there was no significant difference in TSH among different age groups over time (Group*time: $p = 0.999$). During the whole follow-up period, the TSH of the >80 years group was higher than the <60 years and 60–69 years groups, and the difference was statistically significant. The 70–79 years group was higher than the <60 years group at different time points, but there was no significant difference between the 70–79 years and 60–69 years groups. During the follow-up period, TSH showed an upward trend with the increase of the age group. The results of analysis at different time points in each age group showed that the changes in TSH levels in each group were statistically significant ($p < 0.001$). Except for the age group <60 years, the other three groups showed an increasing trend with age, especially in the group of ≥80 years.

Significant differences in FT3 were observed among different age groups (Group: $p < 0.001$), time (Time: $p < 0.001$), and FT3 changes with time in different age groups (Group*time: $p < 0.001$). In 2013, the FT3 of the age ≥80 years group was significantly lower than that of the 70–79 years, 60–69 years, and < 60 years groups ($p < 0.05$). During the whole follow-up period, there was no significant difference in the level of FT3 between the two groups aged 60–69 and <60 years. FT3 in the ≥80 years group was significantly lower than in other low age groups (all $p < 0.05$). The age group of 70–79 years was lower than that of the other two low age groups ($p < 0.05$). The results of analysis at different time points in each age group showed changes in FT3 levels for each group were statistically significant ($p < 0.001$) and showed a downward trend and then an upward trend. The trend of decreasing with age is more significant in the ≥80 years group; the highest value of FT3

Table 1. Initial time general characteristics of 354 study subjects.

Variables	Total (n = 354)	<60 (n = 64)	60~69 (n = 86)	70~79 (n = 124)	≥80 (n = 80)	statistic	*p*
Age	70.97 ± 10.60	55.27 ± 3.35	64.77 ± 2.91	74.48 ± 2.86	84.75 ± 4.21	1090.82	< 0.001
Gender, n (%)						-	-
Male	354 (100)	64 (100)	86 (100)	124 (100)	80 (100)		
BMI	25.18 ± 2.89	25.38 ± 2.53	25.78 ± 2.84	25.02 ± 2.97	24.61 ± 3.00	2.55	0.056
Smoking status, n (%)						12.63	0.006
Never	207 (58.5)	46 (71.9)	49 (57)	77 (62.1)	35 (43.8)		
Current	147 (41.5)	18 (28.1)	37 (43)	47 (37.9)	45 (56.2)		
Diabetes, n (%)	140 (39.5)	11 (17.2)	37 (43)	54 (43.5)	38 (47.5)	16.77	< 0.001
Hypertension, n (%)	244 (68.9)	33 (51.6)	55 (64)	92 (74.2)	64 (80)	16.19	0.001
Endocrine system diseases*, n (%)	54 (15.3)	1 (1.6)	11 (12.8)	20 (16.1)	22 (27.5)	19.04	< 0.001
Malignant tumor, n (%)	80 (22.6)	10 (15.6)	19 (22.1)	27 (21.8)	24 (30)	4.35	0.226

* Endocrine system diseases refer to other endocrine and metabolic diseases except diabetes and thyroid system diseases. BMI, body mass index.

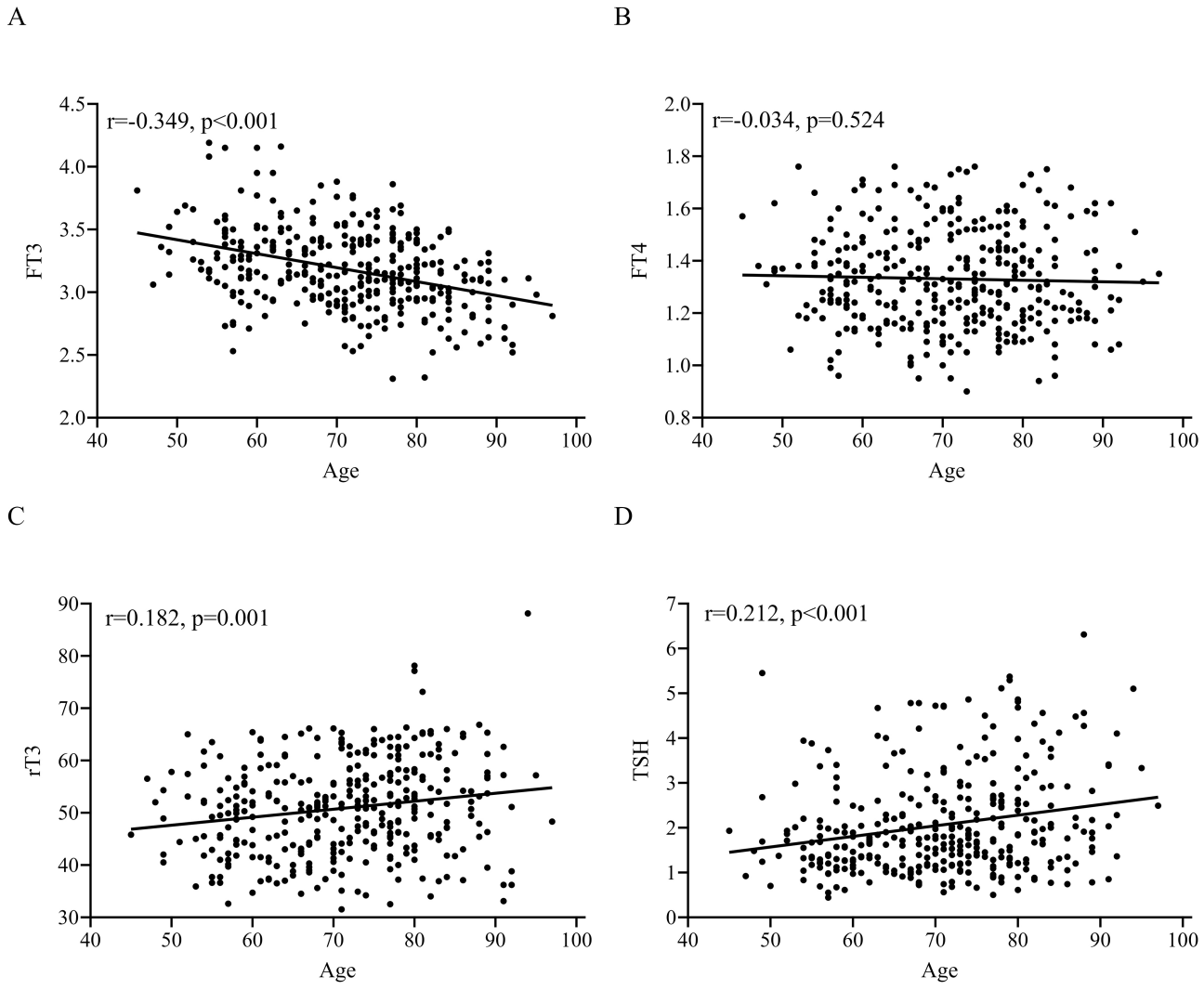

Fig. 2. Scatter plot of correlation analysis between age and initial time free triiodothyronine (FT3) (A), free thyroid hormone (FT4) (B), anti-triiodothyronine (rT3) (C), thyrotropin (TSH) (D).

was in the first year, and the low value was concentrated in the 4th and 5th year of the test, then gradually returned to the initial time level, and the value of the 7th and 8th year did not exceed the initial time level.

Table 2. Generalized estimation variance analysis of each index.

Variables	<60 (n = 64)	60 69 (n = 86)	70 79 (n = 124)	≥80 (n = 80)	GEE
FT3					
2013	3.29 ± 0.33	3.29 ± 0.29	3.17 ± 0.31	3.01 ± 0.26	Group: $\chi^2 = 865.19, p < 0.001$
2014	3.38 ± 0.38	3.27 ± 0.38	3.12 ± 0.36	2.86 ± 0.30	Time: $\chi^2 = 288.89, p < 0.001$
2015	3.13 ± 0.36	3.10 ± 0.35	3.01 ± 0.34	2.80 ± 0.29	Group*Time: $\chi^2 = 66.78, p < 0.001$
2016	3.08 ± 0.25	3.06 ± 0.30	2.95 ± 0.27	2.68 ± 0.26	
2017	3.23 ± 0.32	3.19 ± 0.31	3.00 ± 0.31	2.68 ± 0.28	
2018	3.43 ± 0.31	3.35 ± 0.33	3.19 ± 0.29	2.84 ± 0.30	
2019	3.39 ± 0.32	3.34 ± 0.32	3.17 ± 0.31	2.81 ± 0.32	
2020	3.43 ± 0.32	3.39 ± 0.33	3.22 ± 0.36	2.77 ± 0.34	
FT4					
2013	1.32 ± 0.17	1.35 ± 0.20	1.33 ± 0.18	1.33 ± 0.19	Group: $\chi^2 = 23.52, p < 0.001$
2014	1.33 ± 0.22	1.30 ± 0.19	1.30 ± 0.19	1.27 ± 0.19	Time: $\chi^2 = 108.39, p < 0.001$
2015	1.27 ± 0.17	1.22 ± 0.19	1.24 ± 0.16	1.20 ± 0.18	Group*Time: $\chi^2 = 13.98, p = 0.870$
2016	1.24 ± 0.21	1.22 ± 0.18	1.23 ± 0.18	1.19 ± 0.19	
2017	1.29 ± 0.20	1.27 ± 0.20	1.27 ± 0.17	1.24 ± 0.17	
2018	1.30 ± 0.18	1.31 ± 0.18	1.28 ± 0.18	1.28 ± 0.18	
2019	1.29 ± 0.21	1.25 ± 0.19	1.24 ± 0.17	1.17 ± 0.17	
2020	1.28 ± 0.18	1.30 ± 0.18	1.29 ± 0.17	1.25 ± 0.20	
rT3					
2013	48.76 ± 7.34	48.82 ± 8.44	51.63 ± 8.31	53.33 ± 10.73	Group: $\chi^2 = 168.67, p < 0.001$
2014	49.63 ± 9.63	49.78 ± 11.48	53.93 ± 11.21	56.04 ± 12.32	Time: $\chi^2 = 104.19, p < 0.001$
2015	53.71 ± 9.60	54.78 ± 10.18	57.15 ± 10.54	60.37 ± 12.59	Group*Time: $\chi^2 = 15.74, p = 0.784$
2016	49.86 ± 9.90	51.35 ± 10.87	55.86 ± 11.65	56.89 ± 12.40	
2017	52.41 ± 9.30	52.52 ± 10.02	55.37 ± 10.01	58.48 ± 12.43	
2018	47.28 ± 9.72	48.23 ± 9.89	50.97 ± 9.73	56.13 ± 12.71	
2019	48.26 ± 11.36	48.33 ± 8.91	51.99 ± 10.12	57.55 ± 15.18	
2020	50.56 ± 10.47	51.25 ± 8.07	54.37 ± 10.03	61.35 ± 13.45	
TSH					
2013	1.76 ± 0.95	1.87 ± 0.98	2.09 ± 1.13	2.48 ± 1.27	Group: $\chi^2 = 117.15, p < 0.001$
2014	1.93 ± 1.02	2.05 ± 1.10	2.28 ± 1.43	2.52 ± 1.43	Time: $\chi^2 = 63.92, p < 0.001$
2015	1.93 ± 1.09	2.24 ± 1.58	2.51 ± 2.28	2.62 ± 1.53	Group*Time: $\chi^2 = 6.60, p = 0.999$
2016	1.73 ± 1.07	2.05 ± 1.13	2.13 ± 1.23	2.59 ± 1.61	
2017	2.08 ± 1.06	2.40 ± 1.41	2.56 ± 1.60	2.98 ± 1.71	
2018	1.99 ± 1.00	2.30 ± 1.32	2.52 ± 1.52	2.89 ± 1.94	
2019	2.07 ± 1.02	2.36 ± 1.28	2.60 ± 1.64	3.13 ± 2.02	
2020	2.21 ± 1.05	2.41 ± 1.45	2.69 ± 1.61	3.33 ± 2.30	

GEE, generalized estimation equation.

For FT4, the GEE analysis revealed a significant difference among different age groups (Group: $p < 0.001$), and there was significant difference in FT4 over time (Time: $p < 0.001$), but no significant difference in FT4 among different age groups (Group*time: $p = 0.870$). There was no significant difference in FT4 among different age groups in 2013. Still, during the follow-up period, the age group ≥80 was lower than that of other age groups in 2019 and lower than those of the <60 age groups in 2014, 2015, 2019, and 2020, and the difference was statistically significant ($p < 0.05$). The results of analysis at different time points in each age group showed that the changes in FT4 levels in each group were statistically significant ($p < 0.001$). However, the change in FT4 with increased age was unclear. The measured value decreased in the 3rd, 4th, and 5th years, increased in the 6th year, decreased in the 7th year, and increased again in the 8th year, and did not exceed the initial time level.

For rT3, the results of the GEE showed significant differences in rT3 among different age groups (Group: $p < 0.001$), with time (Time: $p < 0.001$), but there was no significant difference in rT3 among different age groups (Group*time: $p = 0.784$). During the whole follow-up period, the rT3 of the ≥80 years group was higher than the <60 years and the 60–69 years groups, and the difference was statistically significant ($p < 0.05$). Except in 2015, the rT3 of the 70–79 years group was significantly higher than the <60 years and 60–69 years groups ($p < 0.05$). The rT3

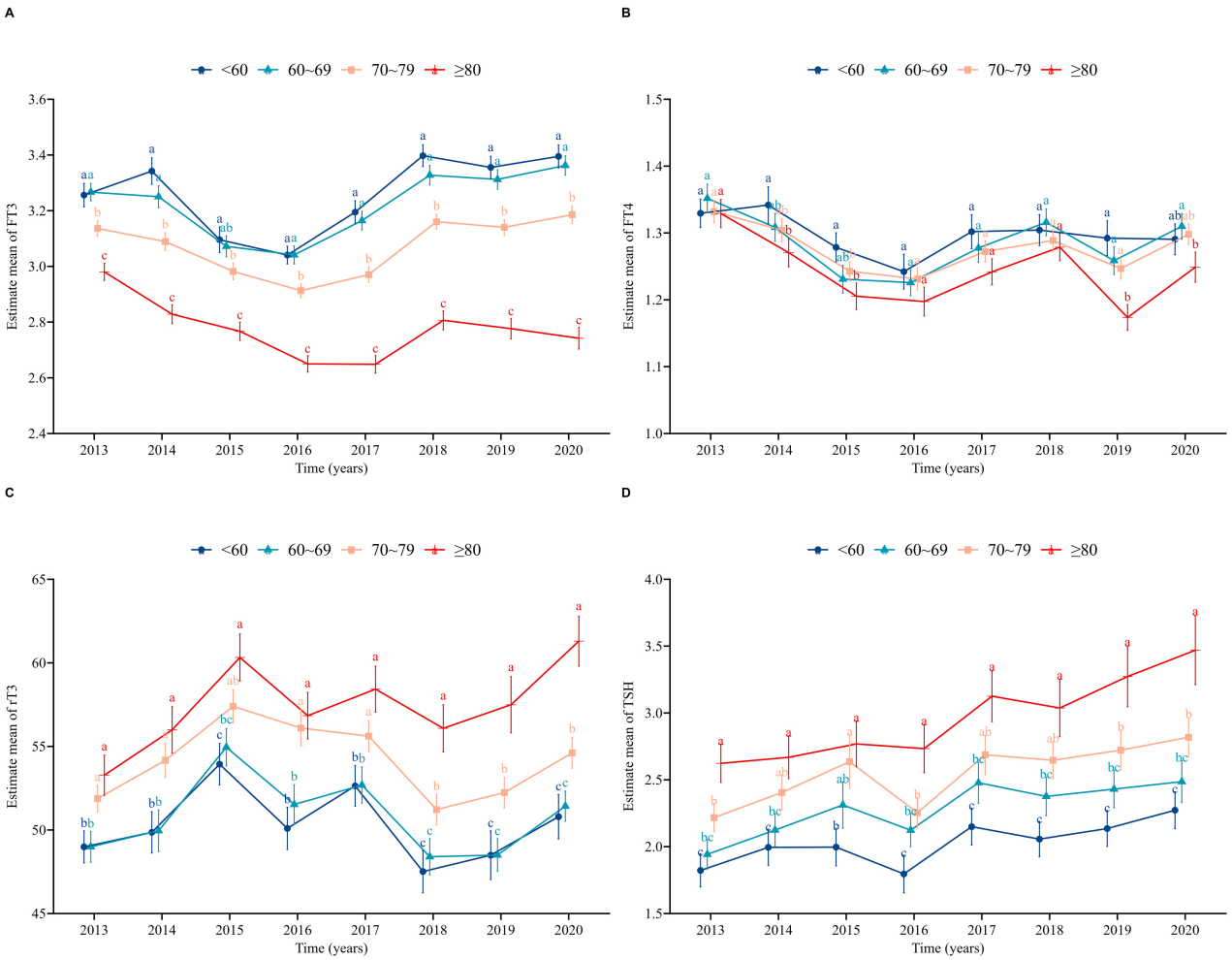

Fig. 3. Estimation mean line chart (mean and SE) of generalized estimation equation: FT3 (A), FT4 (B), rT3 (C), and TSH (D) changes with time in different age groups. abc is significant letter marking method, at the same time point, the difference between groups with the same letter is not statistically significant, otherwise the difference is statistically significant.

of the 70–79 age group in 2015 is only greater than that of the <60 years group ($p < 0.05$), and there is no statistical significance compared with the 60–69 age group ($p > 0.05$). However, there was no significant difference between the 60–69 years group and the other three groups during the whole follow-up period. The results of analysis at different time points in each age group showed that the changes in rT3 levels in each group were statistically significant ($p < 0.001$). They all show a trend of rising first, then falling, and finally rising. After 2017, the rT3 of 70–79 years group and ≥80 years group increased with age, and there are statistical differences ($p < 0.05$). The <60 years group also had an increasing trend after 2017, but there was no statistical difference among the three years ($p > 0.05$).

Discussion

The population included in this study were males with good nutritional status, excluding confounding factors such as thyroid system diseases, the use of drugs affecting thyroid function, and suffering from critical diseases. The thyroid function of the observer was detected in the same laboratory, and the same detection method was used, so the results were more reliable. The number of people in the ≥90 years group who met the conditions for 8 years follow-up and those without critical illness and in the late stage of the disease was relatively small, so the statistics were combined with those in the ≥80 years group.

There are many horizontal comparative studies on thyroid function changes with age at home and abroad, but the results differ [1]. The Barthelton Health Survey in Australia was followed up for 13 years and showed serum TSH increased with age (an average increase of 0.32 mU/L over 13 years) [5]. At present, the vast majority of studies in adults have shown that serum T3 levels decrease with age [6], and a study has shown that T3 levels decrease with age occur mostly after 90 years of age [7]. For serum T4 and FT4 levels, the results are quite different. Due to age, sex, and health conditions, T4 and FT4 can remain unchanged, decrease, or increase, but most studies show that serum T4 and

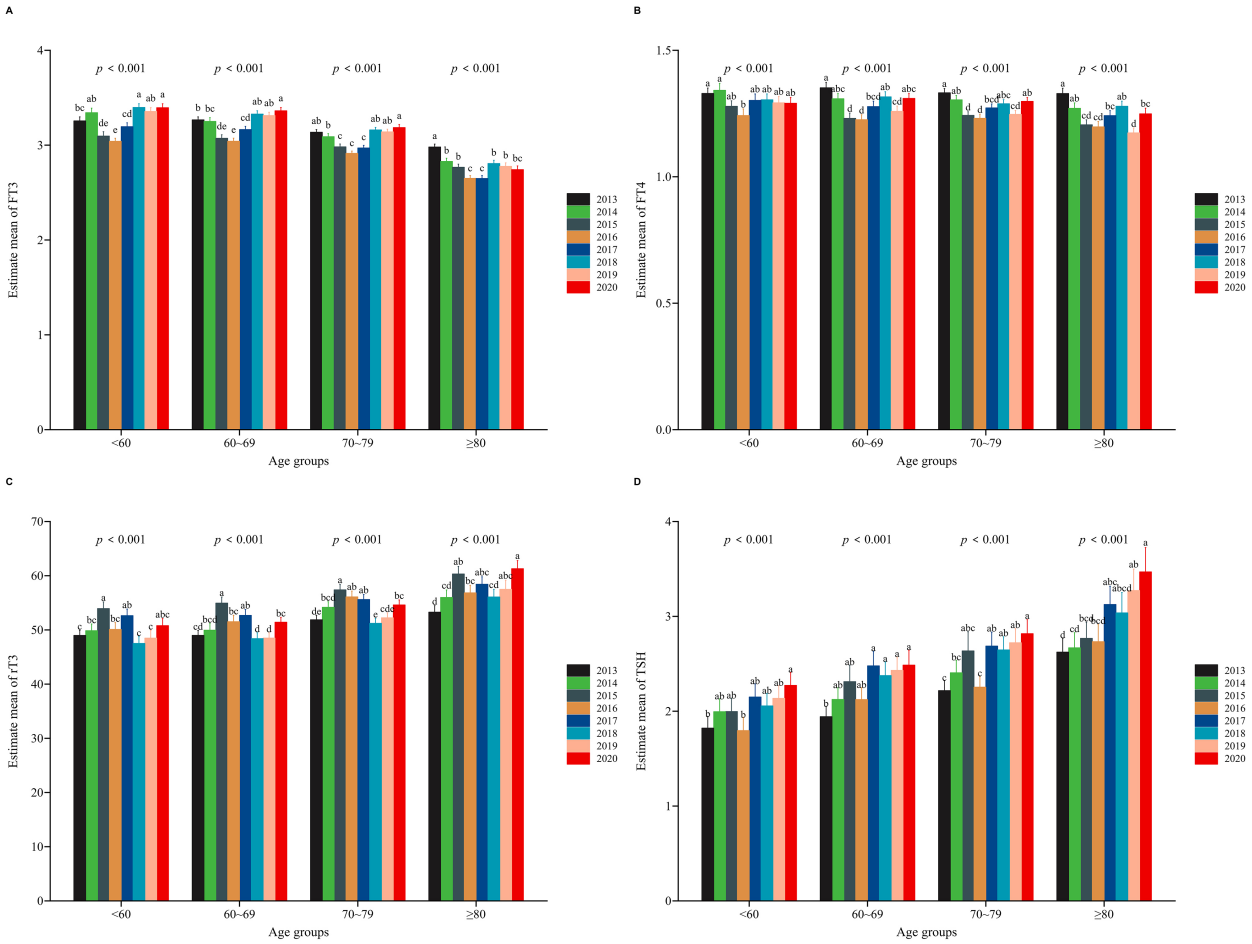

Fig. 4. Estimation mean histogram of generalized estimation equation: Changes of internal FT3 (A), FT4 (B), rT3 (C), and TSH (D) in different age groups with aging. abcde is significant letter marking method, at the same time point, the difference between groups with the same letter is not statistically significant, otherwise the difference is statistically significant.

FT4 levels do not change with age [8,9]. The present study on serum rT3 found that the aging trend was consistent. Peeters's study shows an independent correlation between the increase of rT3 and aging, and the level of rT3 increases with age [10]. The changing trend of thyroid hormone levels in healthy elderly people by Li Xin [11] in China also shows that rT3 is positively correlated with age.

In the correlation analysis, our results show that age has a negative correlation with FT3 and a positive correlation with rT3 and TSH, but no significant correlation with FT4. In the horizontal comparison of this study, during the whole follow-up period, the TSH of ≥80 years group was higher than that of <60 years and 60–69 years groups, and 70–79 years group was higher than that of <60 years group; for FT3, the FT3 of age ≥80 years group was lower than other three groups at initial time (2013); for FT4, there was no significant difference in FT4 among different age groups at initial time (2013). For rT3, during the whole follow-up period, the rT3 of ≥80 years old group was higher than that of <60 years old and 60–69 years groups. This is consistent with the results of most studies [5,8–11].

In the longitudinal analysis of thyroid function in stratified people of the same age for 8 consecutive years, there is a difference between the changing trend and the horizontal comparison. Because longitudinal analysis studies the same individual, it is more suitable to study the effects of aging than other individuals with different characteristics [7].

In the longitudinal comparison for TSH, except for the age group <60 years old, the other three groups showed an increasing trend with age, especially in the group of ≥80 years old. A study has shown that the setting value of pituitary TSH feedback inhibition is gradually reset in the elderly, which becomes apparent only in extreme aging [12]. At present, some scholars at home and abroad have suggested that the reference range of the normal value of TSH in the elderly should be adjusted [13]. Combined with the results of this study, it is suggested that the relevant reference range should be established according to age stratification. There are several explanations for the aging changes of TSH: (1) the sensitivity of TSH to negative feedback of thyroid hormone decreases, (2) the biological activity of

TSH decreases with age, and (3) the responsiveness of the thyroid to TSH decreases. Therefore, higher TSH concentration is needed to maintain the circulating concentration of peripheral thyroid hormone [14]. It is also speculated that the increase in TSH is the result of occult thyroid disease in the elderly [15]. Thyroid disease and the use of drugs affecting thyroid function have been excluded in this study, so it is proved that the age-related increase in TSH is not the result of thyroid disease, suggesting that it is not necessary to treat a mild increase in TSH in elderly patients.

In the horizontal study, most data showed that the serum T3 level decreased with age. The horizontal comparison in this study also supported this view. However, in the longitudinal study, FT3 decreased at first and then increased with age but did not exceed the 2013 level. The trend of decreasing with age is more significant in the group of older people ≥80 years; the highest value of FT3 was in the first year, and the low value was concentrated in the 4th and 5th year of the test, then gradually returned to the initial time level, and the value of the 7th and 8th year did not exceed the initial time level. Although the significant decrease of FT3 in the 4th and 5th years in the longitudinal study does not rule out the reason for different batches of test reagents, the overall trend is still to decline first. The reasons for the decrease of serum FT3 in the elderly may be as follows: (1) the aging changes of the thyroid gland with age, which affects the synthesis of T3 and T4 to a certain extent; (2) the serum 80% T3 of healthy people is caused by the deiodination of T4 in the liver and other tissues. The physical function of the elderly is degraded, and the metabolism and transformation of T4 are affected to a certain extent, which reduces the level of T3; (3) the reduction of food intake in the elderly leads to the decrease of substances needed for T4 deiodination, resulting in the decrease of serum T3 level [13]. In this study, the slow growth of FT3 levels in 2019 and 2020 is presumed to be due to the gradual increase of TSH with age and the gradual rise of FT3 to maintain body function. The specific mechanism needs to be confirmed by follow-up basic research.

In the horizontal comparison in 2013, FT4 did not change with age. Still, during the follow-up period, the age group ≥80 years old was lower than that of other age groups in 2019 and lower than those of the <60 age groups in 2014, 2015, 2019, and 2020, and the difference was statistically significant. In the longitudinal comparison, the change of FT4 fluctuated in a waveform curve with age; the change is irregular. A longitudinal analysis of 908 individuals in the Busselton health survey showed that after a 13-year period, there was no significant change in FT4 [4]. The decrease of peripheral T4 degradation and the reduction of thyroid binding globulin level with age may be the reasons for the constant or normal FT4 value of healthy elderly subjects [16].

In the horizontal comparison, during the whole follow-up period, the rT3 of ≥80 years old group was higher than that of <60 years old and 60–69 years old groups. Except for 2015, the rT3 of the 70–79 years old group was significantly higher than that of the <60 years old and 60–69 years old groups ($p < 0.05$), the rT3 of the 70–79 age group in 2015 was significantly higher than that of <60 years old group ($p < 0.05$), and there was no statistical significance compared with the 60–69 years old group. In the longitudinal study, the rT3 value increased with age at first, then decreased briefly, and then increased again. Especially in the group of ≥80 years old and 70–79 years old groups, the law of rT3 increasing with age is especially obvious in the last three years. Serum rT3 levels are often affected by diseases and other confounding factors. In a study of 403 elderly men without severe acute and chronic diseases (aged 73–94 years), 63 men showed that serum rT3 levels were higher than normal, which had nothing to do with the disease [17]. In this study, critical patients were excluded, and the increase of rT3 was considered related to aging. The reason is that in the process of aging, the demand for calories from human tissue continues to decrease, rT3 has no thermogenic activity, which will lead to the increase of rT3, this may be a protective mechanism for the body to avoid excessive metabolic consumption [12]. Our study found that the increasing trend of rT3 is more significant in the older age group. This is consistent with the results of the Newcastle study involving people over 85 years old, which shows that it has nothing to do with the burden of disease, the study also showed nothing to do with the burden of disease, that high rT3 is a predictor of all-cause mortality [18]. Therefore, the detection of rT3 in the elderly is particularly important.

There are still many limitations in this study; the sample size is relatively small, only the analysis of age and thyroid function, and no related multi-factor analysis. This paper only studies elderly men and cannot represent the female population [19]. In the follow-up study, we can expand the sample size and further study the impact of gender and other related factors on thyroid function.

Conclusions

In conclusion, we analyzed the thyroid function of 354 men without thyroid disease over 8 years. These data were compared not only horizontally in different age groups in the same year, but also longitudinally in the same age group for 8 years. The results of the horizontal comparison were consistent with those reported in most literature. TSH and rT3 increased gradually with age, while FT3 decreased with age. The results of the longitudinal comparison were different from those reported in the literature. FT3 in the same group decreased at first and then increased with age, while TSH and rT3 increased with age in the older group. The law of thyroid function changing with age in different individuals is not the same as that of the same individual with age,

and the specific mechanism needs to be confirmed by more basic research. More attention should be paid to medical research and clinical diagnosis and treatment.

Availability of Data and Materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions

LQ, evolution of overarching research goals and aims, design of methodology, writing — Review & Editing. RZ, design of methodology, formal analysis, writing — Original Draft. JD, data curation, performed the validation. YL, data curation, performed the validation. SX, preparation and presentation of the published work, specifically visualization/data presentation. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study has passed the ethical review of the Beijing Hospital Ethics Committee. The ethical approval number is 2020BJYYEC-242-02. Because the study is a retrospective study and does not require the informed consent of the patient, it has been approved by the Ethics Committee of Beijing Hospital.

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Conflict of Interest

The authors declare no conflict of interest.

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