Study of the relationship of thyroid status and frailty in older Egyptian men

Maha H. El Din Ibrahim[a], Mohamed M. Alsebaie[b], Haidy I. Elbendary[c], Elham M. Yousief[a]

Departments of [a]Internal Medicine, [b]Medical Biochemistry & Molecular Biochemistry, Faculty of Medicine, Cairo University, [c]National Institute of Diabetes and Endocrinal Glands, General Authority for Hospitals and Medical Institutions, Ministry of Health, Egypt

Correspondence Elham M. Yousief, MD, 66 Gaamat Eldwal, Mohandseen, Giza, 12511, Egypt. Tel: +20 122 222 17049; e-mail: drelhamyousief@gmail.com

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Background
This study was conducted in Endocrine and Diabetes Clinic (Cairo University) and National Institute of Diabetes and Endocrinal Glands from 2016 to 2017.
Aim
To recognize the relationship between thyroid status and frailty in older Egyptian men, as distinguishing proof of contrasts in thyroid function as a hazard factor for frailty gives added chances to recognize men in danger of more unfortunate well-being results.
Methods
The study included 100 geriatric Egyptians men without overt thyroid disorder. All patients were subjected to medical history and physical measurement including assessment of frailty by using FRAIL scale (Fatigue, Résistance, Ambulation, Illnesses and Loss of weight, with frailty represented by the presence of three or more of these elements), free thyroxine level and thyroid-stimulating hormone.
Results
The average age of the patients was 67.34±3.42 years. of 100 men, four patients were classified as having overt hyperthyroidism, two patients having overt hypothyroidism (2.0%), 10 patients having subclinical hyperthyroidism (10%), one patient with subclinical hypothyroidism (1.0%), and 83 patients were euthyroid (83%), and 40 men were classified as being frail. The authors found a positive correlation of frailty with age ($P<0.001$).
Conclusion
There is a statistically significant association of frailty with smoking ($P=0.014$) and hypertension ($P=0.003$). There was no factually noteworthy relationship between frailty and thyroid-stimulating hormone, free T4, and free T3, and no measurably statistically significant difference between frailty and change in thyroid function ($P=0.592$).

Keywords:
Egyptian men, frailty, thyroid disorders

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Introduction

Frailty is a condition described by loss of natural holds over numerous organ, loss of homoeostatic components, and vulnerability to function decompensation after minor events [1].

Frailty is firmly identified with the maturing process, which results from the collection of harm brought about by numerous systems at a subatomic and cell level, prompting slow utilitarian decay. However, the underlying process assist in frailty occurrence remain poorly understood in elderly peoples [2].

One phenotype of frailty can be characterized by the nearness of at least three of the accompanying five factors: unexpected weight reduction, depletion, poor hold quality, moderate strolling velocity, or low physical action [3]. Another strategy has been proposed utilizing a tool for assessment of frailty – the FRAIL scale [4]. This tool uses five components, that is, fatigue, resistance, ambulation, illnesses, and loss of weight, with frailty meant by the nearness of at least three of these components. The contributory factors that help advancement of frailty as individual age stay understood [1].

Numerous endocrinal changes happen during life time and are associated with the beginning of frailty [5]. Diminished testosterone levels in elderly men are connected with frailty and may add to exhaustion and muscle shortcoming in older men [6]. Insulin-

like development factor-I is another anabolic hormone that controls muscle bulk, whose levels reduce with increasing age [7].

Thyroid diseases (hyper or hypothyroidism) are normally connected with adverse effects of fatigue, decline in muscle strength, and weight changes, with unmistakable manifestations less regular in older individuals [8].

Subclinical hyperthyroidism happens when thyroid hormone levels are not raised, but thyrotropin [thyroid-stimulating hormone (TSH)] levels are suppressed [9]. This condition predicts expanded danger of cardiovascular events and dysrhythmia [10].

Subclinical hypothyroidism occurs when TSH levels are respectably raised with ordinary circling thyroid hormone levels (TSH >10 mIU/l) and is related with expanded danger of coronary illness [11].

Presently, it has been perceived that even a small change in the thyroid hormones occurring among euthyroid persons might be connected with metabolic disorder [12], atrial fibrillation [13], cardiovascular mortality [14] bone thickness, and the danger of fracture [15]. Nevertheless, there is not much information assessing the possible role of changes in the thyroid function between euthyroid patients and frailty in elderly [16].

The aim of this study was to assess the relationship between thyroid status and frailty in old Egyptians men, as recognizable proof of the distinctions in thyroid function as a hazard factor for frailty would improve the comprehension of the endocrine pathophysiology and give added prospective to discovering patients at risk of adverse well-being results.

Patients and methods

This study was conducted on one group of 100 geriatric Egyptian persons without overt thyroid disorder recruited from Kasr Al Aini Hospital Outpatient Endocrinology Clinic and National Institute of Diabetes and Endocrinal glands in the period from 2016 to 2017.

This cross-sectional study was conducted from April 2017 till April 2018 after approval of the Institutional Ethical Committee. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000.

All participants signed a written informed consent form before enrollment in the study to complete the requirement of the Ethical Committee of the Faculty of Physical Therapy, Cairo University, and to ensure complete satisfaction. All participants of the study were informed about the study, its aim, all risks, and expected benefits and also assured of their anonymity and confidentiality of data obtained before signing the informed consent form.

The exclusion criteria were younger population and geriatrics with existing thyroid diseases at gauge, including those with a background marked by thyroidectomy, treatment with radioactive iodine, or utilization of thyroid-related drugs.

In all patients, thorough clinical evaluation was performed including past history of thyroid diseases, any medical history, use of thyroid medications, weight (in kilograms), height (in centimeters), BMI, any sign of hypothyroidism or hyperthyroidism, and assessment of frailty by using FRAIL scale. Free T3, free T4, and TSH were also assessed for all participants.

Appraisal of frailty was done by utilizing FRAIL scale [4].

Frailty is distinguished by the nearness of at least three of the following measures: fatigue, resistance, ambulation, illnesses, and loss of weight.

Scale's five domains were as follows:

(1) Fatigue.
(2) Resistance (trouble climbing one trip of stairs).
(3) Ambulation (trouble strolling 100 meters).
(4) Illnesses (>5).
(5) Loss of weight (>5%).

Evaluation of exercises of everyday living and instrumental exercises of day by day living

The participants were approached to reply with, being capable, capable with assistance, or not capable about the two key divisions of utilitarian capacity: exercises of everyday living (ADL) and instrumental exercises of day by day living (IADL).

ADL: self-maintenance activities that an individual performs every day (e.g. eating, dressing, washing, moving between the bed and a seat, utilizing the can, and controlling bladder and gut capacities) [17].

IADL: the activities that are expected to live leisurely (e.g. doing housework, planning suppers, taking

meds appropriately, overseeing funds, and utilizing a phone) [18].

Hindrance of hearing or seeing [19]

The participants were approached to reply with Yes or No to 'Difficulty seeing close to articles' and 'Difficulty in hearing a discussion.' Participants were coded as having visual or hearing hindrance on the off chance that they addressed 'Yes' to the previous or last mentioned, separately.

Assessment of memory [20]

The participants were asked to repeat three unrelated words immediately and after some time (recall test).

Assessment of behavior

The participants were asked to answer with Yes or No about having any of anxiety, agitation, irritability, aggressiveness, or any behavioral problem in general.

Timed get up and go test [21] was done for all participants:

The participants were asked to sit in a straight backed high seat chair and they were instructed the following:

(1) Get up (without use of armrests, if possible).
(2) Stand for moments.
(3) Walk forward 10 feet (3 m).
(4) Turn around and stroll back to seat.
(5) Turn and be seated.

The following were noted:

(1) Sitting balance.
(2) Transfer from sitting to standing.
(3) Stability of walking.
(4) Ability to turn steadily.

The hazard to fall was surveyed:

0=no fall chance (all around composed developments, without strolling help).
1=low fall hazard (controlled, however, balanced developments).
2=some fall hazard (awkward developments).
3=high fall chance (supervision fundamental).
4=high fall hazard (physical help of remain by physical help vital) (Table 1).

Table 1 Time of the get up and go test was recorded from initial rising to re-seating and classified according to the age of the participants

Age (years)	Mean time	Yes or no
60–69	8.1 (7.1–9)	
70–79	9.2 (8.2–10.2)	
80–99	11.3 (10–12.7)	

Thyroid-stimulating hormone

The TSH EIA test depends on the rule of a strong stage catalyst connected immunosorbent test. The measure framework uses a one of a kind monoclonal immune response coordinated against an unmistakable antigenic determinant on the flawless TSH particle. Mouse monoclonal enemy of TSH neutralizer is utilized for strong stage (microtiter wells) immobilization and a goat hostile to TSH immune response is in the counteracting agent protein (horseradish peroxidase) conjugate arrangement. The test is permitted to respond at the same time with the two antibodies, bringing about the TSH particles being sandwiched between the strong stage and catalyst connected antibodies. Following hour long brooding at room temperature, the wells are washed with water to expel unbound marked antibodies. An answer of TMB is included and brooded for 20 min, bringing about the improvement of a blue shading. The shading advancement is ceased with the expansion of 2 N HCl, and the shading is changed to yellow and estimated spectrophotometrically at 450 nm. The grouping of TSH is legitimately relative to the shading force of the test. Reference range utilized was 0.4–7 μIU/ml, as an ordinary range.

Free tri-iodothyronine (fT3)

Principle of the method: Competitive Enzyme Immunoassay Analog Method for free T3 was used. The essential reagents required for a solid-phase enzyme immunoassay include immobilized T3 antibody, enzyme-T3 conjugate, and native free T3 antigen. The enzyme-T3 conjugate should have no measurable binding to serum proteins especially thyroid-binding globulin (TBG) and albumin. The method achieves this goal.

Upon mixing immobilized antibody, enzyme-T3 conjugate and a serum containing the native free T3 antigen, a competition reaction results between the native free T3 and the enzyme-T3 conjugate for a limited number of insolubulized binding sites. The interaction is illustrated by the followed equation:

$$\mathrm{EnzAg} + \mathrm{Ag} + \mathrm{Abc.w.} \underset{\mathrm{k-a}}{\overset{\mathrm{ka}}{\rightleftarrows}} \mathrm{AgAbC.W.} + \mathrm{EnzAgAbC.W.}$$

AbC.W.=Monospecific Immobilized Antibody (Constant Quantity).

Ag=Native Antigen (Variable Quantity).

EnzAg=Enzyme-antigen Conjugate (Constant Quantity).

AgAbC.W.=Antigen-Antibody Complex.

EnzAg AbC.W.=Enzyme-antigen Conjugate-Antibody Complex.

Ka=Rate Constant of Association.

K-a=Rate Constant of Dissociation.

K=ka/k-a=Equilibrium Constant.

After harmony is accomplished, the neutralizer bound portion is isolated from unbound antigen by decantation or goal. The compound movement in the immunizer-bound portion is contrarily relative to the local free antigen focus. By using a few diverse serum references of known antigen focus, a portion reaction bend can be created from which the antigen grouping of an obscure can be learned.

Reference range utilized was 1.4–4.2 pg/ml as an ordinary range.

Free thyroxine (fT4)

Standard strategy: The fundamental reagents required for a strong stage compound immunoassay incorporate immobilized counter acting agent, catalyst antigen conjugate, and local antigen. After blending immobilized counteracting agent, compound antigen conjugate, and a serum containing the local free antigen, a challenge response results between the local free antigen and the catalyst antigen conjugate for a set number of insolubulized restricting destinations. After balance is achieved, the immunizer-bound division is isolated from unbound antigen by decantation or goal. The compound movement in the immunizer-bound division is conversely relative to the local free antigen fixation. By using a few diverse serum references of known antigen focus, a portion reaction bend can be produced from which the antigen convergence of an obscure can be determined.

Reference range utilized was 0.65–1.97 ng/dl as a typical range.

Statistical analysis

Information was coded and entered utilizing the measurable bundle SPSS (Statistical Package for the Social Sciences) adaptation 24 (software package that originated at what formerly was the National Opinion Research Center (NORC), at the University of Chicago). Information was abridged using mean, SD, middle, least, and greatest value in quantitative information and utilizing recurrence (tally) and relative recurrence (rate) for all out information. Examinations between quantitative factors were finished utilizing the nonparametric Mann–Whitney test (Chan, 2003a). For looking at all out information, χ^2-test was performed. Accurate test was utilized rather when the normal recurrence is under 5 (Chan, 2003b). Relationships between quantitative factors were finished utilizing Spearman connection coefficient (Chan, 2003c). Multivariate strategic relapse was done to assess connection between fragile as reliant variable and TSH, fT3 and fT4 as free indicators changing for age, sex, smoking, diabetes, ADL, debilitation of seeing or hearing (Chan, 2004). *P* values under 0.05 were considered as factually noteworthy.

Calculated relapse was performed to evaluate relationship of FT4 in quartiles with chances of delicacy.

Results

Demographic, clinical, and laboratory characteristics of participants

The average age of the participants was 67.34±3.42 years. A total of 52 are female participants (52%) and 48 are male participants (48%), of those four participants were classified as having overt hyperthyroidism (4.0%), two participants having overt hypothyroidism (2.0%), 10 participants having subclinical hyperthyroidism (10.0%), one with subclinical hypothyroidism (1.0%), and 83 participants were euthyroid (83.0%). Overall, 40 participants (40.0%) were classified as being frail (Table 2).

Relation between sex, smoking, exercises of everyday living, impairment of hearing or seeing, hypertension, memory, behavior, get up and go test, fall risk in the test, diabetes, and thyroid state and frailty in the study

There was a statistically significant relation between both smoking and get up and go test and frailty (P=0.014 and0.047, respectively); a high statistically significant relation between hypertension (HTN) and behavior and frailty (P=0.003); and very highly statistically significant relation between ADL, impairment of hearing or seeing, memory, and fall risk in the test and frailty (P<0.001). There was no statistically significant relation between sex, diabetes mellitus, and thyroid state and frailty (P>0.05) (Table 3).

Table 2 Demographic data of the participants included in the study

	Count	%
Sex		
Female	52	52
Male	48	48
Smoking		
Smoker	37	37
Nonsmoker	63	63
ADL		
Able	76	76
With help	24	24
Not able	0	0
Impairment of hearing or seeing		
Yes	64	64
No	36	36
DM		
Diabetic	90	90
Non diabetic	10	10
Components of FRAIL scale		
Fatigue		
Yes	76	76
No	24	24
Resistance		
Yes	49	49.0
No	51	51.0
Ambulation		
Yes	43	43.0
No	57	57.0
Illnesses >5		
Yes	3	3.0
No	97	97
Loss of weight >5%		
Yes	8	8.0
No	92	92.0
Total score		
Nonfrail	60	60.0
Frail	40	40.0
BMI		
Obese	23	23.0
Overweight	48	48
Normal	29	29
HTN		
No	53	53.0
Yes	47	47.0
Memory		
Intact	26	26.0
Forgetfulness	74	74.0
Behavior		
No problem	32	32.0
Problem	68	68.0
Get up and go test		
On time	11	11.0
No	89	89.0
Fall risk in the test		
No risk	36	36.0
Low	25	25.0
Some	15	15.0
High	8	8.0
Very high	16	16.0
Thyroid state		
Overt hyperthyroidism	4	4.0
Overt hypothyroidism	2	2.0
Normal	83	83.0
Subclinical hyperthyroidism	10	10.0
Subclinical hypothyroidism	1	1.0

ADL, exercises of everyday living; DM, diabetes mellitus; HTN, hypertension.

Relation between age, thyroid-stimulating hormone, fT3, fT4, and BMI and frailty in the study

There was a very highly statistically significant relation between age and frailty ($P<0.001$).

No statistically significant relation was seen between TSH, free T3, free T4, and BMI and frailty ($P>0.05$).

Correlation coefficient between thyroid-stimulating hormone, fT3, fT4, age, and total score of FRAIL scale

A very high statistically significant positive correlation between age and total score of the FRAIL scale, ($P<0.001$), but fT3 and fT4 were not correlated with total frailty scale score (Figs. 1–4).

Relation between sex, smoking, exercises of everyday living, impairment of hearing or seeing, hypertension, memory, behavior, get up and go test, fall risk in the test, and components of FRAIL scale and subclinical hypothyroidism, overt hypothyroidism, euthyroidism, subclinical hyperthyroidism, and overt hyperthyroidism in the study

No statistically significant relation between sex, smoking, ADL, impairment of hearing or seeing, HTN, memory, behavior, get up and go test, fall risk in the test, and components of FRAIL scale and subclinical hypothyroidism, overt hypothyroidism, euthyroidism, subclinical hyperthyroidism, and overt hyperthyroidism was seen.

Relation between sex, smoking, exercises of everyday living, impairment of hearing or seeing, hypertension, memory, behavior, get up and go test, fall risk in the test, and components of FRAIL scale and diabetes in the study

There was a statistically significant relation between memory and diabetes ($P=0.018$), behavior and diabetes ($P=0.011$), fall risk in the test and diabetes ($P=0.029$), and fatigue and diabetes ($P=0.032$). No statistically significant relation between diabetes and sex, smoking, ADL, impairment of hearing or seeing, HTN, get up and go test, components of FRAIL scale other than fatigue, subclinical hypothyroidism, hypothyroidism,

Table 3 Relation between sex, smoking, exercises of everyday living, impairment of hearing or seeing, hypertension, memory, behavior, get up and go test, fall risk in the test, diabetes, thyroid state, and frailty in the study

	Frailty (total score 3 or more)				*P* value
	Frail		Nonfrail		
	Count	%	Count	%	
Sex					
Female	29	72.5	23	38.3	0.437
Male	11	27.5	37	61.7	
Smoking					
Smoker	9	22.5	28	46.7	0.014
Nonsmoker	31	77.5	32	53.3	
ADL					
Able	17	42.5	59	98.3	<0.001
With help	23	57.5	1	1.7	
Not able	0	0	0	0	
Impairment of hearing or seeing					
Yes	34	85	30	50	<0.001
No	6	15	30	50	
HTN					
Yes	26	65.0	21	35.0	0.003
No	14	35.0	39	65.0	
Memory					
Forgetfulness	39	97.5	35	58.3	<0.001
Intact	1	2.5	25	41.7	
Behavior					
Problem	34	85	34	56.7	0.003
No problem	6	15	26	43.3	
Get up and go test					
On time	1	2.5	10	16.7	0.047
Not	39	97.5	50	83.3	
Fall risk in the test					
Very high	13	32.5	3	5	<0.001
High	6	15	2	3.3	
Some	8	20	7	11.7	
Low	12	30	13	21.7	
No	6	15	30	50	
DM					
Diabetic	38	95.0	52	86.7	0.308
Nondiabetic	2	5.0	8	13.3	
Subclinical hypothyroidism					
Yes	1	2.5	0	0	0.4
No	39	97.5	60	100.0	
Hypothyroidism					
Yes	1	2.5	1	1.7	1
No	39	97.5	59	98.3	
Normal					
Yes	31	77.5	52	86.7	0.232
No	9	22.5	8	13.3	
Subclinical hyperthyroidism					
Yes	5	12.5	5	8.3	0.515
No	35	87.5	55	91.7	
Overt hyperthyroidism					
Yes	2	5.0	2	3.3	1
No	38	95.0	58	96.7	
Thyroid state	–	–	–	–	0.592

ADL, exercises of everyday living; DM, diabetes mellitus; HTN, hypertension.

euthyroidism, subclinical hyperthyroidism, and hyperthyroidism was seen ($P>0.05$) (Table 4).

Discussion

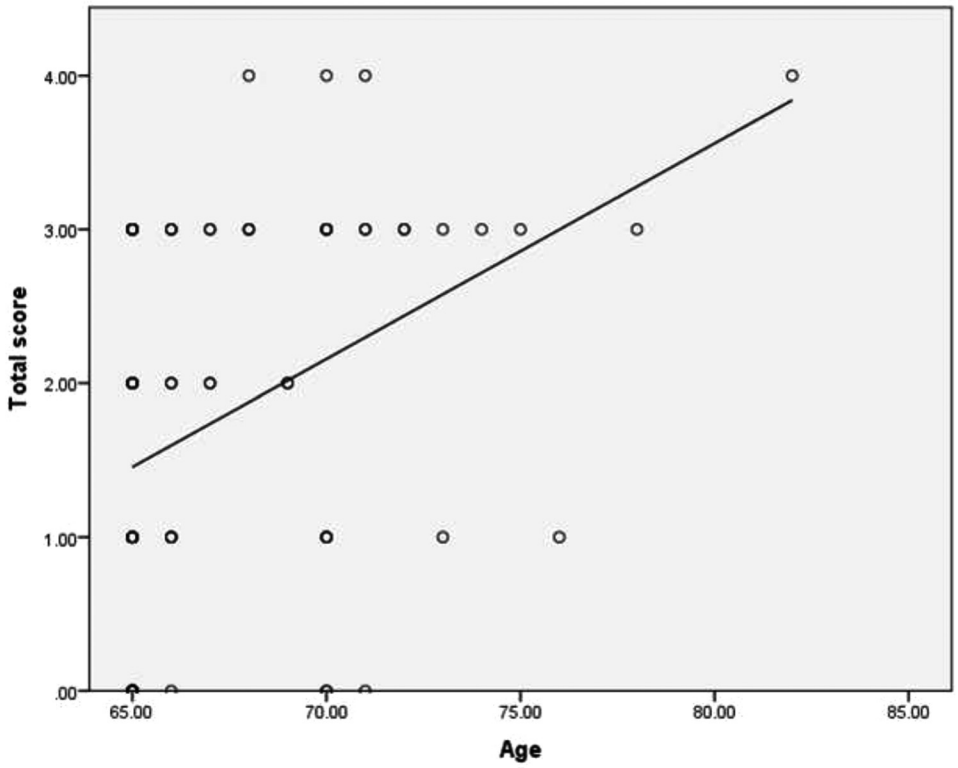
We found a very high statistically significant positive correlation between frailty and age ($P<0.001$), and our results agree with other studies which demonstrated that the commonness of frailty increments with increasing age, and anticipating the advancement of frailty in elderly individuals would be required to save well-being and self-dependence [22]. Moreover, we found a statistically significant association between frailty and smoking ($P=0.014$), and this agrees with another study done by Kojima *et al.* [23] who revealed that present smokers contrasted and nonsmokers were altogether bound to create frailty more than 4 years among community-dwelling elderly individuals and smoking discontinuance may potentially avert or postpone creating frailty, even in old age.

In our study, there is a high measurably noteworthy relation among fragility and HTN ($P=0.003$). Few studies showed the relationship among frailty and HTN prevalence, treatment, and control rates. The study done by Kang *et al.* [24] discovered that frailty status was an independent factor related with poor blood pressure control. Moreover, uncontrolled hypertension was related with pre-frail or frail status of the investigation population. Strangely, the mean frailty record was more noteworthy in older patients who had high or low systolic and diastolic circulatory strain. Considering the criticalness of slightness on future cardiovascular occasions and mortality, more consideration ought to be paid to frail hypertensive patients for the better control of HTN and improvement of forecast.

We found a very high statistically significant relation between frailty and ADL ($P<0.001$), and this agrees with other study done by Al Snih *et al.* [25] who detailed that frailty status in elderly Mexican Americans was related with an expanded danger of exercises of day by day living inability over a 10-year time frame among nondisabled participants.

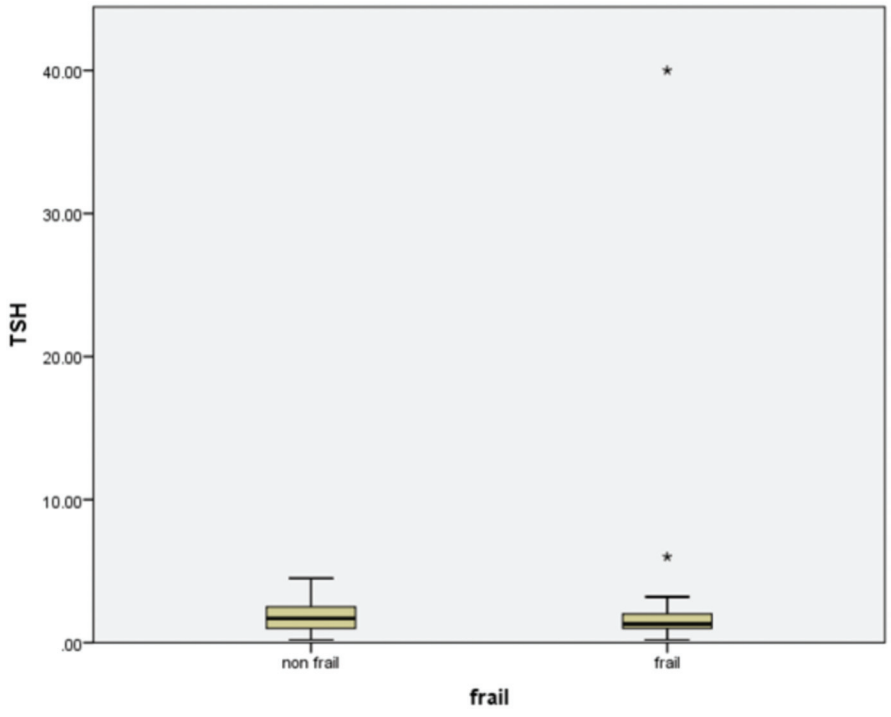
We recognized a highly statistically significant relation among frailty and hindrance of hearing or seeing (P esteem<0.001), and this concur with Liljas *et al.* [26] who demonstrated that older community-dwelling English adults with self-revealed hearing issues and poor vision, separately, have increased dangers of frailty by more than four years. The discoveries recommended that distinguishing and

Figure 1



Relation between age and total score of frail scale in the study ($P<0.001$).

Figure 2

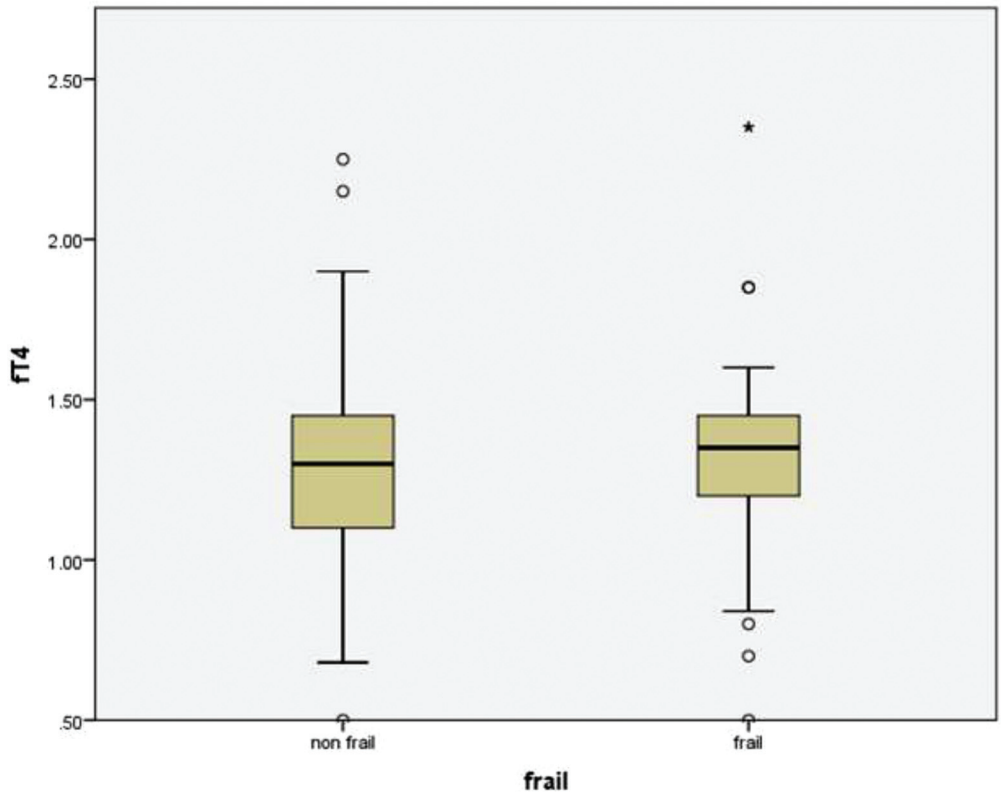


Relation between thyroid-stimulating hormone and frailty in the study ($P=0.091$).

effectively overseeing sensory impairment in elderly might be critical to avoid or postpone further advancement of frailty.

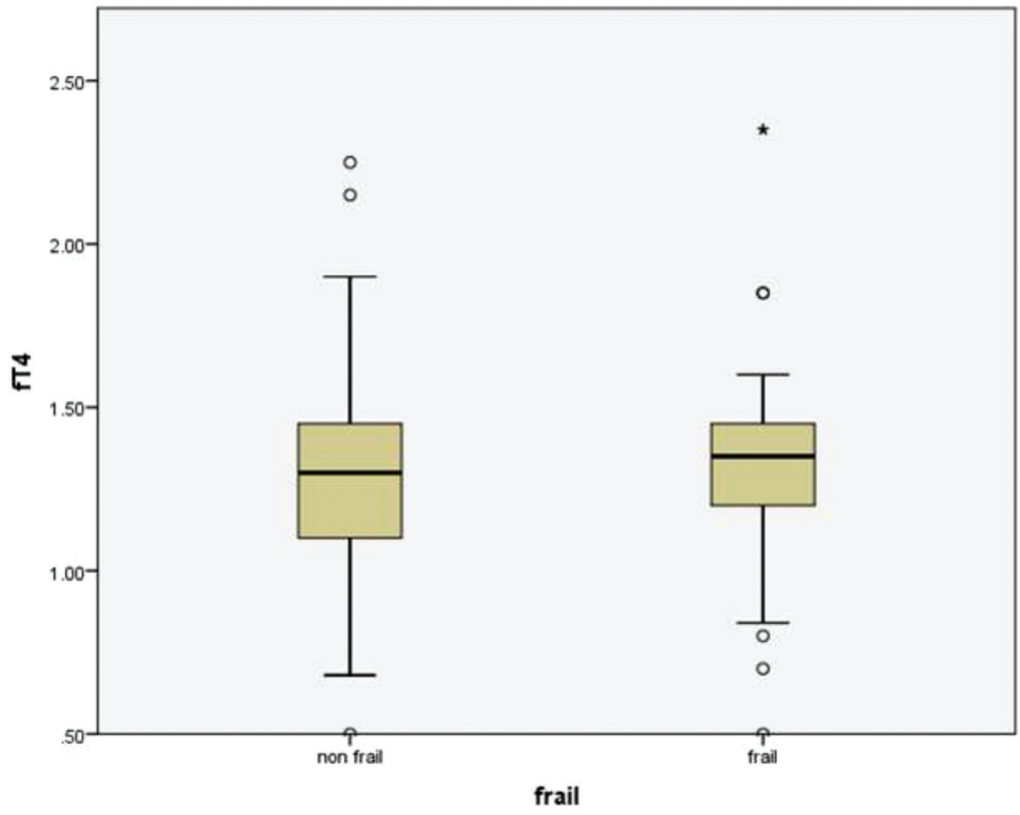
We also found a very high statistically significant relation between frailty and memory impairment ($P<0.001$) furthermore, there was collecting proof

Figure 3



Relation between fT3 and frailty in the study (P=0.955).

Figure 4



Relation between fT4 and frailty in the study (P=0.547).

Table 4 Relation between sex, smoking, exercises of everyday living, impairment of hearing or seeing, hypertension, memory, behavior, get up and go test, fall risk in the test, components of FRAIL scale, and diabetes in the study

	DM				*P* value
	Diabetic		Non		
	Count	%	Count	%	
Sex					
Female	48	53.3	4	40.0	0.514
Male	42	46.7	6	60.0	
Smoking					
Smoker	32	35.6	5	50.0	0.492
Nonsmoker	58	64.4	5	50.0	
ADL					
Able	66	73.3	10	100.0	0.112
With help	24	26.7	0	0	
Not able	0	0	0	0	
Impairment of hearing or seeing					
Yes	57	63.3	7	70.0	1
No	33	36.7	3	30.0	
HTN					
Yes	43	47.8	4	40.0	0.746
No	47	52.2	6	60.0	
Memory					
Forgetfulness	70	77.8	4	40.0	0.018
Intact	20	22.2	6	60.0	
Behavior					
Problem	65	72.2	3	30.0	0.011
No problem	25	27.8	7	70.0	
Get up and go test					
Not	82	91.1	7	70.0	0.078
On time	8	8.9	3	30.0	
Fall risk in the test					
Very high	16	17.8	0	0	0.029
High	8	8.9	0	0	
Some	14	15.6	1	10.0	
Low	18	20.0	7	70.0	
No risk	34	37.8	2	20.0	
Components of FRAIL scale					
Fatigue					
Yes	72	80.0	4	40.0	0.032
No	18	20.0	6	60.0	
Resistance					
Yes	46	51.1	3	30.0	0.158
No	44	48.9	7	70.0	
Ambulation					
Yes	40	44.4	3	30.0	0.289
No	50	55.6	7	70.0	
Illnesses >5					
Yes	3	3.3	0	0	1
No	87	96.7	10	100.0	
Loss of weight >5%					
Yes	7	7.8	1	10.0	0.543
No	83	92.2	9	90.0	
Subclinical hypothyroidism					
Yes	1	1.1	0	0	1
No	89	98.9	10	100.0	
Hypothyroidism					
Yes	1	1.1	1	10.0	0.191
No	89	98.9	9	90.0	
Normal					
Yes	74	82.2	9	90.0	1
No	16	17.8	1	10.0	
Subclinical hyperthyroidism					
Yes	10	11.1	0	0	0.592
No	80	88.9	10	100.0	
Hyperthyroidism					
Yes	4	4.4	0	0	1
No	86	95.6	10	100.0	

ADL, exercises of everyday living; DM, diabetes mellitus; HTN, hypertension.

from observational studies to help the relationship among frailty and cognitive impairment. Community based investigation of elderly individuals without cognitive impairment at standard detailed that frailty was related with an increased danger of creating mild cognitive impairment more than 12 years of follow-up. Increasing level of frailty was additionally related with enhancement of cognitive decline [27].

We found a highly statistically significant relation between frailty and behavioral changes (P=0.003) and this agree with the study done by Jotheeswaran *et al.* [28] who reported the dominant effect of behavioral disorders in frail and dependent older people.

In our study, we found no statistically significant association between sex, TSH, free T4, and free T3 and frailty.

Yeap *et al.* [19] discovered that higher FT4 level is related with frailty in older men, and this affiliation stayed noteworthy when the examination was limited to euthyroid men and there was no relationship between TSH level and frailty. The huge size of the examination permits even unobtrusive relationship to be resolved with consideration to light up potential physiological connections. Moreover, they showed that the relationship of higher fT4 with frailty was not affected by levels of different hormones, for example, testosterone and insulin-like development factor-I. The inquiry emerges whether their outcomes could have been jumbled by the nearness of nonthyroidal disease or sick euthyroid syndrome as men with nonthyroidal illness may likewise show abnormal thyroid hormone levels with diminished total tri-iodothyronine, increased reverse T3, and low,

normal, or high fT4, and they did not assay for either total T3 or reverse T3.

We discovered negative correlation between age and free T3, and no correlation between age and T4 and TSH, and this could be clarified by changes in thyroid function tests happen with advancement of age as free T3 decline with age.

Mariotti *et al.* [29] and Adler *et al.* [30] concentrated on the natural source of thyroid function tests in the older are frequently convoluted by puzzling components, for example, the expanded commonness of autoimmune subclinical hypothyroidism, non-thyroidal illness, and medicine-incited changes in thyroid function tests [31]. After exclusion of these confounders, most studied show comparative outcomes: A reasonable, age-subordinate decrease in serum TSH and free T3, though serum free T4 levels stay unaltered. The latent metabolite rT3 appears to increase likewise with age. Also in a recent longitudinal investigation from Western Australia (Busselton overview), just because, demonstrated that serum TSH increased (mean increment of 0.32 m U/l >13 years) with no critical change in free T4 fixations with maturing [32]. Thus, another longitudinal thyroid capacity assessment in oldest old subgroup (mean age 85 years) of the Cardiovascular Health Study (All Stars Study) found that serum TSH expanded by 13% over a normal of 13 years of line up related with a 1.7% expansion in FT4 and a 13% decrease altogether T3 levels [33].

We did not find statistically significant relation between subclinical or overt hypothyroidism and frailty, which may be owing to our small sample size, and this agrees with other studies done by Virgini *et al.* [34].

Previously, Wang *et al.* [16] detailed an investigation of 641 elderly ladies, in which the nearness of autoantibodies against thyroglobulin or thyroid peroxidase was related with decreased chances of frailty. Ladies positive for Tg or TPO antibodies had higher TSH levels, yet the association of Tg antibody positivity with reduced odds of frailty persisted after modification for TSH. The hidden component for this affiliation stays unsure. The mix of raised TSH and nearness of thyroid antibodies predicts expanded danger of creating hypothyroidism [35]. It is conceivable that the nearness of thyroid antibodies may stamp the nearness of extremely inconspicuous thyroid hypofunction, which may be related with decreased chances of fragility. We did not gauge thyroid antibodies; however, there was no relationship of subclinical hypothyroidism or TSH with frailty in our study participants.

No statistically significant relation was found between subclinical, overt hyperthyroidism, and frailty as well, knowing that hyperthyroidism is usually associated with frailty in older men, and this may be owing to the small sample size in our study.

Virgini *et al.* [34] discovered a conceivable relationship between subclinical hyperthyroidism and frailty at gauge, especially among elderly men less than 74 years. This was explained by several hypotheses. First, subclinical and overt hyperthyroidism had been shown to be associated with an increased risk for developing osteoporosis [36]. Participants with subclinical hyperthyroidism could have a greater likelihood of becoming frail than euthyroid patients. Second, subclinical hyperthyroidism has been associated with cognitive decline [10], which could also contribute to the development of frailty among elderly individuals. Third, because subclinical hyperthyroidism has been previously associated with an increased risk of developing AF [11], it is possible that participants with subclinical hyperthyroidism have decreased physical activity owing to cardiovascular events, such as stroke. Fourth, it has been shown that individuals with overt or subclinical hyperthyroidism have a prothrombotic diathesis, with the activation of various clotting pathways (in particular, increased production of factor VIII and fibrinogen) [37]. Similar hematological changes are also seen in frail individuals [38]. Fifth, elevated free T_4 levels are associated with decreased physical performance and muscular strength, independently of TSH values [31].

It has also been shown that participants with overt hyperthyroidism experience respiratory muscle weakness, leading to decreased exercise capacity [39]. Furthermore, overt hyperthyroidism has been associated with weight loss [40]. Decreased exercise performance and weight loss are both important components of frailty. It is possible that subclinical hyperthyroidism could also be associated with similar pathophysiological changes.

Yeap *et al.* [19] discovered that raised level of fT4 is a critical indicator of frailty among elderly men. This raises the likelihood that even inside the euthyroid range, FT4 adds to weight reduction and decreased physical capacity, and they clarified this by change of the pituitary set point or reaction, where similarly

diminished FT4 level leads to lesser rise of TSH in more established contrasted and more youthful grown-ups with either unconstrained or iatrogenic hypothyroidism [41]. In any case, TSH appropriations and reference limits move to higher levels with increasing age [42]. It may be hypothesized that pituitary affectability to thyroid hormone is decreased in elderly men. If that is indeed the case, a relatively higher level of FT4 are needed to maintain feedback inhibition of TSH in thyrotrophs, but the same level of FT 4in peripheral tissue may represent hidden thyrotoxicosis leading to the symptoms and signs of frailty [43]. In our study, we found that elderly diabetic patients had statistically significant association with components of frailty such as memory (P=0.018), behavior (P=0.011), fall risk in the get up and go test (P=0.029), and fatigue (P=0.032) and this agrees with García-Esquinas *et al.* [44] who found that diabetes mellitus is related with higher risk frailty. This affiliation is mostly clarified by undesirable practices and weight and, to a more noteworthy degree, by poor glucose control and changed serum lipid profile among diabetic people. Then again, diabetes dietary treatment diminishes the risk of frailty.

We also found a high statistically significant relation between diabetes and fT4 (P=0.006) and this may be owing to the effect of the thyroid hormones level on the blood glucose. Thyroid hormones have a role in regulating the body's metabolism; therefore, when fT4 is too high, the blood glucose will be elevated because the body uses up the insulin faster, and when there is a low fT4, the insulin is used up slower so the blood glucose decreases [45].

Conclusion

The incidence of frailty increased with age, and there is a significant association of frailty with smoking and hypertension, but we did not find a relation between frailty and free T3, free T4, and TSH. Moreover, no relation was found between frailty and changes of the thyroid function whether hypothyroidism or hyperthyroidism. Further examinations are expected to explain the utility of the thyroid function testing and the plausibility of switching or avoiding frailty in elderly individuals.

Recommendation

We need large-scale studies to detect the relation of thyroid hormones including free T4, free T3, free thyroid index, and free T3 resin with other factors affecting frailty such as muscle mass, fat mass, and muscle velocity in elderly population to detect patients at risk.

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Conflicts of interest

There are no conflicts of interest.

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