Differences in the Signs and Symptoms of Hyperthyroidism in Older and Younger Patients

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OBJECTIVES: To determine if aging modifies the clinical presentation of hyperthyroidism and the signs of thyrotoxicosis in older people.

DESIGN: Prospective cohort study.

SETTING: A French university hospital.

SUBJECTS: Eighty-four new patients with overt hyperthyroidism confirmed chemically between January 1992 and January 1993. Controls were 68 older euthyroid patients matched to the older hyperthyroid patients.

MEASUREMENTS: Comparison of 19 classical signs of hyperthyroidism between 34 older patients (≥70 years; mean age 80.2) and 50 younger patients (≤50 years; mean age 37.4). Older patients were also compared with controls (mean age 81.3).

RESULTS: Three signs were found in more than 50% of older patients: tachycardia, fatigue, and weight loss. Seven signs were found significantly less frequently in older patients ($P < .001$): hyperactive reflexes, increased sweating, heat intolerance, tremor, nervousness, polydipsia, and increased appetite. Only anorexia (32% vs 4%) and atrial fibrillation (35% vs 2%) were more found frequently in older people ($P < .001$). A goiter was present in 94% of the younger and in 50% of the older patients ($P < .001$). The mean number of clinical signs found in the older subjects was significantly smaller than the number found in younger patients (6 vs 10.8; $P < .001$). Comparison with older controls showed three signs that were highly associated with thyrotoxicosis in older people: apathy (Odd ratio (OR): 14.8), tachycardia (OR: 11.2), and weight loss (OR: 8.7).

CONCLUSION: This study confirms the paucity of clinical signs of hyperthyroidism in older adults. These results suggest the necessity of routine screening for thyroid disease in this age group. **J Am Geriatr Soc 44:50–53, 1996.**

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The reported prevalence of hyperthyroidism in older adults ranges from 0.5 to 4%,[1–5] depending on the population studied and the methods used to assess thyroid function. About 35% of the cases of thyrotoxicosis occur in patients older than 60.[6] The incidence of hyperthyroidism is greater in older patients admitted to the hospital than in those in a community survey.[5,6] In an older US population, the prevalence of hyperthyroidism appears to be 2% overall and 0.7% when iatrogenic causes are excluded.[2]

The clinical diagnosis of thyroid dysfunction is particularly difficult in the older people because of low specificity of so-called characteristic signs and symptoms. Furthermore, older patients with thyrotoxicosis can present subtle and nonspecific signs and symptoms that can be attributed mistakenly to other illnesses or to ageing[6] and, thus, result in a delay in diagnosis and therapy.

Retrospective studies show that although patients may have clinical symptoms that suggest hyperthyroidism, clinicians do not diagnose this condition. Thus, estimates of undiagnosed hyperthyroidism range from 0.5 to 1.5%.[1]

Recent studies[7,8] have tried to show the influence of age on the clinical findings of hyperthyroid patients. In these studies, performed in the United States or other regions of high iodine intake, iodide-induced thyrotoxicosis (IIT) is rare. In Europe, however, IIT is one of the most frequent etiologies of thyrotoxicosis in older adults. This greater frequency of IIT is attributable to marginal iodine intake and to a greater use of amiodarone in older persons.

The aims of this prospective study were (1) to show the role of aging in the differences in clinical signs or symptoms of thyrotoxicosis in old patients compared with those in young patients, independent of etiology, and (2) to study signs that indicate thyrotoxicosis in older people compared with a group of older euthyroid subjects.

PATIENTS AND METHODS

From January 1992 to January 1993, 84 patients with hyperthyroidism were included consecutively in this prospective study. All patients had untreated, newly diagnosed primary hyperthyroidism of different etiologies. These patients consulted with or were hospitalized in the internal medicine and/or endocrinology medical departments of a university hospital. For younger patients, the diagnosis was symptom determined. For older patients, screening was not systematic, but the dosage of serum thyroid-stimulating hormone (TSH) was prescribed widely even when patients had only one of the 19 signs studied.

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Diagnosis of hyperthyroidism was confirmed by two low TSH levels (<0.10 μU/mL) and high serum free thyroxin levels (>26 pmol/L). TSH and serum free thyroxin (FT4) were measured using ultrasensitive immunoluminometric methods in the same laboratory (TSH normal range, 0.1 to 4.5 μU/mL; FT4 normal range, 11 to 26 pmol/L).

Two clinical examinations were performed by the same physician (C.T.), the first at the time of diagnosis and the second after 3 months of specific treatment. During the first examination, the physician did not know the values of TSH and FT4.

A standardized format was used to record the following: age, sex, apparent time of the onset of the disease, history of thyroid disease, and etiology. Nineteen classic signs of hyperthyroidism were studied: general signs (fatigue, anorexia, and weight loss), hypermetabolism signs (tachycardia, increased appetite, increased sweating, polydipsia, heat intolerance, and diarrhea), neuromuscular signs (nervousness, depression, apathy, confusion, tremor, hyperactive reflexes, weakness, and muscular atrophy), and other signs (constipation and dyspnea). Goiter and ophthalmopathy (eyelid retraction or exophthalmos) were considered separately because they depended on etiology.

All these signs or symptoms were defined as described in an endocrinology textbook,[9] a geriatric textbook,[10] and previous studies.[7,8,11] Tachycardia was defined as a pulse greater than 100 beats per minute. Pulse rate was counted at the wrist for 15 seconds if regular and over the precordium for 1 minute if irregular. Atrial fibrillation was defined by electrocardiogram. The thyroid gland was estimated by palpation. Goiter was confirmed by ultrasonography.

Only recent clinical signs of hyperthyroidism, without any other obvious explanation (by clinical examination or laboratory tests), which decreased or disappeared after 3 months of treatment (second examination), were considered for analysis.

We excluded patients less than 20 years of age, patients who had been treated previously for hyperthyroidism, and patients with central hyperthyroidism, subclinical hyperthyroidism (defined by decreased serum TSH only), and those with hyperthyroidism occurring after treatment of hypothyroidism.

Patients were divided into two groups according to age: 34 patients older than 70 (mean age: 80.2 ± 5.6 years; range: 70 to 90 years) and 50 patients younger than 50 (mean age: 37.4 ± 8.0 years; range: 23 to 50 years).

Older patients and younger patients were compared for analysis. Older patients were also compared with 68 controls to determine the specificity of clinical signs. Control subjects were older euthyroid patients (mean age: 81.3 ± 4.1 years) matched to the older hyperthyroid patients on a two-to-one basis by sex, age ± 2 years, date of admission or consultation (within 1 month) and comorbidity. All had normal TSH and FT4 values.

Categorical data were analyzed using a chi-square or Fisher's exact test when samples were not sufficiently large. Because 19 variables were studied, we used Bonferroni correction for multiple comparison.[12] A P value of less than .002 was considered statistically significant. Continuous variables were expressed as mean ± standard deviation (SD) and were compared using the t test or Mann-Whitney test. Odds ratios (OR) and 95% confidence intervals (CI) were calculated by the Miettinen method.[13] Correlation was obtained by calculating the Spearman's rank correlation coefficient. All information was recorded on a Microvax digital II computer. Data were analyzed with the BMDP package.

RESULTS

There were more women in both groups (76% in the older than 70 group and 90% in the younger than 50 group). Mean levels of serum TSH (0.03 ± 0.03 μU/mL and 0.05 ± 0.08 μU/mL, respectively) and FT4 (43.24 ± 21.63 pmol/L and 52.28 ± 22.93 pmol/L, respectively) were not significantly different between the two groups. For older control subjects, the mean levels of serum TSH were 1.92 ± 0.96 μU/mL. The mean duration of evolution was not significantly different between older (5.0 ± 5.4 months) and younger patients (6.7 ± 6.5 months).

Three of the 19 clinical signs studied were were found in more than 50% of older patients (Table 1): tachycardia, fatigue, and weight loss (5.8 ± 2.7 kg). This triad was present in 32% of older patients with hyperthyroidism. Five other signs, tremor, dyspnea, apathy, anorexia and nervousness, were found in more than 30% of older patients.

In young patients, 12 clinical signs were found in more than 50% of patients (Table 1): tachycardia, hyperactive reflexes, increased sweating, heat intolerance, fatigue, tremor, nervousness, polydipsia, weakness, increased appetite, dyspnea, and weight loss (6.25 ± 3 kg). Diarrhea was observed in more than 30% of younger patients.

Seven signs, hyperactive reflexes, increased sweating, heat intolerance, tremor, nervousness, polydipsia and increased appetite, were found significantly less frequently in older than in young patients (Table 1). Only anorexia was found more frequently in older patients (32% vs 4%, $P < .001$).

Table 1. Comparison Between Young and Old Patients with Symptoms and Clinical Signs of Hyperthyroidism

Symptoms and Clinical Signs	Percent Old Patients ≥70 Years (n = 34)	Percent Young Patients ≤50 Years (n = 50)	P Value*
Tachycardia	71	96	.01
Fatigue	56	84	.01
Weight loss	50	51	.87
Tremor	44	84	<.001
Dyspnea	41	56	.20
Apathy	41	25	.20
Anorexia	32	4	<.001
Nervousness	31	84	<.001
Hyperactive reflexes	28	96	<.001
Weakness	27	61	.01
Depression	24	22	87
Increased sweating	24	95	<.001
Polydipsia	21	67	<.001
Diarrhea	18	43	.02
Confusion	16	0	.01
Muscular atrophy	16	10	.52
Heat intolerance	15	92	<.001
Constipation	15	0	.01
Increased appetite	0	57	<.001

* After Bonferroni correction for multiple comparisons, a P value < .002 was considered statistically significant.

For tachycardia, sinusal tachycardia was seen more frequent in young than in older patients (94% vs 41%, $P < .001$). Atrial fibrillation was seen more frequently in older patients (35% vs 2%, $P < .001$).

A goiter (diffuse or nodular) was present in 94% of the younger and in 50% of the older patients ($P < .001$). Ophthalmopathy was present in 46% of the younger and in 6% of the older patients ($P < .001$).

There was a significantly smaller mean number of clinical signs at the time of diagnosis in older patients (6.0 ± 3.5) than in younger patients (10.8 ± 3.1) ($P < .001$).

No significant correlation was found between serum TSH levels and the number of clinical signs in old or young patients.

The comparison between older patients and older controls showed three signs, apathy (OR: 14.8; 95% CI: 3.8–57.5), tachycardia (OR: 11.2,; 95% CI: 4.3–29.4), and weight loss (OR: 8.7; 95% CI: 3.1–24.4), which were highly associated with thyrotoxicosis (Table 2). Five other signs, nervousness, hyperactive reflexes, increased sweating, polydipsia, and muscular atrophy, were more frequent in older hyperthyroid patients. Three percent of our control subjects had goiters ($P < .001$). The odds ratio was not calculated because the prevalence of asymptomatic goiter in the older French population is not known.

Grave's disease was diagnosed in 33% of the older and 92% of the younger patients ($P < .001$), multiheteronodular toxic goiter in 23% and 4%, and solitary toxic nodule in 7% and 4%. IIT (treatment by amiodarone) was observed more frequently in older than in younger patients (37% vs 0%; $P < .001$). There was no statistically significant clinical difference between older patients treated with or without amiodarone.

DISCUSSION

The aim of this prospective study was to determine the relationship between age and clinical findings of hyperthyroidism, independent of etiology, by comparing the frequency of clinical signs in a group of older patients (≥70 of age) and a group of younger patients (≤50 of age). Older patients were also compared with older euthyroid subjects to determine which signs are indicators of hyperthyroidism in older people. Information was obtained using a standardized data collection format for a period of 1 year.

Neither the duration of evolution at the time of diagnosis nor mean serum TSH and FT4 levels were different between the two groups. As in previous studies,[7,14] no correlation was found between serum TSH or FT4 levels and the number of signs and symptoms per patient. Thus, the difference in prevalence of symptoms and signs between the different age groups was not attributable to differences in serum levels of thyroid hormone.

These results suggest that there are four differences in the presentation of hyperthyroidism between older and younger patients. Older patients show (1) fewer signs or symptoms, (2) diminished frequency of seven classical signs, (3) increased frequency of anorexia and atrial fibrillation, and (4) a lack of goiter (in 50% of older hyperthyroid patients). The comparison with older controls showed three signs that were highly associated with thyrotoxicosis in older people.

First, the mean number of clinical signs per patient was significantly smaller in the older patients than in the younger patients (6 vs 10.8; $P < .001$). On the other hand, clinical signs with a frequency greater than 50% were less numerous

Table 2. Comparison Between Old Patients with Hyperthyroidism and Old Controls

Symptoms and Clinical Signs	Percent Old Patients ≥70 Years (n = 34)	Percent Old Controls ≥70 Years (n = 68)	Odds Ratio (95% CI†)	*P* Value*
Tachycardia	71	18	11.2 (4.3–29.4)	<.001
Fatigue	56	32	2.7 (1.1–6.2)	.05
Weight loss	50	10	8.7 (3.1–24.4)	<.001
Tremor	44	31	1.8 (0.8–4.1)	.20
Dyspnea	41	15	4.1 (1.6–10.6)	.01
Apathy	41	4	14.8 (3.8–57.5)	<.001
Anorexia	32	9	4.9 (1.6–14.9)	.01
Nervousness	31	0	ND‡	<.001
Hyperactive reflexes	28	0	ND	<.001
Weakness	27	6	6 (1.7–21.3)	.01
Depression	24	15	1.9 (0.7–5.2)	.30
Increased sweating	24	0	ND	<.001
Polydipsia	21	0	ND	<.001
Diarrhea	18	3	7.1 (1.3–37.2)	.01
Confusion	16	2	6.1 (1.1–33.4)	.05
Muscular atrophy	16	0	ND	<.001
Heat intolerance	15	0	ND	.01
Constipation	15	12	1.3 (0.4–4.3)	.68
Increased appetite	0	0	NA§	NA

* After Bonferroni correction for multiple comparisons, a *P* value < .002 was considered statistically significant.
† CI = confidence interval.
‡ ND = not defined because one cell had value of zero.
§ NA = not accurate.

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