



# Subclinical hyperthyroidism in the course of autonomous nodules — clinical evaluation

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## Abstract

**Introduction:** Subclinical hyperthyroidism (SCH), also known as mildly symptomatic hyperthyroidism, has recently been diagnosed more frequently. One of the main endogenous causes of this disorder is autonomously functioning thyroid nodule (AFTN). Despite the fact that it is usually asymptomatic, SCH entails repercussions on the cardiovascular system and bone, and it carries a risk of progression to overt hyperthyroidism with a typical clinical picture. Treatment is still controversial, and its benefits are widely debated in literature.

**Material and methods:** From 459 patients authors selected a group of 49 patients (10.6% of all subjects with hyperthyroidism), 41 women (83.7%) with AFTN at the stage SCH treated in the Outpatient Endocrinological Clinic and the Department of Endocrinology of the Medical University of Lublin over a three-year period. The method applied in the study was a retrospective analysis of medical records with a particular account of medical history, physical examination, and additional tests obtained during the process of diagnostic and therapeutic procedures.

**Results:** Forty-one patients (83.7%) suffered from typical symptoms of hyperthyroidism; only eight patients (16.3%) were asymptomatic. The most frequently reported symptoms were tachycardia in women (51.2%) and anxiety in men (50%). The type of thyrostatic drugs and the length of therapy did not affect the outcome of iodine-131 therapy. In the vast majority of the patients (87.8%) radioiodine therapy was effective; 30 patients (61.2%) reached euthyrosis and 13 patients (22.5%) developed hypothyroidism.

**Conclusions:** Most patients with SCH in the course of AFTN suffered from typical symptoms of overt hyperthyroidism; only every sixth patient was asymptomatic. The volume of autonomous adenomas did not affect the result of <sup>131</sup>I therapy; however, the impact of AFTN volume as well as the thyroid volume on RIT efficacy requires further investigation. In the vast majority of patients <sup>131</sup>I therapy was an effective method of treatment, and an earlier therapeutic effect was observed more often in the patients with focal lesions located in the right lobe. (*Endokrynol Pol* 2019; 70 (2): 157–164)

**Key words:** subclinical hyperthyroidism; SCH; autonomous nodule; AFTN; <sup>131</sup>I; radioiodine therapy

## Introduction

Subclinical hyperthyroidism (SCH), also called mildly symptomatic hyperthyroidism, in the past years has been diagnosed more frequently. One of the main endogenous causes of this disorder is autonomously functioning thyroid nodule (AFTN) [1, 2]. Diagnosis is established only under certain laboratory criteria, i.e. persistently low TSH level confirmed with third-generation tests and normal level of free thyroid hormones [3]. AFTN, defined as a hot nodule in thyroid scintigraphy, is characterised by excessive production of hormones, which suppresses TSH secretion and leads to inhibition of hormone synthesis by the remainder of the gland and results in either overt or subclinical hyperthyroidism. It is usually a benign follicular lesion (90–95%) or a hyperplastic nodule (5–10%), less often autonomous carcinoma, irrespective of the activity of the hypothalamic–pituitary–adrenal axis [4, 5]. SCH has

gained more attention after publication of the results of a systematic review with a meta-analysis of 10 prospective cohort studies from 2012, pointing to its association with higher total and cardiovascular mortality as well as atrial fibrillation as compared to healthy controls [6, 7]. However, it is emphasised that over 25% of such nodules do not produce symptoms of general thyrotoxicosis. SCH may take the form of a primary onset of the disorder leading to overt hyperthyroidism accompanied by few or even no clinical symptoms. They are mainly associated with cardiovascular diseases like tachycardia or supraventricular arrhythmia, detected in electrocardiographic investigation [8]. An analysis of the clinical symptoms reported by the patients may give valuable information about the expected clinical course of AFTNs. Despite potential cardiovascular and bone complications or even progression to overt hyperthyroidism, the need to treat SCH is still debatable. Treating this form of disease is currently perceived as



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controversial, and arbitrary recommendations of international endocrine associations are questioned by many experts in the field. At the same time the evaluation of the benefits from SCH treatment is often ambiguously presented in literature [9].

The main objective of the study was to evaluate the clinical picture of AFTNs in SCH and its optimal treatment.

## Material and methods

### Study protocol

The method applied in the study was a retrospective analysis of medical records with a particular account of medical history, physical examination, and additional tests obtained during the process of diagnostic and therapeutic procedures.

Medical records of the patients were evaluated for:

- age at diagnosis (patient's age) and duration of the disease;
- family history of thyroid disease;
- subjective clinical signs and co-morbidities;
- TSH, FT<sub>4</sub>, and FT<sub>3</sub> levels at diagnosis and during treatment;
- presence of antithyroid antibodies: anti-thyroid peroxidase antibodies, (anti-TPO antibodies), and TSH-receptor autoantibodies (TRAb);
- thyroid ultrasound and scintiscans;
- ultrasound-guided fine-needle aspiration biopsy (FNAB);
- method of treatment before radioiodine therapy (RIT, <sup>131</sup>I);
- qualification for treatment with RIT;
- evaluation of patient's prognosis after RIT.

The patients underwent physical examination for typical clinical signs of hyperthyroidism.

Diagnosis of SCH was confirmed with the levels of TSH, FT<sub>4</sub>, and FT<sub>3</sub> in accordance with the endocrinological standards. Other causes of low TSH were excluded. They were: overt hyperthyroidism, gestation, thyroiditis, mental illness, central hypothyroidism, and secondary thyroid syndromes in the course of neoplasms, fever, liver disease, and starvation.

The results of biochemical tests and diagnostic imaging (thyroid ultrasound and scintigraphy) performed at the Radiology and Nuclear Medicine Centre of the Medical University of Lublin were used in the study.

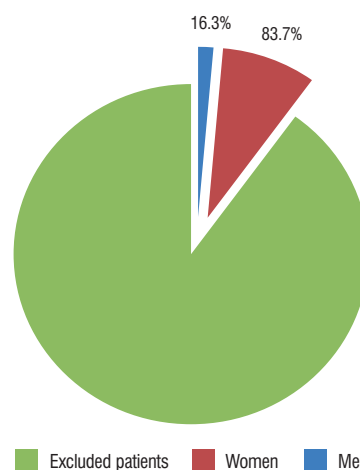
In accordance with the recommendations of the Scientific Committee of the Scientific Conference "Thyroid Cancer", 32 patients (65%) with suspected focal lesions diagnosed by palpation and/or with thyroid ultrasound underwent FNAB. Family history included the prevalence of thyroid disease in first-degree relatives.

### Study population

Initially, we reviewed a group of 459 patients with diagnosed hyperthyroidism (ICD E.05) treated in the Outpatient Endocrinological Clinic and the Department of Endocrinology of the Medical University of Lublin during a three-year-long period, i.e. from October 2010 to June 2013. Next, a group of 291 (63.4%) patients with a toxic goitre was pooled. From this group we singled out 49 patients (10.6% of all subjects with hyperthyroidism), 41 women (83.7%) and 8 men (16.3%), who suffered from AFTN and were qualified for <sup>131</sup>I treatment, as shown in Figure 1. We excluded patients with contraindications to <sup>131</sup>I therapy, with either relative ones (uncontrolled hyperthyroidism, excessive iodine intake induced hyperthyroidism, patients younger than 16 years of age) or with absolute ones (gestation, breastfeeding).

### Methods of laboratory test measurements

Blood serum level of TSH was measured by immunoradiometric assay (B.R.A.H.M.S TSH 1 RIA). The levels of FT<sub>3</sub> and FT<sub>4</sub> in serum



**Figure 1.** Phenotype analysis of the study group

were determined by radioimmunoassay (RIA) with solid phase antigen radioimmunometric technique (SPART) (B.R.A.H.M.S FT<sub>3</sub> SPART RIA, B.R.A.H.M.S FT<sub>4</sub> RIA) with the use of a coated-tube system. The level of TRAb/TSI was measured by radioreceptor assay (RRA) used for the quantitative method of measurement of TRAb (B.R.A.H.M.S) using a human TSH receptor (B.R.A.H.M.S Track human RIA). The levels of antibodies against thyroid peroxidase were determined by RIA with the B.R.A.H.M.S anti-TPO RIA kit.

### Methods of imaging

Thyroid ultrasound was performed using a 7.5-MHz linear probe for the LOGIQ P5 machine. A solution of 74 MBq of <sup>99m</sup>TcO<sub>4</sub> was injected intravenously. Scintigraphy was performed using a gamma camera with a small field of view. For <sup>131</sup>I uptake test, capsules of 4 MBq of sodium iodide Na<sup>131</sup>I were administered orally, and iodine uptake was measured after 24, 48, and 72 hours.

### Ultrasound-guided fine-needle aspiration biopsy

In accordance with the recommendations of the Scientific Committee of the Scientific Conference "Thyroid Cancer", 32 patients (65%) with suspected focal lesions diagnosed by palpation and/or with thyroid ultrasound underwent ultrasound-guided FNAB [10].

### Radioiodine therapy

The therapeutic activity of <sup>131</sup>I was calculated on the basis of Marinelli's formula, in which a dose 300 Gy was for each gram of hyperactive thyroid tissue. The subjects with AFTNs were qualified to RIT in accordance with the official recommendations.

### Criteria for recovery and rules for monitoring patients after administrating <sup>131</sup>I

Criteria of recovery included normal thyroid function (TSH, FT<sub>4</sub>, and FT<sub>3</sub> levels within range) as well as a less expected effect of treatment i.e. hypothyroidism. All patients were evaluated for possible complications, in particular: aggravation of hyperthyroid symptoms including atrial fibrillation, circulatory failure, thyroid crisis, radiation-induced thyroiditis, and symptoms of sialadenitis. In accordance with the procedure of <sup>131</sup>I therapy, each patient was monitored in an outpatient clinic at certain intervals i.e. after one, three, six, and 12 months.

### Statistical analysis

The values of non-measurable parameters were presented by means of numbers and percentages, whereas the measurable ones used the arithmetic mean, standard deviation, median, as well as the 25<sup>th</sup> and 75<sup>th</sup> percentile along with the range of variability. To evaluate

Table I. Characteristics of the study group

Parameter	Women median (range)		Men median (range)		Total median (range)		p
Age [years]	59.0 (52.00–67.00)		63.5 (56.00–75.00)		59.0 (52.00–68.00)		0.28
Treatment length [months]	3.00 (0.00–6.00)		2.5 (0.00–7.50)		3.00 (0.00–7.00)		1.0
Period of time from scintigraphy to iodine administration [days]	37.0 (15.00–113.00)		36.00 (28.00–66.00)		37.0 (17.00–93.00)		0.78
Patients treated with thyrostatics	25 (60.9%) (51.0% of all patients)		5 (62.5%) (10.2% of all patients)		30 (61.2% of all patients)		0.75
TSH before treatment [mIU/L]	< 0.04 (0.04–0.25)		< 0.04 (0.04–0.04)		< 0.04 (0.04–0.18)		0.37
FT <sub>4</sub> before treatment [pmol/L]	18.00 (15.70–19.40)		16.65 (15.60–21.00)		17.60 (15.70–19.40)		0.60
FT <sub>3</sub> before treatment [pmol/L]	6.30 (5.80–6.70)		6.50 (6.00–8.70)		6.30 (5.80–6.80)		0.27
aTPO [U/mL]	30.9 (21.45–75.7)		53.00 (26.00–67.5)		33.25 (22.1–75.2)		0.73
TSI [U/mL]	0.30 (0.30–0.60)		0.35 (0.3–0.65)		0.3 (0.3–0.6)		0.57
Volume of the whole thyroid [mL]	29.22 (15.19–42.23)		46.75 (23.81–68.91)		32.23 (16.09–47.82)		0.09
Size of the right lobe [mL]	13.01 (7.22–24.58)		23.92 (11.59–46.68)		13.1 (8.87–29.49)		0.13
Size of the left lobe [mL]	9.22 (5.48–19.59)		7.51 (3.46–49.36)		9.22 (5.38–19.59)		0.81
Volume of adenoma [mL]	4.24 (0.96–8.88)		4.97 (3.08–36.90)		4.24 (1.27–9.25)		0.39
Size of adenoma in the thyroid (%)	(16.92%) (4.74–2.65)		(23.32%) (12.02–44.74)		(17.1%) (6.72–34.51)		0.42
Location of adenoma	Left lobe 20 (48.8%)	Right lobe 21 (51.2%)	Left lobe 0 (0%)	Right lobe 8 (100%)	Left lobe 20 (40.8%)	Right lobe 29 (59.2%)	0.03
Ultrasound-guided FNAB	26 (63.4%)		6 (75.0%)		32 (65.3%)		0.82

TSH — thyroid stimulating hormone; FT<sub>3</sub> — free triiodothyronine; FT<sub>4</sub> — free thyroxine; aTPO — anti-thyroid peroxidase antibodies; TSI — thyroid stimulating immunoglobulin; FNAB — ultrasound-guided fine-needle aspiration biopsy; Data are presented as median (interquartile range) and N (%)

statistical differences and correlations between the non-measurable parameters, cross tabulation and a chi-squared test were applied. While, to compare the measurable variables, we performed the Mann-Whitney U test for two independent groups, whereas the Kruskal-Wallis test and a post-hoc analysis were used for multiple comparisons. The adopted significance level was 5%. The statistical analysis was performed with the StatSoft, Poland Statistica v. 10.0 software.

## Results

### Clinical characteristics of the study group

The median age in women was insignificantly lower than in men, whereas the median of the time of observation between qualification procedures and RIT in the whole group was 37 days, which was insignificant in terms of gender (Tab. I). Only nine patients (18.4%) reported family history of thyroid disease. Further evaluation showed that the time median was three months and the duration of treatment in women was insignificantly longer than in men, as shown in Table I. In the study group 30 patients (61.2%) were treated with thyrostatics, as shown in Table I.

### Thyroid characteristics of the study group

Thyroid evaluation of the study group included both the results of imaging and biochemical tests, as shown

in Table I. TSH level before the treatment in the whole study group was suppressed, while FT<sub>4</sub> and FT<sub>3</sub> levels were normal. Both in women and in men the right lobe was larger. However, the volume of the left lobe in women was insignificantly greater than in men. The mean volume of the autonomous adenoma was 4.24 ml (1.27–9.25 ml) with no significant difference in terms of gender, which constituted 16.9% and 23.3% of the whole thyroid tissue in women and men, respectively. In most of the patients (29 subjects, 59.2%) adenoma was located in the right lobe, whereas in 20 subjects (40.8%) it was in the left lobe. In all men the nodule was found in the right lobe, and in women it was distributed equally. Thyroid FNAB was performed in 32 patients, which constituted 65% of the whole group, i.e. in 75% of men and 63.4% of women. All biopsy specimens were found benign.

### Clinical symptoms in the course of SCH

Forty-one patients (83.7%) suffered from typical symptoms of hyperthyroidism, and only eight patients (16.3%) were asymptomatic. The most frequently reported symptom in women was tachycardia (51.2%) while in men (50%) it was anxiety — as shown in Table II.

**Table II.** *Clinical symptoms in the study group*

Symptoms	Women	Men	Total
	N (%)	N (%)	N (%)
Periodical heart palpitation	21 (51.2%)	3 (37.5%)	24 (49%)
Weakness	20 (48.9%)	3 (37.5%)	23 (47%)
Unintentional weight loss	14 (34.1%)	3 (37.5%)	17 (34.7%)
Excessive sweating	14 (34.1%)	3 (37.5%)	17 (34.7%)
Emotional lability	13 (31.7%)	4 (50%)	17 (34.7%)
Reduced exercise tolerance	13 (31.7%)	3 (37.5%)	16 (32.7%)
Shortness of breath	11 (26.8%)	0 (0%)	11 (22.4%)
Chest pain	10 (24.4%)	0 (0%)	10 (20.4%)
Insomnia	9 (22%)	0 (0%)	9 (18.4%)
Heat intolerance	7 (17.1%)	2 (25%)	9 (18.4%)
Difficulty swallowing	8 (19.5%)	1 (12.5%)	9 (18.3%)

**Table III.** *Prevalence of coexistent symptoms in one patient*

Number of symptoms	Number of patients	Percentage (%)
0	8	16.3%
1	3	6.1%
2	2	4.1%
3	8	16.3%
4	17	34.7%
5	6	12.2%
6	3	6.1%
7	1	2.0%
8	1	2.0%
Total	49	100%

The occurrence of coexistent symptoms in one patient was analysed as shown in Table III.

Eight patients (16.3%) were completely asymptomatic. Three patients (6.1%) suffered from one symptom, and only one patient (2.0%) suffered from the maximum number of symptoms – nine. Prevalence of four symptoms in one patient was observed in 17 subjects (34.7%).

### *Effects of <sup>131</sup>I treatment*

One month after <sup>131</sup>I therapy 19 patients (38.8%) reverted to euthyroidism, two patients (4.1%) developed hypothyroidism, and 28 patients (57.1%) still suffered from SCH (Tab. IV).

After three months 32 patients (65.3%) reverted to euthyroidism, seven patients (14.3%) developed hypothyroidism, and only 10 patients (20.4%) still suffered from SCH.

After six months as many as 33 patients (67.4%) reverted to euthyroidism, 10 patients (20.4%) developed

hypothyroidism, and only six patients (12.2%) still suffered from SCH.

After 12 months 30 patients (61.2%) reverted to euthyroidism, 13 patients (26.5%) developed hypothyroidism, and six patients (12.2%) still suffered from SCH.

In majority of patients (87.8%) RIT was effective.

To sum up, after the complete follow-up, targeted therapeutic results were observed in 43 patients (87.8%); 30 patients (61.2%) reverted to euthyroidism and 13 patients (22.5%) became hypothyroid, as shown in Table V and Figure 2.

### *Relationship between <sup>131</sup>I therapy efficacy, gender, positive thyroid history, and location of the nodule*

In the analysis of the efficacy of <sup>131</sup>I therapy after one, three, six, and 12 months with regard to patient's gender, positive thyroid history, and location of the nodule as well as whether the subjects reverted to euthyroidism or developed hypothyroidism with regard to patient's gender, positive thyroid history and location of the nodule, the treatment was found effective only one or three months after the therapy in the patients with focal lesions in the right lobe.

## **Discussion**

The results of our study point to the symptomatic course of AFTNs in SCH despite persistent normal thyroid hormones. In the study group most patients (83.7%) suffered from typical symptoms of hyperthyroidism, and only every sixth patient was asymptomatic. Stott et al. presented similar results for patients aged 61–90 years with SCH as compared to healthy controls [11]. In the study by Biondi et al. the scores of the Symptoms Rating Scale and the Short Form 36 Health Survey

Table IV. Effects of <sup>131</sup>I treatment after 1, 3, 6, and 12 months

Parameter	Women N (%)	Men N (%)	Total N (%)	p
<b>1 month after treatment</b>				
Euthyreosis	17 (41.5%) (34.7% of all patients)	2 (25.0%) (4.1% of all patients)	19 (38.8% of all patients)	0.34
Hypothyroidism	1 (2.4%) (2.0% of all patients)	1 (12.5%) (2.0% of all patients)	2 (4.1% of all patients)	
Hyperthyroidism	23 (56.1%) (46.9% of all patients)	5 (62.5%) (10.2% of all patients)	28 (57.1% of all patients)	
<b>3 months after treatment</b>				
Euthyreosis	26 (63.4%) (53.1% of all patients)	6 (75.0%) (12.2% of all patients)	32 (65.3% of all patients)	0.80
Hypothyroidism	6 (14.6%) (12.2% of all patients)	1 (12.5%) (2.0% of all patients)	7 (14.3% of all patients)	
Hyperthyroidism	9 (21.9%) (18.4% of all patients)	1 (12.5%) (2.0% of all patients)	10 (20.4% of all patients)	
<b>6 months after treatment</b>				
Euthyreosis	27 (65.8%) (55.1% of all patients)	6 (75.0%) (12.2% of all patients)	33 (67.4% of all patients)	0.83
Hypothyroidism	9 (21.9%) (18.4% of all patients)	1 (12.5%) (2.0% of all patients)	10 (20.4% of all patients)	
Hyperthyroidism	5 (12.2%) (10.2% of all patients)	1 (12.5%) (2.0% of all patients)	6 (12.2% of all patients)	
<b>12 months after treatment</b>				
Euthyreosis	25 (61%) (51.0% of all patients)	5 (62.5%) (10.2% of all patients)	30 (61.2% of all patients)	0.99
Hypothyroidism	11 (26.8%) (22.4% of all patients)	2 (25.0%) (4.1% of all patients)	13 (26.5% of all patients)	
Hyperthyroidism	5 (12.2%) (10.2% of all patients)	1 (12.5%) (2.0% of all patients)	6 (12.2% of all patients)	

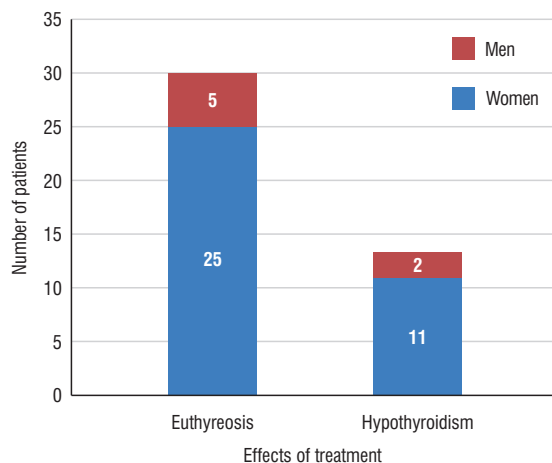
Table V. Effects of <sup>131</sup>I treatment after 12 months

Parameter	Women N (%)	Men N (%)	Total N (%)	p
Effective treatment	36 (87.8%) (73.5% of all patients)	7 (87.5%) (14.3% of all patients)	43 (87.8% of all patients)	0.57
Hypothyroidism	11 (26.8%) (22.4% of all patients)	2 (25.0%) (4.1% of all patients)	13 (22.5% of all patients)	0.74
Euthyreosis	25 (61%) (51.0% of all patients)	5 (62.5%) (10.2% of all patients)	30 (61.2% of all patients)	0.75

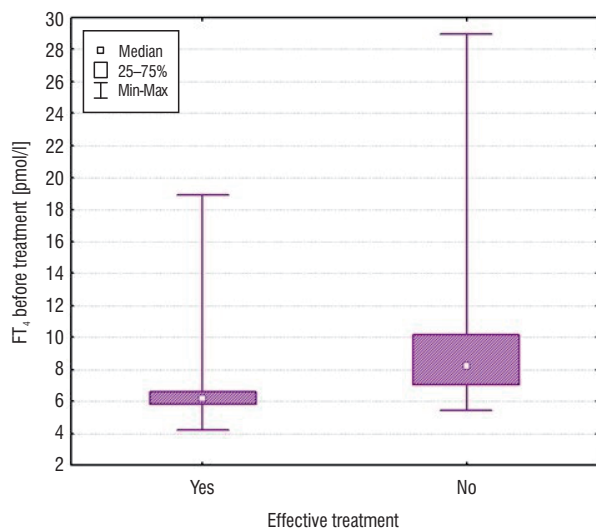
questionnaires showed increasing prevalence of typical symptoms of hyperthyroidism that worsened the quality of life of the patients, which correlated with TSH levels [12, 13]. Gulseren et al. presented worse results of both mental and physical tests performed by SCH patients as compared to the control group [14]. In the clinical picture of hyperthyroidism literature stresses greater frequency of symptoms related to the adrenergic overactivity expressed most often by heart palpitation present particularly in young and middle-aged patients. In the study group the feeling of tachycardia was

the most frequently reported sign in women (52.2%) and one of the most common in men (37.5%). In their study, Sgarbi et al. found a significant increase in atrial and ventricular premature beats in SCH patients and observed that TSH and FT<sub>4</sub> significantly correlated with such premature beats [15]. The meta-analysis conducted by Collet et al. showed higher total and cardiovascular mortality and prevalence of atrial fibrillation in SCH patients as compared to healthy controls [6]. Such documented effect of SCH on the cardiovascular system suggests considering treatment also in young patients





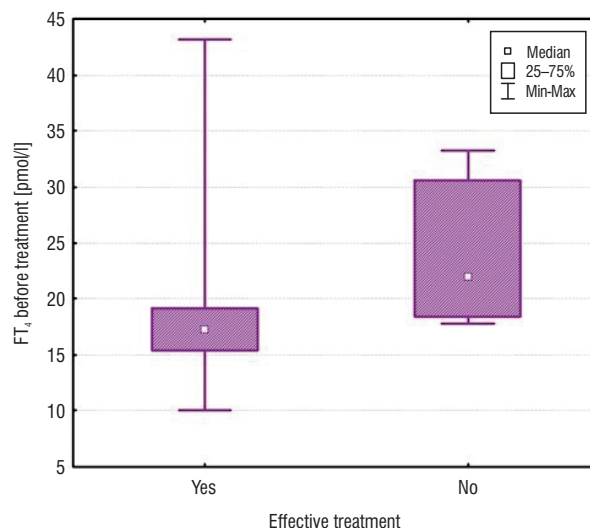
**Figure 2.** Effects of  $^{131}\text{I}$  treatment after 12 months



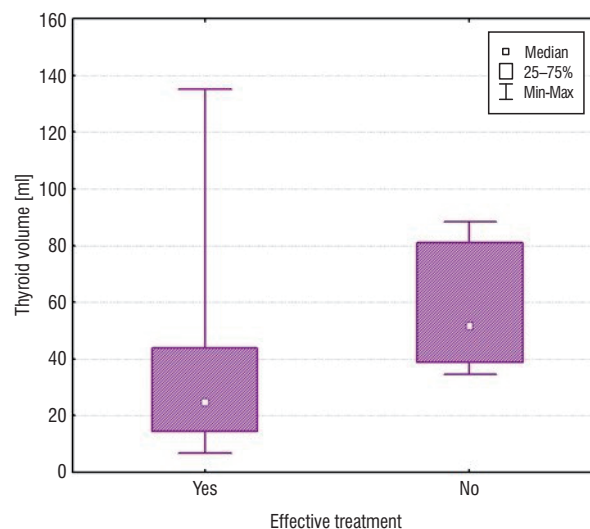
**Figure 4.** Relationship between initial  $\text{FT}_3$  level and effects of  $^{131}\text{I}$  treatment

in order to prevent cardiovascular risk and to improve their quality of life. Our study group showed that the clinical symptoms were not limited to the cardiovascular system. Coexistence of four symptoms in one patient was found in as many as 17 subjects (34.7%), which means that every third patient had at least four symptoms typical for overt hyperthyroidism. In the study group 31.7% of women and 50% of men complained about emotional lability. The study carried out on the basis of the Beck Anxiety Inventory showed that SCH patients had significantly higher scores of anxiety than their healthy controls [16].

In Poland  $^{131}\text{I}$  therapy is the treatment of choice in patients suffering from hyperthyroidism in the course of AFTNs, especially over the age of 60 years, who also suffer from cardiovascular diseases [17]. In our study, in the majority of the patients (87.7%), RIT



**Figure 3.** Relationship between initial  $\text{FT}_4$  level and effects of  $^{131}\text{I}$  treatment



**Figure 5.** Relationship between the volume of the thyroid gland and effects of  $^{131}\text{I}$  treatment

treatment was effective. After the complete follow-up of 12 months from  $^{131}\text{I}$  therapy good therapeutic results were observed in 43 patients (87.8%); 30 patients (61.2%) reverted to euthyroidism and 13 patients (22.5%) developed hypothyroidism. Our results were more encouraging than those of the Australian study (79.5% efficacy) [18]. In the study conducted by Goldstein et al. 35% of SCH patients treated with  $^{131}\text{I}$  observed from 4 to 16.5 years developed hypothyroidism, and its prevalence was not dependent on the size of the nodules, thyroid function, or  $^{131}\text{I}$  dose [19]. However, Mariotti et al. reported hypothyroidism only in 4% of the patients and found no correlation between the development of hypothyroidism and the size of the nodules or the therapeutic dose of  $^{131}\text{I}$  [20]. Bolu-

sani et al. included 105 patients with AFTNs in their study and observed a rising rate of hypothyroidism over time, i.e. in 11% after one year, in 33% after five years, and in 49% after 10 years following treatment. The development of hypothyroidism did not correlate with age, gender, radioiodine uptake, and activity in therapy [21].

Our study showed correlation between the number of coexistent symptoms before the treatment and the result of SCH therapy in the course of AFTNs. The patients who reported the largest number of symptoms reverted to euthyrosis or still suffered from SCH. However, the patients who reported the smallest number of symptoms developed hypothyroidism. In the analysis of these symptoms and their impact on the effect of treatment significant correlation was found only in terms of emotional lability. We demonstrated that high initial free thyroid hormone levels predisposed patients to poorer therapeutic effects. In most of the patients the nodule was found in the right lobe (59.2%), whereas in 20 (40.8%) patients it was found in the left one; in 48.8% of women the nodule was located in the left lobe. Interestingly, all AFTNs in men were located in the right lobe, for which the literature found no explanation either in terms of anatomy or genetics.

Our results showed no link between the volume of the nodule and treatment efficacy probably due to the small volume of the nodule in our study group.

Although  $^{131}\text{I}$  therapy was performed when extranodular thyroid tissue was suppressed, the larger thyroid volume translated into poorer treatment effect. This is a surprising observation of the studied population, which requires confirmation in further studies with larger groups of patients. Nonetheless, Rong et al., who examined the above relationship, found no such correlation [22]. Also, Massaroi et al. reported no link between the size of the thyroid and the effect of  $^{131}\text{I}$  therapy [23].

In our study group the targeted therapeutic effect one and three months after treatment was significantly more frequent in patients with focal lesions located in the right lobe. Such a finding may allow selection of a group of patients who reach therapeutic effects much faster, and at the same time it may serve as a reason to consider various follow-up periods in patients with nodules in the left and right lobe. It seems that such observations should be confirmed in further studies with a larger number of patients because the available literature reports no associations between the quality and quantity of clinical symptoms and the effect of  $^{131}\text{I}$  therapy.

The coexistence of symptoms typical for overt hyperthyroidism, which was observed in every third patient with SCH, may serve as a basis for modifying

the definition of this endocrinopathy and consequently changing the qualifications for treatment. Distinct clinical pictures of SCH point to the necessity for thorough and early diagnostics and treatment, especially in patients with high cardiovascular risk. Because the treatment of this form of disease is currently controversial and the recommendations of international endocrine associations are heterogeneous and often questioned by renowned endocrinologists, our conclusions could serve as valid input in the current debate.

## Conclusions

1. Most patients with SCH in the course of AFTNs suffer from typical symptoms of overt hyperthyroidism; only every sixth patient was asymptomatic.
2. The volume of autonomous adenomas does not affect the result of  $^{131}\text{I}$  therapy; however, the impact of the thyroid volume on RIT efficacy requires further investigation.
3. In the vast majority of the patients  $^{131}\text{I}$  therapy is an effective method of treatment and an earlier therapeutic effect is observed more often in patients with focal lesions located in the right lobe.

## References

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