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*Atrial fibrillation and subclinical hyper- and hypothyroidism  
in patients hospitalized in the Department of Internal Diseases*

Cardiovascular symptoms in hyperthyroidism have been known for 200 years, when Caleb Parry described thyreocardiac syndrome. Its clinical manifestations are: cardiac rhythm disorders, circulatory insufficiency, stenocardia. They occur in elderly patients and are the cause of hospitalization. Subclinical hypo- and hyperthyroidism are defined as abnormal TSH levels in blood with the absence of other clinical manifestations (5, 6, 7, 11, 15).

Analysis of thyroid functional status in atrial fibrillation in subjects treated in the Department of Internal Diseases in 2004–2006 is the objective of the study.

MATERIAL AND METHODS

Data of patients treated in the Clinic of Internal Diseases in the period of 2004–2006 were collected according to the international disease classification. The patients admitted were brought by ambulance or from an outpatients' clinic with the initial diagnosis of paroxysmal atrial fibrillation which could not be put under control in the hospital admission room.

Patients with atrial fibrillation or flutter who did not regain sinus rhythm during the therapy in the hospital emergency room were hospitalized in the Department of Internal Diseases. TSH levels in blood serum were determined; if TSH levels were not within the acceptable range, the levels of free thyroid hormones: triiodothyronine (FT3) and thyroxine (FT4) were determined. To determine TSH and thyroid hormones in blood immunofluorescent method was applied using BioMERIUS kit. Statistical analysis of the obtained data was carried out, with  $P < 0.05$  assumed as statistically significant. The groups were compared using Student's T-test and Pearson's chi-square test.

RESULTS

In the analysed group there were 313 patients: 183 women (56.47%) and 130 men (41.53%) The average age was  $69.0 \pm 11.6$ ;  $70.7 \pm 11.2$  in women and  $66.6 \pm 11.6$  in men. Up to 50 years of age there were 18 patients (5.8%), 65 were aged 51–60 (20.8%), 68 were aged 61–70 (21.7%), 162 were over 70 years of age (51.7%). TSH levels were determined in 313 hospitalized patients with atrial fibrillation. Mean TSH values in particular age groups are shown in Table 1.

Mean TSH levels in blood in particular age groups were not statistically different among men or women, no statistically significant differences were observed between women (TSH  $1.73 \pm 2.22 \mu\text{g/l}$ )

Table 1. Mean TSH values in blood serum in age groups of hospitalized patients with atrial fibrillation

Age groups	TSH ( $\mu\text{g/l}$ )	TSH N	TSH ( $\mu\text{g/l}$ )	TSH N	TSH ( $\mu\text{g/l}$ )	TSH N
	women and men		women		men	
Entire group	1.60 $\pm$ 1.90	313	1.73 $\pm$ 2.22	183	1.42 $\pm$ 1.99	130
<50	1.31 $\pm$ 1.95	18	0.59 $\pm$ 0.25	10	2.21 $\pm$ 2.74	8
51-60	1.40 $\pm$ 1.23	65	1.59 $\pm$ 1.41	29	1.25 $\pm$ 1.06	36
61-70	1.28 $\pm$ 1.20	68	1.30 $\pm$ 1.25	36	1.26 $\pm$ 1.16	32
>70	1.84 $\pm$ 2.29	162	2.01 $\pm$ 2.66	108	1.51 $\pm$ 1.20	54
P	0.12		0.11		0.22	

and men (TSH 1.73  $\pm$  1.30  $\mu\text{g/l}$ ), P was not statistically significant. In 262 (83.7%) patients with atrial fibrillation, including 153 women (83.61%) and 109 men (83.85%), TSH levels assumed to be correct were found (0.5-5  $\mu\text{g/l}$ ) and euthyroidism was diagnosed (EU). In the other 51 patients TSH values were not within the normal range. To determine their thyroid functional status, FT3 and FT4 levels in blood serum were determined. Among the patients with atrial fibrillation manifest hyperthyroidism (TT) occurred in 14 (4.5%), subclinical thyreotoxicosis (STT) in 30 (9.6%) and subclinical or manifest hypothyreosis (HY) in 7 (2.2%). Among women manifest hyperthyroidism occurred in 10 (5.4%), subclinical thyreotoxicosis in 15 (8.20%), subclinical or manifest hypothyreosis in 5 (2.73%). Among men manifest hyperthyroidism was diagnosed in 4 (3.08%), subclinical thyreotoxicosis in 15 (11.54%), subclinical or manifest hypothyreosis in 2 (1.54%). The incidence of various thyroid functional states in age groups in patients with atrial fibrillation is shown in Table 2.

Table 2. Incidence of various thyroid functional states in age groups in patients with atrial fibrillation

Age groups	Thyroid functional states			
	manifest thyreotoxicosis	subclinical thyreotoxicosis	euthyrosis	subclinical / manifest hypothyreosis
< 50 yrs	1 (0.32%)	1 (0.32%)	15 (4.79%)	1 (0.32%)
51-60 yrs	2 (0.64%)	5 (1.6%)	57 (18.21%)	1 (0.32%)
61-70 yrs	3 (0.96%)	11 (3.51%)	54 (17.25%)	0 (0%)
>70 yrs	8 (2.58%)	13 (4.15%)	136 (43.45%)	5 (1.6%)
Total	14 (4.47%)	30 (9.58)	262 (83.71)	7 (0.64)

Statistically significant differences in the incidence of various thyroid functional states in age groups ( $P=0.25$ ) or the correlation of TSH levels with the age were not observed. Among all the hospitalized subjects with atrial fibrillation circulatory insufficiency was diagnosed in 31.6%.

## DISCUSSION

The incidence of cardiac rhythm disorders in the Polish population was evaluated in the epidemiological studies of K. Kocemba et al. on the basis of 2,487 ECGs analysis. AF was observed in 1.4% and also the increase in the incidence of rhythm disorders with age was found, especially after 60 years of age (7). In our population there were 8.32% patients with paroxysmal atrial fibrillation (AF) and nearly 75% over 60 years of age. Simultaneously, according to Wilson et al. (15) the

incidence of subclinical thyreotoxicosis is estimated at 2% of population, hypothyreosis at 4–8.5%, and in women over 60 years of age even at 20%. Many authors think that in patients over 60 low TSH levels are connected with a several times higher probability of AF appearance (1, 2, 4, 9, 10).

The above can apply to our studied population because the majority of patients with atrial fibrillation (almost 70%) were over 60 years of age. At the same time in this group of patients with AF TSH levels within the acceptable normal range (TSH 0.5–5.0  $\mu\text{g/l}$ ) occurred in 175 (76.09%) patients over 60 years of age, the values below 0.5  $\mu\text{g/l}$  were in 46 (20.0%) patients and above 5  $\mu\text{g/l}$  in 4 (1.74%). Similar observations in patients with AF are made by other authors (1, 6).

Subclinical thyreotoxicosis as the cause of atrial fibrillation can be excluded in almost 100% if TSH is within acceptable range (0.5–5.0  $\mu\text{g/l}$ ) (9); among our patients with AF this concerned 239 (76.36%). Epidemiological studies of Auer et al. (2) on the correlation of atrial fibrillation incidence and various TSH values in 23,638 patients showed the occurrence of AF in 2.3% (513 patients) in the group with normal TSH values, in 12.7% (78 patients) in the group with subclinical thyreotoxicosis and in 13.8% (100 patients) in the group with fully manifest thyreotoxicosis. The authors conclude that low TSH levels were connected with five times greater probability of AF occurrence, with a slight difference between manifested and subclinical thyreotoxicosis (2).

The observations of Sawin et al. (14) show that low TSH levels (below 0.4  $\mu\text{g/l}$ ) and even slightly lowered levels (TSH 0.1–0.4  $\mu\text{g/l}$ ) increase the risk of AF occurrence three times. In our population, if we exclude the patients with manifest thyreotoxicosis, TSH levels in blood serum up to 0.1  $\mu\text{g/l}$  were in 12 patients (3.83%) with AF, from 0.1 to 0.5  $\mu\text{g/l}$  in 3 patients (11.18%) with AF. Significant differences in the incidence of various TSH values in patients with AF were not observed.

Long-term studies of Osman et al. (10) showed an increase in mortality for cardiovascular and cerebro-vascular reasons in patients with recurrent and subclinical hyperthyroidism, through the influence of thyroid hormones on the autonomous nervous system and proarrhythmic action. In the deliberations on the dependence of cardiac rhythm and thyroid function, the influence of Amiodaron on their incidence cannot be omitted. According to Barbisan et al. (3) it causes thyroid dysfunction in 16.6% of the treated subjects (hyperthyroidism in 6.9%, hypothyroidism in 5.6% and FT4 level increase in 4.2%). On the other hand, TSH levels just below 1.5  $\mu\text{g/l}$  can be a risk factor for AF at normal levels of thyroid hormones (13), which in our case concerns 62 patients (19.81%) with AF. The diagnosis of subclinical thyreotoxicosis can be a problem because of the absence of clinically manifest symptoms or domination of circulatory system symptoms. If we diagnose subclinical hyperthyroidism, there is still left the problem of thyreostatic treatment to solve. Many authors think that in such cases it should be applied individually (5, 8, 12, 15).

Manifest hyperthyroidism is developed in 4% of patients with subclinical thyreotoxicosis. The decision about the thyreostatic treatment should take into account many aspects, particularly in patients from the groups of high risk of thyroid functional disorders and AF. However, some authors claim that early treatment does not prevent from the development of hyperthyroidism (5, 11). According to Romaldini et al. (11) subclinical thyreotoxicosis should be treated if TSH level is below 0.1  $\mu\text{g/l}$  with existing clinical symptoms and in elderly patients, whereas hypothyreosis should be treated if TSH is above 8  $\mu\text{g/l}$ .

In the studied population, according to Romaldini et al. (11), thyreostatic treatment should be applied in 15 patients (4.8%) with AF and subclinical thyreotoxicosis, whereas hypothyreosis should be treated in 6 (1.9%) patients, including 5 patients over 70 years of age. In hospitalized subjects with AF and circulatory insufficiency thyreostatic treatment can cause favourable hemodynamic changes in the case of co-existing subclinical thyreotoxicosis (13).

Thyreotoxicosis, clinically manifested and confirmed by laboratory tests, does not raise doubts as to the role of metabolic factor in the occurrence of cardiovascular disorders and the necessity of thyreostatic treatment. In our studies in 12 patients with cardiac rhythm disorders (3.83%) lowered TSH levels and highered free thyroid hormone levels were observed. However, until now no indications have been worked out regarding taking up thyreostatic treatment in subclinical disorders of thyroid functions and still it is the doctor's individual decision.

Taking into account the fact, described in the literature, of the increased mortality of patients with subclinical hyperthyroidism and cardiac rhythm disorders (10), we should find the answer to the questions concerning indications for thyreostatic treatment in those patients. However, this requires further population studies.

### CONCLUSIONS

In about 10% of patients with atrial fibrillation, cardiac rhythm disorders can be caused by subclinical hyperthyroidism, hence the necessity to evaluate the thyroid function in patients with cardiac rhythm disorders. At the same time, further epidemiological studies would make it possible to work out indications to take up thyreostatic treatment in patients with subclinical thyreotoxicosis and cardiovascular disorders.

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## SUMMARY

Analysis of thyroid function in patients with atrial fibrillation hospitalized in the Clinic of Internal Diseases was the aim of the paper. Patients' data were collected according to the international classification of diseases. TSH, FT3, FT4 levels in blood serum were determined in the hospital laboratory using the immunofluorescent method and BioMERIUS kit. In the analysed group there were 313 patients with atrial fibrillation, 183 women (58.47%) and 130 men (41.53%). The average age was  $69.0 \pm 11.6$ , in women  $70.7 \pm 11.2$  and in men  $66.6 \pm 11.6$ . In 262 (83.7%) patients with atrial fibrillation euthyroidism was diagnosed on the basis of TSH levels, which were from 0.5 to  $5.0 \mu\text{g/l}$ . In 51 patients TSH values were not within acceptable normal range; to establish the functional thyroid status, FT3 and FT4 levels in blood serum were determined. Among the patients with atrial fibrillation manifested hyperthyroidism (TT) occurred in 14 patients (4.5%), subclinical thyrotoxicosis (STT) in 30 patients (9.6%) and subclinical or manifest hypothyroidism (HY) in 7 patients (2.2%). According to various authors subclinical thyrotoxicosis should be treated when TSH level is below  $0.1 \mu\text{g/l}$  in the presence of clinical manifestations and in elderly patients; hypothyroidism should be treated when TSH is above  $8 \mu\text{g/l}$ . In the studied population thyrostatic treatment should be taken up in 15 (4.8%) patients with AF and subclinical thyrotoxicosis, and hypothyroidism should be treated in 6 (1.9%) patients, including 5 patients above 70 years of age. Subclinical hyperthyroidism was diagnosed in about 10% of patients with atrial fibrillations. Literature data point to the increased mortality of patients with hyperthyroidism and cardiovascular disorders, hence the need to evaluate the thyroid function in atrial fibrillation. Indications to take up thyrostatic treatment require the evaluation in large population studies.

### Migotanie przedsionków a subkliniczna hyper- i hypotyreoza u hospitalizowanych w Klinice Chorób Wewnętrznych

Celem pracy była ocena funkcji tarczycy u pacjentów z migotaniem przedsionków, hospitalizowanych w Klinice Chorób Wewnętrznych. Dane o hospitalizowanych zbierano wg międzynarodowej klasyfikacji chorób. Poziom TSH, trójjodotyroniny (FT3), czterojodotyroniny (FT4) w surowicy krwi oznaczono w Laboratorium Szpitalnym metodą immunofluorescencyjną z użyciem zestawu Bio MERIUS. W analizowanej grupie było 313 osób z migotaniem przedsionków, w tym 183 (58,47%) kobiet i 130 (41,53%) mężczyzn. Średni wiek badanych wynosił  $69,0 \pm 11,6$  lat, kobiet  $70,7 \pm 11,2$ , mężczyzn  $66,6 \pm 11,6$  lat. U 262 (83,7%) pacjentów z migotaniem przedsionków rozpoznano eutyreozę na podstawie poziomu TSH od 0,5 do  $5 (\mu\text{g/l})$ . U 51 pacjentów wartości TSH nie mieściły się w wartościach przyjętych za normę, oznaczano poziom FT3 i FT4 w surowicy krwi celem ustalenia stanu czynnościowego tarczycy. Spośród pacjentów z migotaniem przedsionków jawną nadczynność tarczycy (TT) wykazywało 14 (4,5%) osób, subkliniczną tyreotoksykozę (STT) 30 (9,6%) pacjentów, a subkliniczną lub jawną hypotyreozę (HY) 7 (2,2%) osób. Zdaniem różnych autorów subkliniczną tyreotoksykozę leczymy, jeśli TSH jest poniżej  $0,1 \mu\text{g/l}$ . z obecnymi objawami klinicznymi oraz u starszych pacjentów, a hypotyreozę jeśli TSH jest powyżej  $8 \mu\text{g/l}$ . W badanej

populacji leczenie tyreostatyczne powinno otrzymywać 15 (4,8%) pacjentów z FA i subkliniczną tyreotoksykozą, a leczenie hypotyreozy powinno być prowadzone u 6 (1,9%) pacjentów, w tym u 5 pacjentów powyżej 70 roku życia. U około 10% pacjentów z migotaniem przedsionków rozpoznano subkliniczną nadczynność tarczycy. Dane z piśmiennictwa wskazują na zwiększoną śmiertelność pacjentów z nadczynnością tarczycy i zaburzeniami w układzie sercowo-naczyniowym, stąd konieczność oceny funkcji tarczycy w migotaniu przedsionków. Wskazania do podjęcia leczenia tyreostatycznego wymagają oceny w dużych badaniach populacyjnych.