Introduction
In hypothyroid patients, pericardial effusion represents a common finding (1, 2). The incidence of pericarditis in patients with mild hypothyroidism ranges from 3% to 6%, but in those with severe deficiency, the incidence raises to 30% or even 80%. However, pericardial effusion has also been associated with subclinical hypothyroidism (3).

Hypothyroidism induces accumulation of effusions in various body cavities including peritoneum, pericardium, pleura, middle ear, uvea, joints and scrotum. These are exudates and the incriminated pathophysiological mechanism is an increase in the volume of distribution of albumin, with extravasation of hygroscopic mucopolysaccharides into the body cavities, combined with increased permeability and decreased lymphatic clearance, associated with increased retention of salt and water (4, 5). In hypothyroidism, the pericardial effusion contains high levels of cholesterol.

Methodology
We studied 192 patients with hypothyroidism, admitted in the Clinic of Endocrinology of the County Emergency Hospital, University of Medicine and Pharmacy, Victor Babes, Timisoara, in a period of 3 years, January 2010 – January 2013. The study was approved by the ethics committee of the hospital and all patients gave their consent. The study group contained 169 women and 23 men, aged between 21 and 79 years (mean age = 54.27 ± 21.5 years).

All patients were first evaluated by an endocrinologist, with hormonal determinations (thyroid stimulating hormone - TSH, free thyroxin - FT4, free triiodothyronin - FT3) and so on, in order to establish the etiology and severity of thyroid disorder. Subsequently, they underwent cardiac evaluation: physical examination, ECG, chest x-ray and echocardiography, done with an Acuson Sequoia C512 echocardiography. We established by echocardiography the presence and amount of pericardial effusion with its hemodynamic consequences, eventually the signs of tamponade. A particular aspect, noticed in some cases, was the presence of a thick, hyperreflecting pericardium.

Results
From the 192 patients included in our study, 156 (81.25%) had overt hypothyroidism and 36 (18.75%) subclinical disease (SHT). Because of the inhomogeneity of patients with overt hypothyroidism we divided them into two categories: 77 subjects (49.35%) with severe thyroid insufficiency (STI), with TSH levels > 70 μmol/ml and FT4 < 6 pmol/ml, and 79 (50.64%) patients with moderate forms of clinical hypothyroidism (MCHT).

In our patients, pericarditis had an insidious onset, evolved without significant hemodynamic manifestations, and echocardiography was the primary method of diagnosis. Suggestive EKG findings were microvolt, ST – segment changes, negative T – waves and electrical alternans. The results of the laboratory examinations are presented in table 1.

Except for patients with prolonged hypothyroidism, pericardial effusion was detected in a minor or moderate amount, symptoms were minimal and alleviated with hormonal replacement therapy. Occasionally, pericardial effusion was substantial with cardiomegaly on chest X-ray and echocardiography revealed signs of tamponade.

Patients with overt hypothyroidism had the highest incidence of pericarditis: from the 77 subjects with STI, 59 (76.62 %) had pericardial effusions, of which 37 (62.71%) were small, 16 (21.11%) moderate and only 6 (7.90%) large, with signs of tamponade; from the 79 patients with MCHT, 22 (27.84%) had pericarditis: 15 (68.18%), small, 5 (22.72%) moderate and in 2 cases (9.09%) large. In patients with SHT, only 8 (22.22%) had pericardial effusion, but 6 (75%) had mild forms and 2 (25%) moderate ones, see fig.1.

Table 1: Results of laboratory examinations

| Laboratory examination | 192 patients (1) | 36 patients with SHT |
|------------------------|----------------|---------------------|
| TSH                    | 156 p with overt hypothyroidism | 36 p with SHT |
| FT4                    | 77 p with STI | 79 p with MCHT |
| FT3                    | 14 - 17,72% | 8 - 10,12% |
| Chest X-ray: Normal Cardiomegaly | 41 - 53,24% | 8 - 22,22% |

| Normal Cardiomegaly | 18 – 23,37% |
ECG:
- Negative T wave
- ST segment changes

Microvolt

|            | 23 – 29,87% | 19 – 24,67% | 11 – 14,28% |
|------------|-------------|-------------|-------------|

|            | 12 – 15,18% | 9 – 11,39%  | 5 – 6,32%   |
|------------|-------------|-------------|-------------|

|            | 1 - 2,77%   | 2 – 5,55%   | 1 – 2,77%   |
|------------|-------------|-------------|-------------|

Echocardiography: Pericardial effusion:
- Small (3-8 mm)
- Moderate (8-15 mm)
- Large (>15 mm)

| Protodiastolic collapse of RV Thickened pericardium |
|-----------------------------------------------------|
| 59 – 76.62% | 37 – 62.71% | 16 – 27.11% |
| 16 – 10,16% | 6 – 10,16%  | 6 – 10,16%  |
| 18 – 23.37% | 13 – 16,45% | 8 – 22.22%  |
| 8 – 22.22%  | 6 – 75%     | 2 – 25%     |
| 6 – 10,16%  | 2 – 9,09%   | 0           |
| 1 – 2,77%   | 2 – 9,09%   | 0           |
| 18 – 23,37% | 13 – 16,45% | 8 – 22.22%  |
| 8 – 22.22%  | 6 – 75%     | 2 – 25%     |
| 6 – 10,16%  | 2 – 9,09%   | 0           |
| 1 – 2,77%   | 2 – 9,09%   | 0           |
| 18 – 23.37% | 13 – 16,45% | 8 – 22.22%  |
| 8 – 22.22%  | 6 – 75%     | 2 – 25%     |
| 6 – 10,16%  | 2 – 9,09%   | 0           |
| 1 – 2,77%   | 2 – 9,09%   | 0           |
| 18 – 23.37% | 13 – 16,45% | 8 – 22.22%  |
| 8 – 22.22%  | 6 – 75%     | 2 – 25%     |
| 6 – 10,16%  | 2 – 9,09%   | 0           |
| 1 – 2,77%   | 2 – 9,09%   | 0           |

Fig. 1: Incidence of pericarditis

We looked for correlations between the amount of pericardial effusion and the levels of TSH; our results are plotted in fig. 2.

The statistical analyses using GraphPad InStat revealed, through the Mann-Whitney test, an extremely significant correlation (p<0.0001) between the amount of pericardial effusion (expressed in mm) and the level of seric TSH (μUI/ml).

Most patients had a favorable evolution under hormonal therapy and pericardial effusion reduced slowly and disappeared in time. Echocardiography performed at 1, 3, 6 and 12 month after starting L-thyroxine therapy revealed graduated reduction of pericardial effusion, parallel with the improvement of thyroid dysfunction, see fig 3.

Fig. 2: Correlations between the amount of pericardial effusion and TSH level

Fig. 3: Peculiar aspect, found mostly in patients with overt hypothyroidism, especially STI, was a thickened pericardium. This aspect was found in 17.70% of patients caused probably by long lasting or/and repeated episodes of pericarditis.

Discussions

Our study group contained 192 hypothyroid patients, mainly women (88.02%) and less men (11.97%) with mean age 54.27 ± 21.5 years, with prevalence of overt (81.25%) and few subclinical forms (18,75%) (6, 7, 8). The high incidence of severe forms can be explained by the fact that we included only hospitalized patients.

In our study group the incidence of pericarditis due to hypothyroidism was 46.35%, with large variations, from 22.22% in SHT, to 76.62% STI. Our results regarding the incidence of pericarditis were similar with those described in different studies, which ranges from 3% to 80% (9, 10).

We found a very significant correlation (p<0.0001) between the severity of thyroid dysfunction (expressed by the level of TSH) and the amount of pericardial effusion (in mm).

In our patients, the pericardial effusion regressed slowly and disappeared in time after reversion to euthyroid status (11, 12, 13, 14). Even in patients with signs of tamponade, pericardial effusion reduced gradually under therapy, so that no pericardiocentesis was needed (7, 15).

In hypothyroidism, pericardial fluid accumulates slowly, in most cases, allowing stretching of the pericardium, accommodating a large volume. That is why pericardial tamponade is a rather rare presentation in hypothyroidism, occurring mostly after many years of symptomatic disease or in patients who do not respond well to replacement therapy (16, 17).

Regarding the amount of pericardial effusion, most patients diagnosed with pericarditis (65.16%) had small amounts and 25.84% moderate ones. In our group the incidence of pericardial tamponade was 9.16%.

It has been thought that the size of the pericardial effusion depends on the severity and duration of hypothyroidism. Most cases of tamponade have been reported in the elderly where diagnosis of hypothyroidism is difficult because of its slow onset, and clinical signs and symptoms are subtle and non-specific (16, 18, 19).

Occasionally, cardiac function may be further compromised by the development of pericarditis, occurring in severe, long-standing overt hypothyroidism (20). In addition, overt hypothyroidism may be associated with other cardiovascular complications such as left ventricular hypertrophy and diastolic dysfunction. (21, 22).
Conclusions
In hypothyroid patients, pericarditis represents a frequent feature, found by echocardiography. The incidence and amount of pericardial effusion correlates with the severity and duration of disease and regresses slowly under hormonal replacement therapy. In some cases, with long lasting STI, a thickened pericardium developed.

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