DOI: 10.21802/acm.2022.1.9

CLINICAL COURSE AND LIPID METABOLISM INDICATORS IN PATIENTS WITH CHRONIC HEART FAILURE OF ISCHEMIC GENESIS AND COEXISTING HYPOTHYROIDISM

Iryna Kupnovytska, Yuliia Mykula
Ivano-Frankivsk National Medical University, Ivano-Frankivsk, Ukraine

Abstract. Cardiac diseases, especially chronic heart failure which, according to the World Health Organization, affects 1.5-2% of the global population, are the number one cause of mortality and morbidity worldwide, including Ukraine. Chronic heart failure is often accompanied by endocrine disorders, especially hypothyroidism, the diagnosis of which has increased over the past 10 years, and which facilitates the rapid progression of heart failure due to reduced metabolic processes and altered lipid metabolism.

The objective of the research was to study clinical manifestations, lipid metabolism indicators and their relationship in patients with chronic heart failure of ischemic genesis and coexisting primary hypothyroidism.

Materials and Methods. 73 patients with the average age of 55.92±2.66 years were examined. They were divided into 2 groups: Group I included 38 patients with chronic heart failure and coexisting hypothyroidism; Group II comprised 35 heart failure patients without hypothyroidism. The clinical course of chronic heart failure itself and chronic heart failure with coexisting hypothyroidism was studied, the patients' quality of life was evaluated, the myocardial function was studied by means of the 6-minute walk test, the indicators of lipid profile were analyzed by determining the serum levels of total cholesterol, low-density lipoprotein cholesterol. To assess thyroid function, thyroid-stimulating hormone and thyroxine levels were determined by the electrochemiluminescence immunoassay.

Results and Discussion. The clinical course and quality of life of patients with chronic heart failure and coexisting hypothyroidism were worse as compared to patients without hypothyroidism. The serum levels of total cholesterol, low-density lipoprotein cholesterol differed between both groups of patients ($p<0.05$).

Conclusions. Blood lipid profile was more significantly impaired in the patients with chronic heart failure of ischemic genesis and coexisting primary hypothyroidism that could result in the rapid progression of chronic heart failure, a more severe clinical course, and more frequent complications. The quality of life was higher in patients with heart failure without hypothyroidism and their condition was significantly better.

Keywords: chronic heart failure; hypothyroidism; lipid profile; patient's quality of life.

Problem statement and analysis of the latest research

The number of adults with chronic heart failure (CHF) is increasing worldwide, including Ukraine, with the tendency to rise with age. According to different countries, the average prevalence rate of CHF among the adult population ranges from 1.5 to 5.5% [1]. The prevalence of CHF progressively increases with age, accounting for more than 10% among people over 70 years of age. According to various sources, the incidence of CHF is estimated between 150 to 500 cases per 100,000 population (0.15 – 0.5%) each year, with the indicator doubling every 10 years among people over 45 years of age [2].

The clinical course of CHF is characterized by increased dyspnea, peripheral edema, reduced exercise tolerance, limited self-management capacity, psycho-emotional disorders, resulting in a deterioration in quality of life (QoL) which reflects the multidimensional influence of a clinical condition and its treatment on patients' daily lives. Maintaining a high QoL is as important as survival to most patients living with CHF [4, 5]. A low QoL is associated with high hospitalization and mortality rates [5].

The concept of QoL is related to health and is an integral part of a comprehensive assessment of the patient's condition, as well as the efficacy of therapeutic and preventive measures. The main approach to measure QoL is the use of generic and specific questionnaires. Generic questionnaires evaluate QoL as a whole, while specific questionnaires determine the impact of the disease or therapeutic method on specific QoL components.

Among disease-specific questionnaires, the Minnesota Living with Heart Failure Questionnaire (MLHFQ) is the gold standard for patients with CHF as it has the highest validity and sensitivity [4, 5].

Coronary artery disease (CAD) secondary to atherosclerosis is one of the most common causes of CHF. The National Chronic Heart Failure Registry database (2011), involving 2,820 patients from different regions of Ukraine, confirmed the important role of CAD and coronary artery atherosclerosis as their etiological factor (68% of patients had angina pectoris, 72% of patients were diagnosed with past myocardial infarction) [6].

Thyroid dysfunction has a great impact on the cardiovascular system and lipid profile. Hypothyroidism has been proven to be associated with increased risk of CAD, atherosclerosis, and mortality, as well as to depend directly on the degree of thyroid dysfunction, especially in patients with thyroid-stimulating hormone (TSH) ≥ 10

mIU/l [7].

Hypothyroidism, both overt and subclinical, affects lipid metabolism that has been well-documented in the literature. Decreasing thyroid function is associated with an increase in the risk of cardiovascular diseases. On the other hand, the prevalence of hypothyroidism in patients with hypercholesterolemia is reported to be 4.3% [8]. Therefore, the American Association of Clinical Endocrinologists and the American Thyroid Association recommend screening for hypothyroidism in patients with newly diagnosed hyperlipidemia [8-10].

Hypothyroidism is associated with an atherogenic lipid profile, including elevated total cholesterol (TC) levels due to elevated levels of low-density lipoprotein cholesterol (LDL-C), hypertriglyceridemia [8-10]. There are several mechanisms involved in the pathophysiology of hyperlipidemia in hypothyroidism, such as the decreased number of LDL receptors in the liver, resulting in decreasing LDL uptake and accumulation, reduced activity of the LDL receptor, increased LDL oxidation [11].

The objective of the research was to study clinical manifestations and QoL level in patients with CHF of ischemic genesis and coexisting primary hypothyroidism; to investigate the indicators of lipid profile in patients with hypothyroidism and those without hypothyroidism; to establish the relationship between the indicators and serum levels of TSH and thyroxine (T4).

Materials and Methods

73 patients with CHF, the New York Heart Association (NYHA) Functional Class (FC) I-II were examined. They were hospitalized to the Department of Arterial Hypertension of the Ivano-Frankivsk Regional Clinical Cardiology Centre of Ivano-Frankivsk Regional Council. The patients were divided into 2 groups: Group I comprised 38 patients with CHF and coexisting hypothyroidism; Group II included 35 HF patients without hypothyroidism. The average patients' age was 54.31±2.21 years in Group I and 57.54±3.12 years in Group II, respectively. The duration of CHF was on average 5.8±1.32 years. The exclusion criteria were diabetes mellitus, acute myocardial infarction, CHF NYHA FC III-IV, secondary and tertiary hypothyroidism.

All the patients underwent clinical and laboratory testing according to the Unified Clinical Protocol of Primary, Secondary (Specialized) and Tertiary (Highly Specialized) Medical Care "Chronic Heart Failure" (2016), the European Society of Cardiology Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 and the Guidelines of the Ukrainian Association of Cardiologists 2017.

During clinical examination, typical CHF symptoms were studied: the incidence of peripheral edema, dyspnea on exertion, general weakness, and fatigue. The 21-item MLHFQ was used to evaluate QoL in patients with CHF. The total score can range from 0 (very high QoL) to 105 (very low QoL) points.

The NYHA functional class of CHF was assessed using the 6-minute walk test (6MWT) in a 35-m long corridor with the measurement of peak oxygen uptake by the following formula:

$$V0_2 = (5.8xM+151+10.1xW)/M$$

where $V0_2$ is the value of oxygen uptake, ml/(kg-min); M is the patient's mass, kg; W is the power of the work done, W. The power of the work done was calculated by the formula:

$$W = M \times L/t$$

where M is the patient's mass, kg; L is the distance covered during the 6MWT, m; t is the test time, sec.

The serum level of TC was determined by the enzymatic colorimetric method. The plasma concentration of LDL-C was measured by the direct enzymatic method, without precipitation.

The blood lipid profile was determined on the GBS Stat Fax 4500 analyzer (USA), using the ELITech reagent kit (France).

The serum concentration of TSH and T4 was determined by the electrochemiluminescence immunoassay (ECLIA) on the Cobas 8000 modular analyzer (Switzerland), using Roche Diagnostics reagents (Switzerland).

The results obtained were statistically processed using an advanced analytics software package Statistica 6.0, the Student's t-test. The correlation was assessed using the Spearman rank correlation coefficient. A p-value less than 0.05 was considered statistically significant.

Results and Discussion

When analyzing clinical symptoms in patients with CHF and coexisting hypothyroidism, peripheral edema was found in 72.1% of cases, dyspnea on exertion was detected in 61.8% of patients, general weakness and fatigue were observed in 88.7% of cases. In Group II, these indicators were significantly lower: lower extremity edema was found in 65.4% of cases, dyspnea on exertion was detected in 54.9% of patients, general weakness and fatigue were observed in 75.3% of cases that was 6.7%, 6.8% and 13.4% lower, respectively, as compared to Group I.

According to the MLHFQ, QoL in patients with coexisting hypothyroidism was 36.5% lower as compared to those with no comorbidity ($p<0.001$) (Table 1).

When evaluating different QoL aspects, in patients of Group I, the number of points scored for functional capacity was found to be 36.2% higher as compared to

Group II (p<0.001). Psycho-emotional disorders were 14.1% more often observed in patients with comorbidity; patients with CHF and coexisting hypothyroidism reported social limitation 26.3% more often (p<0.001) (Table 2).

Table 1. Quality of life in patients with chronic heart failure of ischemic genesis and coexisting hypothyroidism and those with chronic heart failure and no comorbidity, points (M±m)

Group	Points
Group I, n = 38	62.31±1.68*
Group II, n = 35	40.82±1.32

Notes: *p<0.001- a significant difference between patients of Group I and Group II

Table 2. Evaluation of different quality of life aspects in patients with chronic heart failure of ischemic genesis and coexisting hypothyroidism and those with chronic heart failure and no comorbidity according to the Minnesota questionnaire, points (M±m)

Quality of life aspects	Patients under study, n = 73	
	Group I, n = 38	Group II, n = 35
Physical	24.12±1.53*	16.42±0.95
Emotional	15.22±0.91*	13.12±0.76
Social	6.21±0.37*	3.68±0.18

Notes: *p<0.001- a significant difference between patients of Group I and Group II

Exercise tolerance was significantly lower in patients with coexisting hypothyroidism indicating a great impact of comorbid pathology on the cardiovascular system functioning (Table 3).

Table 3. Exercise tolerance according to the 6-minute walk test in patients with chronic heart failure of ischemic genesis and coexisting hypothyroidism and those with chronic heart failure and no comorbidity (M±m)

Indicator	Patients under study, n = 73	
	Group I, n = 38	Group II, n = 35
Distance, m	384.17±15.91*	453.18±13.41
Oxygen uptake, ml/kg/min	14.02±0.94*	16.74±0.98

Notes: *p<0.001- a significant difference between the patients of Group I and Group II

The distance walked by the patients during the 6MWT ranged from 341 to 427 m (384±15.9 m); the average value of oxygen uptake ranged between 14.2 and 17.1 ml/kg/min (14.02±1.3 ml/kg/min) (p<0.05). In the comparison group, this distance was 17.6% greater and the value of oxygen uptake was 6.3% higher as compared to patients with hypothyroidism (p<0.05).

The elevated serum levels of TC and LDL-C were observed in the patients of both groups; however, these indicators were 21% and 18% higher in patients of Group I, respectively, as compared to patients with no hypothyroidism. There was a strong positive correlation between the serum levels of TSH and TC (r=0.72, p<0.05), a moderate positive correlation between the levels of TSH and LDL-C (r=0.61, p<0.05), a moderate negative correlation between the levels of T4 and LDL-C (r=- 0.32, p<0.05). In the patients with CHF and without hypothyroidism, there was a weak positive correlation between the levels of TSH, TC and LDL-C (r=0.21 and r=0.24, respectively, p<0.05), a weak negative correlation between the levels of T4 and TC (r=0.18, p<0.05) (Table 4).

These results indicated that impaired lipid profile contributed to the rapid progression of CHF, a more severe clinical course in the patients with comorbid pathology leading to more frequent complications.

Table 4. Blood lipid profile in patients with chronic heart failure of ischemic genesis and coexisting hypothyroidism

Indicators	Group I, n=38	Group II, n=35	Apparently healthy, n=10
TC, mmol/l	6.32±0.31*°	5.22±0.23*	4.24±0.18
LDL-C, mmol/l	3.87±0.21*°	2.69±0.19*	2.18±0.14
TSH, mIU/ml	12.96±0.51*	1.17±0.32	0.91±0.21
T4 pg/mL	5.32±0.81*	13.68±1.28	14.21±1.84

Notes: *- statistically significant as compared to apparently healthy individuals; ° - statistically significant as compared to Group I and Group II

Coexistence of CHF and thyroid dysfunction is becoming more common today, therefore, both cardiologists and endocrinologists are required to focus on this condition more precisely; correlation with hormonal status is necessary as there is a close pathogenetic relationship between both pathologies that results in their mutual aggravation and rapid progression.

Conclusions

1. CHF of ischemic genesis and coexisting hypothyroidism had a significantly worse clinical course as compared to CHF with no endocrine pathology, manifesting itself as reduced exercise tolerance as well.

2. Quality of life was 35.5% lower in the patients with comorbid pathology; the patients experienced social and psycho-emotional limitations more often.

3. Blood lipid profile was impaired in the patients with hypothyroidism resulting in rapid CHF progression. There was a strong correlation between the serum levels of TSH and T4 and the levels of TC and LDL-C.

Conflict of Interest: The authors declare that there is no conflict of interest.

Funding: The authors have no funding to report.

Acknowledgements: The authors have no support to report.

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Received: 17.01.2022
Revised: 03.05.2022
Accepted: 25.05.2022