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## Syndrome of hypothyroidism as a factor of cardiovascular pathology development (literature review)

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**Abstract.** *The article presents pathogenetic data on the development of cardiovascular pathology in reduced thyroid function. Hypothyroidism is associated with an increased risk of coronary heart disease, myocardial infarction, chronic heart failure and cardiovascular mortality, regardless of gender, age and previous cardiovascular disease. This leads to the search for additional influence on the pathogenetic mechanisms of hypothyroidism in order to effectively treat these threatening manifestations and consequences of the disease.*

**Keywords:** *hypothyroidism; coronary heart disease; review*

### Introduction

In modern medical science the thyroid dysfunction is one of the risk factors for cardiovascular disease. This fact is unpredictably underestimated, unfortunately [1].

Many studies, devoted to the mechanisms of the influence of reduced function of the thyroid gland on the cardiovascular system, have been organized. Slight disorders of the thyroid function may be accompanied by an increasing of cardiometabolic risk [2, 3]. It has been shown that hypothyroidism has a significant impact on the formation and development of cardiovascular diseases even at the early (subclinical) phase. The results of large-scale studies show that subclinical hypothyroidism is associated with an increased risk of coronary heart disease, myocardial infarction, chronic heart failure and cardiovascular mortality, regardless of gender, age and previous cardiovascular disease [4]. Metabolic relationships are found between hypothyroidism and the risk factors of cardiovascular diseases, that accompany by obesity, arterial hypertension, lipid and carbohydrate metabolism disorder [5].

The increasing of the coronary atherosclerosis prevalence in patients with hypothyroidism compared to patients with euthyroidism has led to the emergence of studies that examine the thyroid hormones effect on the synthesis of lipids. The hypothyroidism was detected in 30–45 % of cases in patients with chronic forms of

coronary heart disease [6]. Secondary dyslipidemia is a pathogenetic factor that binds hypothyroidism and the development of atherosclerosis [7].

According to the Colorado population study, which included 25 862 patients, the prevalence of hypothyroidism was 4–21 % for women and 3–16 % for men, depending on their age. The severity of hypercholesterolemia was directly related to the increased levels of the TSH. The medium levels of total cholesterol and low-density lipoprotein cholesterol were significantly higher in patients with TSH 5.1–10 mIU/l than in patients with euthyroidism [8]. The low levels of thyroid hormones slow down the decomposition of lipids however the synthesis of lipids is preserved, which leading to hyperlipidemia [9].

Hypothyroidism reduces expression of the SREBP-gene, which regulates the absorption and synthesis of the cholesterol. The authors demonstrate that this gene is regulated by the thyroid hormones [10]. The thyroid hormones induce of the 3-hydroxy-3-methylglutaric-coenzyme-A-reductase and are involved in the process of the first stage of cholesterol synthesis. Triiodothyronine also regulates the activity of the receptors of low density lipoprotein and controls the activity of the genes responsible for them [11], and protects low-density lipoprotein from oxidation [12]. It is responsible for reducing the amount and sensitivity of the receptors of low density lipoprotein

in the liver; impairs renal glomerular function (decreased glomerular filtration) and slows down the clearance of low density lipoprotein [13].

Thyroid hormones stimulate the conversion of the cholesterol to bile acids. The  $T_3$  regulates the activity of the main enzyme in the synthesis of bile acids — cholesterol-7 $\alpha$ -hydroxylase, which in conditions of hypothyroidism, accelerates the disintegration of cholesterol in the liver and increases its level in the blood [14].

The hypothyroidism leads to the decrease of the activity of cholesterol-ester transport protein, which is a primary factor of the metabolism of high-density lipoprotein and hepatic lipase, providing 30 % of the reverse transport of cholesterol [15].

At the stage of the subclinical hypothyroidism increased concentrations of lipoprotein-associated phospholipase A2 (Lp-PLA2), known as marker of coronary heart disease [16], and decreased activity of Lp-PLA2 HDL, which is associated with anti-atherogenic effects of the high-density lipoprotein observed. In addition,  $T_3$  regulates apolipoprotein A, which plays a major role in controlling triglyceride levels [17].

Thus, insufficiency of the thyroid hormones leads to the hypercholesterolemia, and it is a characteristic symptom of the hypothyroidism. Than higher is the level of the TSH, the higher is the content of cholesterol [18].

Hormones of the thyroid gland are vasodilators, that influence on the smooth muscle of vessels and are a non-lipid risk factor of cardiovascular disease [19]. The hypothyroidism leads to an increased peripheral vascular resistance, which leads to vasoconstriction of the vessels, promotes the development of hypertension. In addition, thyroid hormones are stimulating the activity of the 5-deoxyadenosine phosphatase of the second type in smooth muscle cells, which provide the conversion of  $T_4$  to active  $T_3$  and contribute to the relaxation of the blood vessels [20]. Also with hypothyroidism, products of protein metabolism (glycosaminoglycans, derivatives of protein, glucuronic acid and chondroitin sulfuric acids) accumulates in the interstitium, which causes the mucinous edema and vascular dysfunction [14].

The deficiency of NO in hypothyroidism leads to the development of arterial hypertension. Together with the endothelial dysfunction it leads to the stimulation of the proliferation of the vascular cell wall, what promotes the development of fibrosis and changes vascular adaptation mechanisms, increases the risk of atherosclerosis [6, 9, 13].

Another factor in hypothyroidism, which contributes into the increased cardiovascular risk — is a disorder in the hemostasis: microthrombus slab, increased viscosity and density of blood, which changes the microcirculation, promotes perivascular edema, the emergence of the blood resistance and increased blood pressure [4, 8].

It was established that the decrease in the concentration of thyroid hormones leads to changes in metabolism of the energy and neurotransmitter, forms a syndrome of secondary immunological deficiency, promotes the activation of lipid peroxidation processes and the appearance of hypercholesterolemia [3, 17].

It has been proved that in patients with autoimmune thyroiditis and hypothyroidism, the presence of systemic inflammation of the low activity causes the development of the endothelial dysfunction [7]. The thickness of the intima-medial complex of carotid arteries in women with obesity and autoimmune thyroiditis, which confirms the important participation of hypothyroidism in the progression of atherosclerotic vascular damage, is demonstrated [20].

In patients with hypothyroidism an increased thickness of intima-media of carotid arteries, in comparison with euthyroid individuals, was found. And the degree of thickening is closely correlated with the low-density lipoprotein and TSH [32, 39].

## Conclusions

Thus, the influence of the hypothyroidism on the cardiovascular system is carried out by mechanisms such as atherogenic dyslipidemia, endothelial dysfunction, activation of the system of hemocoagulation, the increase of peripheral vascular support, the increase of the tone of the sympathoadrenal system, the decrease vasodilatational properties of blood vessels. This leads to the search for additional influence on the pathogenetic mechanisms of the hypothyroidism in order to effectively treat these threatening manifestations and consequences of the disease.

**Conflicts of interests.** Authors declare the absence of any conflicts of interests that might be construed to influence the results or interpretation of their manuscript.

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### Синдром гіпотиреозу як фактор розвитку патології серцево-судинної системи (огляд літератури)

**Резюме.** У статті наведені дані про патогенетичні аспекти розвитку патології серцево-судинної системи при зниженні функції щитоподібної залози. Гіпотиреоз асоціюється з підвищенням ризику розвитку ішемічної хвороби серця, інфаркту міокарда, хронічної серцевої недостатності й смертності від серцево-судинних захворювань не-

залежно від статі, віку й попередніх серцево-судинних захворювань. Це спонукає до пошуку додаткового впливу на патогенетичні механізми гіпотиреозу з метою ефективної терапії вказаних загрозливих проявів та наслідків хвороби.

**Ключові слова:** гіпотиреоз; ішемічна хвороба серця; огляд

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**Резюме.** В статье приведены данные о патогенетических аспектах развития патологии сердечно-сосудистой системы при снижении функции щитовидной железы. Гипотиреоз ассоциируется с повышением риска развития ишемической болезни сердца, инфаркта миокарда, хронической сердечной недостаточности и смертности от сердечно-сосудистых заболеваний независимо от пола,

возраста и предыдущих сердечно-сосудистых заболеваний. Это побуждает к поиску дополнительного воздействия на патогенетические механизмы гипотиреоза с целью эффективной терапии указанных угрожающих проявлений и последствий болезни.

**Ключевые слова:** гипотиреоз; ишемическая болезнь сердца; обзор