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FEATURES OF DYSLIPIDEMIA IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND ITS COMBINATION WITH CONCOMITANT HYPOTHYROIDISM

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Abstract. Features of dyslipidemia in chronic obstructive pulmonary disease and its combination with concomitant hypothyroidism. Kashul S.V., Khukhlina O.S. *Systemic inflammation and external respiration dysfunction lead to blood lipid profile shift. As the frequent concomitant pathology, hypothyroidism causes lipid metabolism deviations as well. In this study, we aimed to investigate lipid metabolism features in chronic obstructive pulmonary disease including the presence of concomitant hypothyroidism. A direct method for determining total cholesterol and high- and low-density lipoproteins in blood serum, an enzymatic method for determining triacylglycerols in serum, automatic counting of the absolute number of the peripheral blood monocytes by a hematology analyzer, a fluorescent immunoassay method for determining thyroid-stimulating hormone and free thyroxine in serum were used. All patients underwent postbronchodilator forced spirometry using a portable spirometer to obtain forced expiratory volume in the first second and forced vital capacity. There were assesed 65 patients with chronic obstructive pulmonary disease, 43 of them without concomitant hypothyroidism (research group A), and the other 22 – with concomitant hypothyroidism (research group B); and 24 healthy controls. Comparing to controls, both research groups had significantly higher levels of total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol and triacylglycerols ($p<0.05$ for each parameter). Research group B patients had significantly higher serum concentrations of total cholesterol, low-density lipoprotein cholesterol and triacylglycerols and lower – of high-density lipoprotein cholesterol ($p<0.05$ for each), compared with research group A. Forward stepwise regression analysis revealed that forced vital capacity decrease could be associated with total cholesterol content rise in all patients ($p<0.001$). We ascertained a negative correlation between total cholesterol level and forced expiratory volume during the first second, and also between total cholesterol level and forced vital capacity in both research groups ($p<0.05$). We also established a significant relationship between increased thyroid-stimulating hormone levels and increased total cholesterol concentrations based on stepwise regression analysis ($p<0.001$). A calculated monocytes-high density lipoprotein cholesterol ratio is perspective prognostic indicator of development of the final result of dyslipidemia – atherosclerosis, it was higher in the research group of patients with COPD and comorbidity ($p<0.05$). Investigation of blood lipid profile and the aforementioned index not only illustrates pathogenetic mutual burden of respiratory and thyroid pathologies, but also gives an opportunity to predict clinical parameters in chronic obstructive pulmonary disease patients like state of external ventilation function of lungs and cardiovascular risk.*

Реферат. Особливості дисліпідемії за хронічного обструктивного захворювання легень і його поєднання із супутнім гіпотиреозом. Кашул С.В., Хухліна О.С. *Системне запалення та порушення функції зовнішнього дихання спричинюють зрушення ліпідного профілю крові. Гіпотиреоз як часта супутня патологія також викликає порушення ліпідного метаболізму. У цьому дослідженні ми мали за мету дослідити особливості обміну ліпідів за хронічного обструктивного захворювання легень, зокрема і за наявності супутнього гіпотиреозу. Були застосовані прямий метод визначення холестеролу загального та ліпопротеїдів високої та низької щільності в сироватці крові, ферментативний метод визначення тріацилгліцеролів у сироватці, автоматичний підрахунок абсолютної кількості моноцитів периферичної крові гематологічним аналізатором, метод флуоресцентного імуноаналізу для визначення в сироватці тиреотропного гормону та вільного тироксину, а також пацієнтами була здійснена постбронходилатаційна форсована спірометрія з використанням портативного спірометра для отримання об'єму форсованого видиху за першу секунду та форсованої життєвої ємності легень. Було обстежено 65 пацієнтів із хронічним обструктивним захворюванням легень, з яких у 43 не було супутнього*

гіпотиреозу (I дослідна група), а інші 22 мали супутній гіпотиреоз (II дослідна група); а також 24 практично здорові особи контрольної групи. Порівняно з контрольною групою, в обох дослідних групах спостерігалися значно вищі показники вмісту холестеролу загального та ліпопротеїдів високої та низької щільності, а також тріацилгліцеролів (p<0,05 для кожного параметра). У пацієнтів II дослідної групи були достовірно вищі концентрації холестеролу загального й ліпопротеїдів низької щільності, та тріацилгліцеролів (p<0,05 для кожного параметра), і нижча – холестеролу ліпопротеїдів високої щільності (p<0,05) порівняно з I дослідною групою. За результатами покрокового регресійного аналізу, зниження функціональної життєвої ємності легень могло бути пов'язане з підвищенням вмісту холестеролу загального у всіх пацієнтів (p<0,001). Ми встановили негативний кореляційний зв'язок між концентрацією холестеролу загального та об'єму форсованого видиху за першу секунду (p<0,05) та між концентрацією холестеролу загального та функціональною життєвою ємністю легень (p<0,05) в обох дослідних групах. Також нами був встановлений достовірний зв'язок між підвищенням вмісту тиреотропного гормону та зростанням концентрації холестеролу загального на основі покрокового регресійного аналізу (p<0,001). Визначене нами співвідношення абсолютної кількості моноцитів до холестеролу ліпопротеїдів високої щільності, який є перспективним прогностичним показником для одного з кінцевих результатів дисліпідемії, а саме – розвитку атеросклерозу, було достовірно вищим у тій дослідній групі, у яку входили пацієнти із хронічним обструктивним захворюванням легень, які мали супутній гіпотиреоз (p<0,05). Дослідження ліпідного профілю крові та визначення згаданого вище індекса не лише відображає патогенетичне взаємообтяження розглянутих респіраторної та тиреоїдної патологій, але й дає змогу прогнозувати клінічні параметри пацієнтів із хронічним обструктивним захворюванням легень, такі як стан зовнішньовентиляційної функції легень та кардіоваскулярний ризик.

Decade by decade, chronic obstructive pulmonary disease (COPD) becomes more ubiquitous in the world. It is known that COPD world prevalence may be from 2.5 to 10.3%, according to different estimates [1]. It is prognosed that COPD world prevalence will raise by 23% till the year 2050, and its burden will become more in women and in developping countries [2]. In recent years, COPD is more frequently diagnosed at age of 20-30 years [3]. According to Global Burden of Disease Study, COPD mortality in Ukraine in 2019 was 25.79 per 100,000 population [4].

Hypothyroidism is one of the leading endocrinological pathologies. First of all, its prevalence depends on iodine defficiency in particular area. Thus, in iodine sufficient areas (US, Europe) it is from 4.6% to 5.3% [5], and it is drastically higher in countries with iodine deficiency (Saudi Arabia) – 17.9% and 18.9% for subclinical and overt hypothyroidism, respectively [6]. The hypothyroidism and thyroid pathology issue is current and less studied in Ukraine where there are a number of regions with at least moderate iodine deficiency [7, 8]. Thus, the data given in the most recent available sources show that from 2013 till 2017 [9] hypothyroidism prevalence raised from 251.6 to 302.8 per 100,000 population.

One systematic review mentions that hypothyroidism prevalence among COPD patients is much higher than in general population and can reach 37% [10].

Dyslipidemias are almostly the most global problem of modern healthcare. Thus, 4.4 millions of deaths all over the world were associated with high level of low-density lipoprotein cholesterol (LDL-C), and it was by 46.7% higher than in 1990 [11]. It is reported that lipid metabolism disruption is also present in COPD [12] and in hypothyroidism [13].

The purpose of our research is to study serum lipid profile parameters in COPD patients depending on concomitant hypothyroidism; to analyze the role of lipid metabolism and monocytes in pathogenetic mutual burden in this comorbidity.

MATERIALS AND METHODS OF RESEARCH

The study is based on observation of 65 inpatients hospitalized to Internal Medicine departments of one healthcare establishment in city of Chernivtsi, Ukraine, due to severe COPD exacerbation. They were divided into two research groups depending on hypothyroidism presence. Research group A included 43 COPD patients without concomitant hypothyroidism, 22 males and 21 females, average age 62.71(3.87) years. Research group B included 22 COPD patients with concomitant hypothyroidism, 11 males and 11 females, average age 65.13 [45.70;74.20] years, with primary subclinical hypothyroidism. In particular, it was caused by autoimmune (Hashimoto) thyroiditis in 5 (22.73%) patients, postoperative – in 2 (9.09%) patients and the hypothyroidism etiological factor was unknown in the rest of patients. The COPD diagnosis was made according to Unified Clinical Protocol for Primary, Specialized and Emergency Medical Care "Chronic Obstructive Pulmonary Disease", approved by Ukraine Ministry of Health order dated 20 September 2024, No. 1610 [14]. Patients were hospitalized as stated by indications included in paragraph 3.4 of part IV of this protocol. Hypothyroidism was diagnosed by UK National Institute for Health and Care Excellence (NICE) guideline NG145 "Thyroid disease: assessment and management", published 20 November 2019, updated 12 October 2023 [15].

24 healthy people, 12 males and 12 females, average age 28.26 [21.32;37.89], were also involved in the control group.

Exclusion criteria in this research were: oncological disease with any localization of tumour and regardless of metastases, pneumonia, tuberculosis, sarcoidosis, bronchiectasis, idiopathic lung fibrosis, acquired immunodeficiency syndrome, individual 400 mcg salbutamol intolerance, subclinical or overt hyperthyroidism, decompensated acute or chronic heart failure and (or) unstable angina pectoris or stable angina pectoris grade 3-4 according to Canadian Cardiovascular Society classification, all types of obesity and (or) diabetes mellitus, and chronic kidney disease as well.

Serum contents of total cholesterol (TC), LDL-C, high-density lipoprotein cholesterol (HDL-C) were evaluated by direct method, and serum triacylglycerols (TG) content was evaluated by enzymatic method with GPO-PAP monoreagent, ready-for-service sets were used (PrJSC "Reahent", Dnipro, Ukraine). Monocyte count was performed on automatical haematology analyzer Diatron Abacus 360 (manufacturer "Diatron Mi Zrt.", Hungary). We also used them for determining following derivative indices.

Atherogenic coefficient (AC) was calculated using a formula [16]:

$$AC = \frac{TC - (HDL\text{–}C)}{(HDL\text{–}C)}$$

Atherogenic index of plasma (AIP) was calculated using a formula [17]:

$$\text{AIP} = \lg(\frac{TG}{HDL\text{–}C})$$

MHR was calculated using a formula [18]:

$$\text{MHR} = \frac{monocyte\ count\ (10^9 \times l^{-1})}{HDL\text{–}C\ (mmol\ \times\ l^{-1})}$$

In order to assess thyroid function, blood contents of free thyroxin (fT4) and thyroid-stimulating hormone (TSH) were evaluated by fluorescent immunoanalysis method using quantative express tests on Finecare FIA Meter Plus FS-113 analyzer (manufacturer Guangzhou Wondfo Biotech Co., Ltd., People's Republic of China).

Patients performed forced spirometry 15 minutes after inhalation of 400 mcg beta-2-adrenergic agonist salbutamol, and heathy controls did not perform bronchodilator inhalation, in order to estimate forced expiratory volume in one second (FEV1) and forced vital capacity (FVC). The portative spirometer BTL-08 SPIRO PRO (manufacturer BTL zdravotnická technika, a.s., Czech Republic) was used for this purpose.

For a clinical blood test and biochemical investigation, 10 ml of venous blood was collected fasting in the morning on the following day after determining shortness of breath by modified Medical Research Council its grade fell from 4 to 3 [19]. Forced spirometry was conducted in the patients' ward the same day when the blood was taken.

We offered patients and controls to get acquainted with an informed consent and sign it. We received a positive conclusion of Bukovinian State Medical University Biomedical Ethics Comission (protocol No. 1 dated 21 September 2023) about abidance of moral and legal rules of conducting medical scientific researches. During carrying out all diagnostic procedures including invasive ones basic ethical principles were followed according to World Medical Association Declaration of Helsinki "Ethical principles for medical research involving human subjects", basic statements of Good Clinical Practice, and Order of the Ministry of Health of Ukraine No. 690 of 23.09.2009.

Obtained research results were statistically processed with a licenced program StatSoft STATISTICA 10.0.1011 Enterprise edition (Stat Soft inc., United States of America, serial No. GFR205F354521FA-5). Gender homogeneity in groups was substantiated using Pearson χ^2 criterion. Kruskal-Wallis H-criterion was used in order to substantiate age similarity between research groups A, B, and controls, Mann-Witney U-criterion was used to in research groups A and B. Having compared gender distribution in research groups A, B, and controls, we did not find significant differences between all of them (p=0.994). Considering groups' differences by age, we revealed that research groups and controls differed significantly (p=0.027), but there was no difference between research groups A and B while controls were excluded (p=0.781).

Data distribution was normal in research group A, so their average (M) and standart deviation (SD) were defined like M(SD). Since research group B and the control one had less than 30 participants, so that they couldn't have normal data distribution and in these groups Me[25%;75%], Me stands for median and [25%;75%] stands for the interquartile range.

Research groups A, B, and controls were compared using Kruskal-Wallis H-criterion. Research groups were compared separately using Mann-Witney U-criterion. In the research group A, we evaluated possible relations between parameters by

Pearson correlations and in research group B – by Spearman correlations. Differences between groups and correlations were considered as significant at $p<0.05$ [20]. We also performed forward stepwise multiple regression [21] for FVC and TC.

RESULTS AND DISCUSSION

Our research results' analysis indicates that all blood lipids, AC, monocyte count, MHR were significantly higher, and FEV1 and FVC were significantly lower in both research groups than in controls. We also observed significantly higher blood concentrations of TC, LDL-C, AC, MHR and significantly lower blood level of HDL-C and FVC in research group B than in research group A (Table 1).

Table 1

Parameters of blood lipid spectrum, monocytes, derivative coefficients and FEV1 and FVC findings between research groups and controls M(SD), Me[25%;75%]

Parameter	Research group A n=43	Research group B n=22	*p*-level of significance due to U-criterion	Control group n=24	*p*-level of significance due to H-criterion
TC, mmol/L	5.60 (0.17)	6.04 [4.40;7.73]	p=0.034	4.57 [3.28;6.24]	p=0.019
HDL-C, mmol/L	2.66 (0.16)	2.27 [1.32;3.15]	p=0.042	1.29 [0.92;2.06]	p=0.021
LDL-C, mmol/L	3.10 (0.11)	3.56 [2.70;4.24]	p=0.029	2.44 [1.64;3.15]	p=0.013
TG, mmol/L	1.98 (0.19)	2.44 [1.95;2.87]	p=0.021	1.36 [0.85;1.81]	p=0.014
AC	2.71 (0.29)	3.19 [2.69;3.57]	p=0.044	2.41 [1.84;2.87]	p=0.031
AIP	-0.09 (0.20)	-0.11 [-0.16;0.24]	p=0.687	-0.07 [-0.23;0.09]	p=0.491
Monocyte count, 10^9/L	0.55 (0.22)	0.37 [0.19;0.65]	p=0.084	0.21 [0.04;0.37]	p=0.039
MHR	0.202 (0.11)	0.270 [0.164;0.353]	p=0.025	0.166 [0.113;0.221]	p=0.041
FEV1, % of predicted	45.11 (1.78)	43.03 [28.02;56.34]	p=0.236	95.47 [90.16;99.78]	p=0.007
FVC, % of predicted	66.94 (1.51)	60.25 [47.69;68.11]	p=0.037	86.75 [76.31;95.47]	p=0.009

Notes: n – number of patients in each group; the significance level according to the U-criterion was computed in order to determine whether the difference between research groups A and B is significant; the significance level according to the H-criterion was computed in order to determine whether the difference between both research groups and controls is different.

We also analyzed possibility of statistical relationships between lipid profile parameters and derivative indices on one side, and TSH, fT4, FEV1 and FVC on the other side, in both research groups A (Table 2) and B (Table 3) seperately.

In research group A (Table 2), we revealed significant correlations between TC and FEV1 ($r=-0.575$, $p<0.05$) and FVC ($r=-0.459$, $p<0.05$), between HDL-C level and FEV1 ($r=-0.478$, $p<0.05$), and between TG level with fT4 ($r=-0.554$, $p<0.05$) and TSH ($r=0.469$, $p<0.05$) as well.

TC level correlation with FEV1 and FVC mentioned before were stronger in a research group B ($r=-0.814$, $p<0.01$ and $r=-0.854$, $p<0.01$, respectively) compared to research group A (Table 3). There were also negative correlations of TG with FEV1 ($r=-0.670$, $p<0.05$) and FVC ($r=-0.677$, $p<0.05$) in research group B patients. We also observed negative correlations of AIP with fT4 level ($r=-0.581$, $p<0.05$), FEV1 ($r=-0.497$, $p<0.05$) and FVC ($r=-0.494$, $p<0.05$).

Table 2

Matrix of Pearson correlations of serum lipid parameters with thyroid function rates and certain spirometric rates in the research group A

	TSH, μIU/mL	fT4, pmol/L	FEV1, %pred.	FVC, %pred.
TC, mmol/L	**0.297**	**-0.292**	**-0.575***	**-0.459***
HDL-C, mmol/L	**-0.098**	**0.113**	**-0.478***	**-0.411**
LDL-C, mmol/L	**0.359**	**-0.328**	**-0.231**	**-0.101**
TG, mmol/L	**0.469***	**-0.554***	**-0.434**	**-0.345**
AC	**-0.120**	**0.039**	**-0.074**	**-0.050**
AIP	**0.304**	**-0.416**	**-0.242**	**-0.171**
MHR	**0.201**	**-0.316**	**-0.332**	**-0.396**

Note. * – correlation rate significance at p<0.05.

Table 3

Matrix of Spearman correlations of serum lipid parameters with thyroid function rates and certain spirometric rates in the research group B

	TSH, μIU/mL	fT4, pmol/L	FEV1, %pred.	FVC, %pred.
TC, mmol/L	**0.151**	**-0.263**	**-0.814****	**-0.854****
HDL-C, mmol/L	**-0.280**	**0.273**	**-0.367**	**-0.412**
LDL-C, mmol/L	**0.025**	**-0.389**	**-0.007**	**-0.007**
TG, mmol/L	**0.070**	**-0.350**	**-0.670***	**-0.677***
AC	**-0.238**	**0.427**	**-0.039**	**-0.070**
AIP	**0.112**	**-0.581***	**-0.497***	**-0.494***
MHR	**0.140**	**-0.063**	**-0.193**	**-0.119**

Notes: * – correlation rate significance at p<0.05; ** – correlation rate significance at p<0.01/

Separately it is worth noting there were no correlation between fT4, TSH and both spirometric parameters in both research groups (Tables 2,3).

Using these massives data, we eventually performed multiple forward stepwise regression, and identified FVC (dependent variable) statistical dependence on serum lipid levels, monocytes, TSH and fT4 concentrations (independent variables) on (Table 4).

Due to absence of statistical significance, all independent variables except TC were dismissed. We obtained a pattern, defined by a formula:

$$y = 105.152 - 5.4533 * x_1 ,$$

where y stands for FVC in % of predicted, x_1 stands for serum TC level, mmol/L. Probability of rejecting the hypothesis p=0.000197.

Table 4

Multiple regression of potential factors of FVC decreasing in COPD patients

Independent variables	B-coefficient	Standard deviation	Significance p-level
TC, x_1		2.068	p=0.024
HDL-C, x_2	-4.949	6.757	p=0.472
LDL-C, x_3	0.962	3.156	p=0.764
TG, x_4	0.352	2.150	p=0.871
Monocyte count, x_5	19.745	22.343	p=0.387
fT4, x_6	-3.354	8.690	p=0.704
TSH, x_7	0.388	1.326	p=0.773
Constant	108.137	16.892	p<0.001

In turn, we performed multiple forward stepwise regression, accepting TC as the dependent variable, and fT4, TSH, monocyte count, MHR, FEV1 and FVC as the independent ones, in order to determinate probable factors of serum TC concentration alterations (Table 5).

Table 5

Multiple regression of potential factors of TC increasing in COPD patients

Independent variables	B-coefficient	Standard deviation	Significance p-level
fT4, u_1	0.387	0.878	p=0.663
TSH, u_2	0.225	0.134	p=0.108
Monocyte count, u_3	1.670	1.256	p=0.197
MHR, u_4	-1.445	1.795	p=0.430
FEV1, u_5	-0.094	0.053	p=0.091
FVC, u_6	0.000	0.046	p=0.988
Constant	8.676	2.110	p<0.001

After gradual rejection of insignificant independent variables, association between TC on the one side and TSH (p=0.047) with FEV1 (p<0.001) one the other, was defined as follows:

$$v = 9.280 + 0.196 * u_2 - 0.097 * u_5 \ ,$$

where v stands for serum TC level in mmol/L, u_2 stands for serum TSH level in μIU/mL, u_5 stands for FEV1 % of predicted. Probability of rejecting the hypothesis p=0.00035.

Thus, while performing forward stepwise multiple regression analysis, we identified potential connections between pathogenetic mutual burden links of COPD and hypothyroidism like inflammation, bronchial obstruction, lung restriction, dyslipidemia, decreased thyroid function and hypersecretion of thyroid-stimulating hormone secretion by anterior pituitary gland.

We can find little literary data about dyslipiidemia in COPD. It is known about high blood concentrations of

TC, LDL-C, TG, and also HDL-C in COPD patients [12, 22, 23], as it was in our obtained results. There were some statements about HDL-C decrease due to FEV1 decline [24], and, vice versa, FEV1 levels were significantly lower in COPD patients with verified coronary atherosclerosis [25]. We also revealed the reversed statistical dependence between FEV1 and blood TC content in regression analysis. In other study a negative correlation between TC and FVC in COPD patients was revealed [26].

Mechanism of dyslipidemia in COPD remains obscured by now [27]. A noteworthy assumption is decreased expression of gamma-receptors which are activated by proliferator peroxisome (PPARγ) in COPD. They signal absorption of oxidated LDL by macrophages [28, 29]. It should also be highlighted that acute phase proteins like C-reactive protein enhance insulin resistance, which leads to dyslipidemia, especially in COPD [12, 30].

Besides more intensive dyslipidemia, we also detected significantly lower FVC, which indicated on enhancing restrictive ventilatory impairment in patients with COPD and concomitant hypothyroidism. Fibrosing processes in lungs is one of the pulmonary restriction causes. Respective morphological alterations in the lungs were revealed in patients with COPD, in patients with steatotic liver disease and obesity, which are linked with dyslipidemia [31].

We did not identify any significant correlations between thyroid function and spirometric parameters in COPD patients, this is supported by other researches [32, 33]. But, using regressions, we revealed that, due to rise of TSH level, there was a tendency of TC concentration increase, which could be statistically linked to the FVC decrease. Recent cross-sectional study also reports about nonlinear association between high blood content of TSH and FVC decrease [34].

Hypothyroidism is one of secondary dyslipidemia causes [35]. Significantly higher serum levels of TC, LDL-C, TG, and significantly lower HDL-C content are revealed in patients with sublinical hypothyroidism compared to euthyroid subjects [36]. Vice versa, decreasing of TC, LDL-C and TG serum levels were also ascertained during hormone-replacement therapy of hypothyroidism [37]. There are also data about positive correlation of TC, LDL-C and TG with TSH level [38]. It is known that thyroid hormones inhibit TG synthesis in the liver [39], and TSH enhances activity of 3-hydroxy-3-methylglutaryl-CoA reductase – enzyme which is responsible for cholesterol synthesis owing to kinase signalization [40].

On the other hand, there is information about toxic effects of high TG doses on thyroid gland such as downregulation of thyroglobulin, sodium iodide symporter, and thyroperoxidase [41]. According to that, and on the background of dyslipidemia in COPD, we can find likely explanation of higher hypothyroid prevance in COPD patients compared to general population [10].

We also need to pay attention to monocytes, which implement atherogenic lipids impact on arteries by participating in atherosclerotic plaques formation [42]. Monocyte count is increased in COPD patients compared to healthy subjects [43], and is associated with higher risk of COPD exacerbation [44]. MHR was also increased in this pathology [25].

There was no statistically significant difference in peripheral blood momonocyte count due to hypothyroidism accession, and there were no meaningful correlations between monocyte count and thyroid function neither in our research (Table 2,3) nor in the other one [45]. But it was revealed that thyroxin promotes monocytes proliferation and migration to tissues with their transition to macrophages. Thyroxin also inhibits their senescence and pro-inflammatory factors secretion. Migration slowdown, which can be caused by oxidated LDL, in particular, results in macrophages transformation into foam cells because of cholesterol uptake, and these cells are captured by atherosclerotic plaques [46]. Lastly we were particularly interested in the data about possible MHR association with thyroid nodule formation irrespectively of the gender [47].

CONCLUSIONS

1. In chronic obstructive pulmonary disease, irrespectively of hypothyroidism presence, all serum lipid levels were increased compared to healthy controls ($p<0.05$). Further increasing of atherogenic lipids (by 7.86% for total cholesterol, $p<0.05$, by 14.84% for low-density lipoprotein cholesterol, $p<0.05$, and by 23.23% for triacylglycerols, $p<0.05$) and antiatherogenic high-density lipoprotein cholesterol decreasing by 14.66% ($p<0.05$) was present in patients with chronic obstructive pulmonary disease combined with hypothyroidism.
2. Restrictive ventilatory impairment was intensified in patients with comorbidity. Compared to patients with chronic obstructive pulmonary disease who did not have concomitant hypothyroidism, in those with hypothyroidism forced vital capacity was 9.99% lower ($p<0.05$). Due to correlation analysis there was also revealed significant negative relationship between blood total cholesterol concentration and forced vital capacity both in patients with COPD without hypothyroidism ($p<0.05$) and those with hypothyroidism ($p<0.01$). Forward stepwise regression analysis demonstrated the possibility to predict the decrease of forced vital capacity on the strength of the rise of total cholesterol content in blood ($p<0.001$), as well as increase of total cholesterol content based upon the rise

of thyroid-stimulating hormone level and decrease of first second forced expiratory volume ($p<0.001$).

3. Except ventilatory failure, there is an important clinical aspect like cardiovascular risk, which is impacted by monocytes, in particular, with their possibility to turn into macrophages or foam cells, and especially their ratio to high-density lipoprotein cholesterol, which was higher by 33.66% in patients with chronic obstructive pulmonary disease who had concomitant hypothyroidism compared to others ($p<0.05$).

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