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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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THE SIGNIFICANCE OF CIRCULATING SURFACTANT PROTEIN D(SP-D) AND DYSLIPIDEMIA IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD), CORONARY HEART DISEASE (CHD) AND THEIR COMBINATION

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Abstract.

Background: As it is widely known, cardiovascular diseases represent one of the leading causes of mortality. In the coexistence of chronic obstructive pulmonary disease, the mortality rate is increasing as well. The research conducted reviews the effect of SP-D on the coronary heart disease and chronic obstructive pulmonary disease.

Methods: The cohort of 90 patients was included in the study. The patients were divided into five groups: group I (the patients with CHD); group II (the patients with dyslipidemia); group III (the patients with COPD); group IV (the patients suffering from the combination of CHD and COPD); group V (control group). The laboratory (dyslipidemia – through enzymatic method) as well as the instrumental methods (echocardiography, spirometric examination) were applied in the study.

Results: In consequence of the statistical processing of materials within the study, the relatively high level of SP-D values determined in groups was revealed in group II (the patients with dyslipidemia), SP-D-25.9±19.6 ng/ml. Similar data were identified in practically healthy individuals – control group (group V). Performing the comparative analysis of data, the statistically high value of anti-atherogenic HDLC (52.5±10.5mg/dl) was observed in group II (the patients with dyslipidemia) compared to group IV ($p=0.002$). It is worth noting that in the patients of group IV (COPD+CHD) the quantitative HDLC was statistically lower (43.6±6.5mg/dL) in comparison with the data of all other groups: (group I - HDLC-51,6±6,8; group II -52.5±10.5; group III-50.7±9.5; group V – 50.3±8.4) $p1\text{-}4<0.001$; $p2\text{-}4=0.002$; $p3\text{-}4=0.005$; $p4\text{-}5=0.02$. Considering the above-mentioned data, we can draw the conclusion that along with the elevated level of circulated SP-D, the low HDLC value can be utilized as a marker of the severe course of disease in relation to COPD as well as CHD.

Conclusion: The high level of SP-D, which does not have the significant atherogenic effect (due to the presence of high HDLC), was detected in individuals with isolated dyslipidemia. The study has established that in the presence of CHD, in line with the increase in atherogenic lipoproteins and relatively low HDLC value, there is detected the high level of SP-D, which is correlated with lung function indices (FEV 1 and FVC). And in case of the coexistence of COPD and CHD where dyslipidemia, the elevated level of SP-D and corresponding changes in pulmonary function tests are manifested, there were identified the high risks of severe course of disease, the development of heart failure and mortality.

Key words. circulating surfactant protein D (SP-D), dyslipidemia, chronic obstructive pulmonary disease (COPD), coronary heart disease (CHD), cardiovascular diseases (CVDs).

Introduction.

The combination of two chronic diseases widespread in the world: coronary heart disease (CHD) and chronic obstructive pulmonary disease (COPD) represents an important challenge to modern medicine. By British Heart Foundation 2023 statistics, CHD kills an estimated nine million people each year – in 2019 it was the world's single biggest killer. Around 1 in 6 deaths globally are caused by coronary heart disease. And COPD kills 3.3 million people [1].

A systematic analysis of the Global Burden of Disease Study found that the most common cause for early mortality in COPD was CAD, accounting for more than one million deaths worldwide [2]. The frequency of CHD among stable COPD patients seems to range between 7.1% and 33% [3-5] and reaches 17–22% in patients admitted to the hospital for COPD exacerbations [6]. 10.0% to 17.0% of patients with a confirmed diagnosis of COPD have experienced an acute myocardial infarction, and COPD roughly doubles the risk of myocardial infarction, a clinical outcome associated with a worse prognosis [7,8]. Although the data vary across different studies, 20.0–60.0% of COPD patients suffer from CAD [9,10].

There has been established the high correlation existing between the cardiovascular mortality and the decreased indicators of lung function tests (FVC, FEVI) [11]. The systemic inflammatory factors get involved in the pathogenesis of these two diseases [12]. COPD reveals the existence of correlation between FEV1 or FVC [13] and the level of some of the systemic inflammatory markers, such as C-reactive protein (CRP), fibrinogen, leukocytes, tumor necrosis factor-αTNF-α, IL6, and IL8. As stated by the studies, the indicators of lung dysfunction denote not only the presence of respiratory disease, but they may also predict the risk of CHD, for example, spirometry data (SPF1). There exist the data evidencing the close relationship between CHD and the incidence of pulmonary dysfunction [12]. According to the studies, upon the existence of atherosclerosis, FVC and FEV1 indicators of the forced vital capacity amounts to 74-75%.

Identification of common risk factors and their prevention defines a successful prognosis for the combination of two diseases. The close association between COPD and CHD is conditioned by the existence of common risk factors (e.g. aging, smoking), the development of increased systemic inflammatory processes, such as hypoxemia and elevated pulmonary vascular resistance. Dyslipidemia is the major risk factor of CHD may influence of the lung damage too [14]. However, it's essential, that the lungs perform an important role in the metabolism of lipids and biologically active substances [15] as well as in local and general immunologic reactions of the body. Lipids

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independently affect the morpho-functional state of the lungs and even in the early stages of atherosclerosis they can trigger lung diseases [13,16].

According to the recent studies focused on lipid spectrum and circulating surfactant protein D (SP- D) [17], COPD exacerbation triggers the elevated risk of cardiovascular events [18]. The pathology of the surfactant system assumes the particular importance for the pathology of the lung itself and, in particular, of COPD. Among the various forms of surfactant, serum SP-D is known as a prognostic marker for the clinical course of COPD [19], adult respiratory distress syndrome [19] and pneumonia [19,20]. The research findings confirm the presence of correlation of serum SP-D with the following risk factors for atherosclerosis: high density lipoprotein cholesterol (HDLC), arterial hypertension, BMI, and smoking [21]. The surfactant homeostasis significantly depends on the pathogenic ring- the oxidative stress existing in CHD and COPD, the main cause of which is the oxidation of DSLC [22]. Surfactant protein D (SP-D) is essential innate immune molecule with important roles in lung health. Dual role SP-D affects the process of oxidative vascular damage and represents the potent inhibitor of the oxidative process [23]. At the same time, in case of atherogenesis and COPD, the oxidative stress affects the important compound such as NO, an endogenous vasodilator, which contributes to the systemic hypertension, myocardial ischemia, chronic heart failure, and pulmonary artery damage.

The association between the pulmonary dysfunction and increased CHD risk has been previously studied, however, the risk factors (dyslipidemia, SP-D) and lung functional tests (FVC, FEVI) correlation in cases of combination of CHD and COPD have not yet been fully established [16].

The aim of the study. is to determine the role of circulating surfactant protein D (SP-D) and its correlation with dyslipidemia in the course of chronic obstructive pulmonary disease (COPD), coronary heart disease (CHD) and their combined course as well as to define its role in the progression of the above-mentioned diseases.

Materials and Methods.

The cohort of ninety patients of both sexes (mean age of patients averaged 68.6± 8.53 years). The patients were divided into 5 groups.

The patients included in groups:

1. Group I: 23 patients with ischemic heart disease
2. Group II: 11 patients with lipid metabolic disorders (who were not diagnosed CHD by clinical trials)
3. Group III: 24 patients with chronic obstructive pulmonary disease
4. Group IV: 22 patients suffering from the combined course of chronic obstructive pulmonary disease and ischemic heart disease
5. Group V: 10 patients represented the control group.

In order to diagnose CHD, the recommendations [24] of the European Society of Cardiology (ESC) were followed, according to which ECG, the results of angiographic study and the confirmed history of myocardial infarction were utilized. And the methods provided by the recommendations of the European Respiratory Society (ERS), such as spirometry, chest radiography, and computed tomography [25] were used, so as to identify CVDs. The patients included in the study were not taking statins within the last 1 month prior to the study.

The study encompassed the evaluation of patients' anthropometric data as well as the laboratory and instrumental investigations. The blood pressure of patients included in the study was monitored at rest through the mechanical manometer according to the international protocol provided [26].

Body mass index (BMI) was determined after completing the corresponding questionnaire on the basis of the patient's height and weight defined according to the formula –body weight (kg)/ height (m2). BMI (20-25kg/m2) – obesity was associated with shorter life expectancy and the risk for early development of cardiovascular diseases [27].

With the aim to assess the risk for developing dyslipidemia and CHD, there was determined the waist circumference (>80cm (>35 inch) in women; >94 cm (>40 inch) in men), which increased the probability of developing the above-mentioned diseases. In order to obtain the correctly measured readings, the measurement was performed upon exhalation with the measuring device placed slightly above the hips [28].

The following were examined and determined:

General blood analysis - the total blood test was performed on the automatic hematology analyzer- MEK-6500K NIHON KOHDEN (Japan). The full blood count formula was stained with Gimza – Romanovsky dye and calculated through the microscope.

Surfactant protein D (SP-D) –SP-D concentration was determined in blood serum applying the immune-enzymatic method (ELISA – solid –phase enzyme immunoassay, the so-called antibody "sandwich method"). The optical density of the stained complex was determined on the enzyme immunoassay analyzer using Strip-Reader-das reagent kit (Italy) and MyBiosource reagent kit (USA) ng/ml.

Lipid spectrum in all the groups (on an empty stomach, after a 13-hour fast). The total cholesterol (TC), triglycerides (Tg) were investigated by enzymatic-colorimetric method through 5010 photometers. And the high-density lipoprotein (HDL) cholesterol was determined following the precipitation of low-density lipoprotein (LDL) and very low-density lipoprotein (VLDL) cholesterol.

VLDL cholesterol was determined using the formula: Tg/5 (mg/dL) (Vinogradov A.V. Klimov A.N., 1987). And LDLC was counted through Friedwald (1972) formula: LDLC= TC-(HDLC+VLDLC (Klimov A.N., Nikulcheva N.G., 1995). Atherogenic index (Ai) was calculated using the following formula: AI= LDLC/HDLC

The instrumental method of investigation applied was electrocardiography (ECG) in standard and transthoracic slices through Mindray BeneHeart R3 12 lead ECG-electrocardiograph FK-3B001810 apparatus.

Doppler echocardiography: the echocardiographic study was performed on Philips ClearVue 550 machine and the following data were determined: end-diastolic dimension (LVEDd-cm); left ventricular ejection fraction EF (%); interventricular septum thickness during diastole (IVS-cm); posterior wall thickness during diastole (LVPW-cm); left atrial size during systole - the

parasternal long-axis view (LA-cm); right ventricular dimension during diastole – the parasternal long-axis view (RV-cm); right atrial size – the apical five chamber view (RA-cm); pulmonary artery size - parasternal short-axis view (PA-cm).

The pulmonary functional status was determined on the basis of spirometry, which was performed according to the protocol: the study was conducted in a seated position, the technique of performance met ATS/ERS 2005 quality control criteria (acceptable, repeatable maneuvers, good start, end; exhalation time >6 s); During the test there were determined the forced vital capacity of lungs- FVC-l; forced exhalation volume in 1 second-FEV-l; forced expiratory volume ratio-FEV-l/FVC [29].

Pulmonary function tests included forced expiratory volume in one second (FEV1), forced vital capacity (FVC) and the ratio of these values (FEV1/FVC). Both FEV1 and FVC decline with age; the FEV1/FVC ratio also declines with age. The FEV1/FVC ratio is useful in the diagnosis of obstructive lung diseases [30]. The main results of spirometry are forced vital capacity (FVC), forced expiratory volume exhaled in the first second (FEV1), and the FEV1/FVC ratio [31].

The investigation of cardiovascular system was performed using ECG, echocardiography and coronarography data.

Statistical processing of materials of the conducted research was carried out using the computer program SPSS-22.0. The quantitative parameters are presented in the form of Mean and Standard Deviation (SD). The difference in the quantitative parameters of the groups was statistically tested through t-test. The null hypothesis (the parameters do not differ between the groups) was rejected only when the criterion $p<0.05$ was met. The statistical study of correlative relationships between parameters was performed using Pearson coefficients (r) and (R2). The null hypothesis (parameters do not correlate) was rejected only when the criterion $p<0.05$ was met.

Results and Discussion.

The increase in circulating SP-D is associated with the pathogenesis of COPD and its role in the course of CHD [32]. The common risk factors for COPD and CHD, age, and smoking, are in positive correlated relationship with circulating SP-D, however, they negatively correlate with BMI, FVC, and FEV1/FGF indicators.

According to the clinical data of our study (Table 1) no statistical difference was detected age-wise between the groups. Body mass index was maintained within the normal range only in the control group and amounted to 24.45±3.6 kg/m2, according to the average data in the rest of groups the overweight was detected in: group 1, patients with CHD (28.4±3.6 kg/m2); group II, patients with dyslipidemia (29.9±3.7 kg/m2); group III, patients with COPD (29.7±5.6 kg/m2); group IV, patients with the combined CHD and COPD (28.9±6.5 kg/m2). There was not identified any statistical difference between the groups ($p>0.05$). Thus, upon conducting the comparative analysis on other parameters among the groups, the effect of age and weight on them was excluded.

As a result of the study, in the group of patients with COPD (group III), whose age amounts to 69.3±11 years, the indices of both systolic and diastolic blood pressure are within normal limits as well as in the patients of group II (with dyslipidemia) and those included in group V. As regards the patients in the other two groups (CHD and CHD+COPD), the elevated mean values of higher blood pressure readings were identified (152.8±16.8 mm.Hg/ 88.9±11.9 mm.Hg and 151± 15.5 mm.Hg/86.6±9.3 mm.Hg, respectively), which did not vary statistically from each other ($p>0.05$), however, the difference with the other groups was statistically significant (see Table). Thus, compared to group III, in the patients of group IV the presence of CHD in combination with elevated arterial pressure conditions the complicated clinical course, which is manifested by the decreased ejection fraction during heart failure: 35.8%±6.2%, which does not statistically differ from the data of patients in the main group (36.8%±6.9%).

The authors attribute the increase of SP-D [32] in circulation to the impaired pulmonary lipid metabolism, which participates in the development of lung diseases. Alveoli represent the most active niche of lipid metabolic T2C cells, where the surfactant lipids, essential for respiration, are synthesized. Following its synthesis and secretion in the alveoli, surfactant is recycled by T2C or catabolized by alveolar macrophages (AM). Circulating SP-D is considered to be the product of translocation from the impaired lung and atherosclerotic artery wall. Due to the inflammation during atherogenesis the factor of tumor necrosis α (TNFα) induces SP-D expression in the endothelium [33].

The elevated amount of surfactant protein D (SP-D) and lipid-loaded foamy macrophages (FM) are often found in the state of oxidative stress and/or in patients with CHD and COPD as well as in chronic smokers. Studies demonstrate that the exogenous recombinant fragment of human SP-D(rfhSP-D) prevents the production of FM induced by oxidized LDL (oxLDL) in vitro and affects the inflammation and emphysematous changes of respiratory tract in vivo. SP-D regulates the expression of genes of bone marrow-derived macrophages (BMDM) involved in combating the oxLDL-induced oxidative stress and lipid metabolism disorders.

As a result of the study conducted by us, the denominator of circulating SP-D was determined in all the groups (See Table 2). According to the material analysis, its highest rate (35.1±16.7) was revealed in group IV of patients with combined CHD and COPD, the difference between CHD and control group was statistically significant - p4-1=0.006; p4-5=0.013, respectively as well as compared with the COPD group - p4-3=0.003 (See Table 2). Given that group IV represents the association of two comorbidities, it becomes clear that SP-D can be deemed as a marker of the severity of disease, which is supported by the results of other authors' studies conducted on SP-D, according to which circulating SP-D is a good predictor for the development of CVDs and mortality. It also carries the additional prognostic information along with the risk factors, such as age, gender, lipids, and putative biomarkers of the association between the pulmonary inflammation/damage and cardiovascular diseases [33].

The coexistence of CHD and COPD, which is conditioned by atherosclerosis, highlights the issue about the effect of the main risk factors of CHD atherosclerosis - lipid profile- on the elevation of the value of circulating SP-D.

The solution of the above-mentioned question is clarified by the data of group II. This group consisted of the patients with expressed parameters of dyslipidemia, however, according to

Table 1. *Clinical characteristics of the groups.*

Parameter	Group I		Group II		Group III		Group IV		Group V		p-value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Age, years	68.2	8.2	66.5	5.8	69.3	11.0	69.3	8.0	68.8	7.0	p>0.05 for all groups
BMI, kg/m2	28.4	3.6	29.9	3.7	29.7	5.6	28.9	6.5	24.5	3.6	P_{2-5}=0.003; p_{1-5}=0.007; p_{3-5}=0.011; p_{4-5}=0.055
T/A (S), mm.Hg	152.8	16.8	131.4	12.7	129.8	14.9	151.0	15.5	118.5	11.3	P_{1-2}<0.001; p_{2-4}<0.001; p_{2-5}=0.020; p_{3-5}=0.039
T/A (D), mm.Hg	88.9	11.9	77.3	9.0	77.7	9.0	86.6	9.3	74.0	9.4	P_{1-2}<0.001; p_{1-3}<0.001; p_{1-5}<0.001; p_{2-4}=0.010; P_{3-5}<0.001; p_{4-5}<0.001
Body mass, kg	86.1	15.9	80.5	15.0	87.4	17.7	88.2	18.7	67.0	8.2	P_{1-2}=0.030; p_{1-5}=0.040; p_{2-3}=0.020; p_{2-4}=0.020; P_{2-5}=0.030; p_{3-5}=0.040
Body height, cm	174.2	7.2	167.6	8.2	170.2	5.2	173.6	7.5	173.7	7.6	P_{1-2}=0.020; p_{1-3}=0.030; p_{2-4}=0.040; p_{2-5}=0.009
EF, %	36.8	6.9	56.1	2.0	55.4	2.5	35.8	6.2	56.2	2.5	P_{1-2}<0.001; p_{1-3}<0.001; p_{1-5}<0.001; p_{2-5}<0.001; p_{3-5}<0.001; p_{4-5}<0.001

Note: *BMI-body mass index (kg/m²); BSA-body surface area (m²); T/A(S)-systolic blood pressure (mmHg); T/A(D)-diastolic blood pressure (mmHg); HR'-heart rate (in a minute); EF-ejection fraction (%); P-confidence coefficient. M ± SD- Mean value ± Standard Deviation; Group 1, patients with CHD; Group II, patients with dyslipidemia; Group III, patients with COPD; Group IV-CHD +COPD; Group V- practically healthy people.*

Table 2. *Surfactant protein D (SP-D) and lipid profile parameters in groups.*

Parameter	Group I		Group II		Group III		Group IV		Group V		p-value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
SPD	22.0	14.0	25.9	19.6	19.9	15.4	35.1	16.7	20.0	9.8	P_{4-1}=0.006; p_{4-3}=0.003; p_{4-5}=0.013
TC,mg/dl	199.5	74.4	276.3	48.2	206.4	53.5	184.6	39.7	171.8	38.2	P_{2-1}=0.004; p_{2-3}<0.001; p_{2-4}<0.001; p_{2-5}<0.001
LDL-C,mg/dl	119.5	48.3	187.9	43.6	129.0	44.4	116.0	35.0	100.4	35.4	P_{1-2}=0.005; p_{2-3}<0.001; p_{2-4}<0.001; p_{2-5}<0.001
TG,mg/dl	150.3	34.4	182.7	58.8	134.5	60.2	125.0	48.5	106.9	36.4	p_{1-4}=0.005; p_{1-5}=0.003; p_{2-3}=0.030; p_{2-4}=0.005; p_{2-5}=0.002
HDL-C,mg/dl	51.6	6.8	52.5	10.5	50.7	9.5	43.6	6.5	50.3	8.4	p_{1-4}<0.001; p_{2-4}=0.002; p_{3-4}=0.005; p_{4-5}=0.020

Note: *SPD- surfactant protein D; TC - total cholesterol (mg/dL); LDLC - low-density lipoprotein cholesterol (mg/dL); HDLC- high-density lipoprotein cholesterol (mg/dL); TG- triglycerides (mg/dL); P-confidence coefficient. M ± SD- mean value ± standard deviation. Group 1- patients with CHD; Group II- patients with dyslipidemia; Group III - patients with COPD; Group IV- CHD+ COPD; Group V- practically healthy individuals.*

Table 3. *The values of FEV1, FVC and FEV1/FVC in study Groups.*

Parameter	Group I		Group II		Group III		Group IV		Group V		p-value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
FEV1	95.0	19.7	97.5	12.4	57.1	12.6	56.2	12.7	97.4	18.6	P_{1-3}<0.001; p_{1-4}<0.001; P_{2-3}<0.001; p_{2-4}<0.001; P_{3-5}=0.020; p_{4-5}=0.020
FVC	91.1	16.2	97.4	13.0	68.2	24.5	61.2	11.4	96.9	18.8	P_{1-3}<0.001; p_{1-4}<0.001; p_{2-3}<0.001; p_{2-4}<0.001 P_{3-5}=0.020; p_{4-5}=0.020
FEV1/FVC	0.81	0.06	0.8	0.09	0.65	0.13	0.709	0.10	0.80	0.04	P_{1-3}<0.001; p_{1-4}<0.001; p_{2-3}<0.001; p_{2-4}<0.001 P_{3-5}=0.020; p_{4-5}=0.020
FEV1/FVC, %	81.3	5.9	79.8	8.7	65.1	13.4	70.9	10.3	79.3	4.3	

Note: *FEV1: forced expiratory volume in 1 second (maximal forced expiratory volume in one second); FVC: forced vital capacity; FEV1/FVC; p-confidence coefficient; M±SD- Mean ± Standard Deviation.*

the clinical investigation they were identified neither CHD nor COPD. In terms of lipid profile, OX (276.3±48.2 mg/dL), LDL (187.9±43.6 mg/dL) and TG (182.7±58.8 mg/dL) values in this group were statistically different from the data of the rest of the groups (except for the TG value in CHD group, where P>0.5), among them compared to the data of CHD+COPD group (TC 184,6±39,7 LDLC 116,0±35,0 TG 125,0±48,5) where the high level of statistical difference was revealed p=0.005 (See Table 2). Exactly in this group of patients with high dyslipidemia, the level of circulating SP-D (25.9±19.6) did not statistically differ from COPD+CHD group (p2-4=0.169). The mentioned indicates the increase in pulmonary tissue damage and the value of circulating SPD in case of existing dyslipidemia, particularly, during the high ratio of atherogenic lipoproteins - OX and LDL.

The experimental model of atherosclerosis conducted on rabbits confirms the disruption of T2P lamellar structures [34] that represents the main source of surfactant, induced by the damage to the microcirculatory network developed during hypercholesterolemia and hyperbeta-lipoproteinemia. Such a view is also confirmed by studies indicating that surfactant lipid metabolism genes are transcriptionally regulated by the same factors that control lipid metabolism and lipogenesis in other tissues, and the surfactant lipid synthesis and secretion in T2C are related to lipid availability. T2C obtains lipid precursors from the plasma using the proteins capable of transporting and interacting with lipids, such as CD36 and the high-density lipoprotein-binding protein anchored by glycosylphosphatidylinositol [32]. During atherosclerosis the micro-vessels are also damaged in parallel with the large blood vessels and at this time the level of circulating SPD is elevated as well [33].

Despite the relatively high level of SP-D in group II, the patients of this group are not detected either any clinically confirmed CHD or the presence of obstruction that is evidenced by the lung function tests - spirometric data of FEV1 (97.5±12.4), FVC (97.4±12.4) 13) and FEV1/FVC (79.8±8.7), which is also observed (p>0.5) in practically healthy individuals (group V) FEV1(97.4±18.6), FVC (96,9±18.8) and FEV1/FVC (79,3±4,3). Upon conducting the comparative analysis of data, compared with group IV (43.6±6.5 mg/dL) (P<0.002 the statistically higher value of antiatherogenic HDLC (52.5±10.5 mg/dL) is highlighted in group II of patients with dyslipidemia (See Table 2). The parallel can be drawn with the study conducted on theoretically healthy adults where pulmonary function tests were correlated with HDLC [JiHye Park1]. It is worth noting that the amount of HDLC in the patients with COPD+CHD is statistically lower (43.6±6.5 mg/dL) compared with the data of all other groups: p1-4<0.001; p2-4=0.002; p3-4=0.005; p4-5=0.02 (See Table 2), that gives grounds to conclude that along with the increasing value of circulating SP-D, the low value of HDLC can be considered as risk markers of severe course both in terms of COPD and CHD. In this case the lung functional indices are decreased: FEV1-(56.2±12.7), FVC (61,2±11.4) (group IV) (see Table 3). The early stages of atherogenesis illustrates the picture of permeability of the aero-hematic barrier and impaired surfactant synthesis of lungs. In case of prolonged hypercholesterolemia, foci of dis- and atelectasis, emphysema, develop which is explained by surfactant deficiency [34].

The view, that the elevation of atherogenic lipoproteins causes the oxidative stress and has the atherogenic effect, is countered by the highly significant dual effect of increased circulating SP-D -atherogenic and anti-atherogenic [35].

If we compare the CHD (group I) and dyslipidemia groups (group II) with each other, there is no statistical difference between the data in terms of TG (P>0.5) (see Table 2), however, it is worth noting, that there exists the direct correlation between the value of SP-D and the age in CHD (I) group (Pearson correlation index) r=0.53 p=0.009 (see Table 4). During CHD, the age - related increase is identified in circulating SP-D and the elevation of the latter parameter can be explained by the experimental studies conducted on atherosclerosis [34] in the case of and resulting from the microvessels located parallel to large blood vessels as well as due to the damaged lung alveolocytes, the rupture of lamellar membrane, the activation of macrophages and increase in inflammatory cytokines, especially since the surfactant has the ability to immunomodulatory capacity. Thus, in the CHD group, the age and elevated circulating SP-D can be considered as factors for the progression of atherosclerosis. Such correlation does not exist in any other group.

Table 4. *Correlation matrix of SP-D with analyzed parameters.*
Group 1 (n=23 significance p<0.05 at r>0.4132)
Group II (n=11 significance p<0.05 at r>0.6020)

Parameter	Pearson r	P	Parameter	Pearson r	P
Age	0,5340	0,009	Age	-0,2712	0,420
BMI	-0,0145	0,948	BMI	-0,2240	0,508
TC	0,2411	0,268	TC	-0,1119	0,743
TG	-0,0581	0,792	TG	0,0305	0,929
HDLC	0,1656	0,450	HDLC	-0,0941	0,783
LDLC	0,3259	0,129	LDLC	-0,1115	0,744
FEV1	0,5359	0,008	VLDLC	0,0399	0,907
FVC	0,4576	0,028	FEV1	-0,1581	0,642
FEV1/FVC	0,1298	0,555	FEV1/FVC	-0,4148	0,205

Note: SPD – surfactant protein D; TC – total cholesterol(mg/dL); LDLC-low-density lipoprotein cholesterol (mg/dL); HDLC- high-density lipoprotein cholesterol (mg/dL); TG - triglycerides (mg/dL); FEV1: forced expiratory volume in 1 second(maximal forced expiratory volume in one second); FVC-forced vital capacity; FEV1/FVC; Pearson's r- Pearson correlation coefficient; p-confidence ratio.

Table 5. *Correlation matrix of SP-D with analyzed parameters.*
Group V (n=10 significance p<0.05 at r>0.6319).

Parameter	Pearson r	P
Age	-0,0601	0,869
BMI	-0,2257	0,531
TC	0,4226	0,224
TG	0,1990	0,582
HDLC	0,2654	0,459
LDLC	0,3594	0,308
FEV1	0,2230	0,536
FVC	0,2251	0,532
FEV1/FVC	-0,1029	0,777

Note: SP-D – surfactant protein D; TC – total cholesterol(mg/dL); LDLC-low-density lipoprotein cholesterol (mg/dL); HDLC- high-density lipoprotein cholesterol (mg/dL); TG - triglycerides (mg/dL); FEV1: maximal forced expiratory volume in one second); FVC-forced vital capacity; FEV1/FVC; Pearson's r- Pearson correlation coefficient; p-confidence ratio.

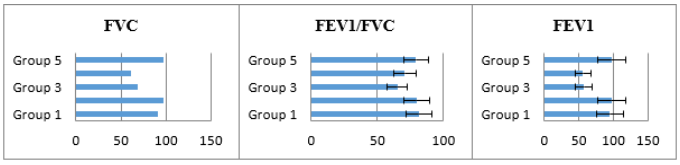

Figure 1. *The values of FVC, FEV1, FEV1/FVC in groups.*
Note: *FEV1: forced expiratory volume in 1 second (maximal forced expiratory volume in one second); FVC: forced vital capacity; FEV1/FVC; P- confidence coefficient. Group 1 – patients with CHD; Group II - patients with dyslipidemia; Group III - patients with COPD; Group IV-CHD+COPD; Group V - practically healthy individuals.*

In group V, in the conditions of normal lipid profile, circulating SP-D could be considered as normal, when SP-D value (19.9±15.4) was revealed in COPD(III) group and did not statistically vary from that of the of practically healthy group (20.0±9.8) (P>0.5).

The existence of relation among lipid profile, pulmonary function indices and circulating SP-D ratio acquires the great salience in case of CHD, PCOD and their combination.

The diagnosis of PCOD is confirmed by spirometry (PFV1/FGEF <70%). And the assessment of severity of airflow limitation is based on the value of PFV1 (% predicted percentage) resulting from post-bronchodilators. However, the severity of airflow obstruction is weakly correlated with the symptoms developed during PCOD.

If we take into account the two, statistically different from other groups, values implying the high levels of atherogenic lipoprotein cholesterol (group II) in atherosclerosis and that of the circulating SP-D in the combined FCOD+GID group (IV), there is demonstrated the effect of dyslipidemia on the surfactant value, on the one hand, and on the other hand, on the patient's clinical condition in combined CHD and PCOD, during which the lung function disorders FEV1-56.2±12.7, FVC 61.2±11.4 and FEV1/FVC 70.9±10.3 as well as the presence of positive correlation between SP-D and FEVI are identified denoting the exacerbation of obstruction during the concomitant CHD.

Like PCOD+CHD group (group IV), the low values of pulmonary function tests of FEV1-57.1±21.6, FVC 68.2±24 and FEV1/FVC 65.1±13.4 were identified in the PCOD group (group III) (P>0.5) (see Table. 3), however, in conditions of normolipidemia and preserved SP-D the difference between groups is statistically significant (P=0.003) indicating that the circulating SP-D does not have an atherogenic effect at that time, however, it affects the lung function, which is confirmed by the presence of correlation between SP-D and FGEL (r>0.4576; p=0.028) (in group I).

Conclusion.

When existing the high level of atherogenic lipoprotein cholesterol, the increased value of SP-D, which may not have the atherogenic inflammatory effect, is detected in essentially healthy individuals due to the presence of high-density lipoprotein cholesterol, which has the protective effect. In case of the elevated value of atherogenic lipoproteins existing during CHD, whereas the decline is identified in high density lipoprotein cholesterol, the SP-D is elevated in line with the age and has the correlation with the pulmonary function indices of FEV1 and FVC. The combination of CHD and COPD is accompanied by dyslipidemia, arterial hypertension, the elevated circulating SP-D, the transformation of pulmonary spirometric data FEV 1 and FVC, heart failure, which determine the severity of the disease and the risk of mortality. The participation of circulating SP-D in the process of atherogenesis requires further investigation.

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