



TOSHKENT TIBBIYOT AKADEMIYASI URGANCH FILIALI
JANUBIY OROLBO'YI TIBBIYOT JURNALI

1-TOM, 3-SON. 2025

14.00.00 - TIBBIYOT FANLARI ISSN: 3093-8740

**GIPERTONIYA VA 2-TIP QANDLI DIABETGA CHALINGAN BEMORLARDA YURAK-
QON TOMIR TIZIMI REMODELLASHUVINI DAVOLASHNING ZAMONAVIY
YONDASHUVLARI.**



Islomov Inomjon Islomovich,

Urganch davlat tibbiyot instituti, ichki kasalliklar kafedrasida katta o'qituvchisi, PhD.

Email : md.inomjon.islomov@gmail.com

ORCID : <https://orcid.org/0000-0002-0634-7895>

Tel: +998972207530



Fayzullayev Baxrom Rustamovich,

Urganch davlat tibbiyot instituti, ichki kasalliklar kafedrasida dotsenti, t.f.n.

Email: md.baxrom.fayzullayev@gmail.com

ORCID: <https://orcid.org/0009-0006-2935-9940>

Tel: +998975168520



Djumaniyazova Zulxumor Farxadovna,

Urganch davlat tibbiyot instituti, ichki kasalliklar kafedrasida mudiri, dotsent, t.f.n.

zulxumor01.67@gmail.com

ORCID <https://orcid.org/0009-0009-0689-2904>

Tel: +998919120022



Xusainov Adham Shuhratovich,

Urganch TTB endokrinologi.

khusainovadham@gmail.com

ORCID <https://orcid.org/0009-0007-5203-4965>

Tel: +998995416534



Yuldashev Otabek Sabirovich,

Urganch davlat tibbiyot instituti, ichki kasalliklar propedevtikasi va endokrinologiya kafedrasida dotsenti, PhD.

otabek.sabirovich1989@gmail.com

<https://orcid.org/0000-0002-5503-9661>

Tel +998977200329



Normatova Umida Yo'ldosh qizi,

Urganch davlat tibbiyot instituti, ichki kasalliklar kafedrası kardiolog-magistranti.

unormatova7@gmail.com

<https://orcid.org/0009-0001-0123-2749>

Tel: +998973606203

ANNOTATSIYA

Kirish: Arterial gipertenziya (AG) va 2-tip qandli diabet (QD2) yurak-qon tomir kasalliklarining rivojlanishini keskin kuchaytiruvchi asosiy xavf omillari hisoblanadi. Ayniqsa, ekologik va ijtimoiy-iqtisodiy sharoitlari murakkab bo'lgan Xorazm viloyati sharoitida ushbu muammo yanada dolzarbdır.

Maqsad: AG va QD2 bilan og'riqan bemorlarda yurak-qon tomir tizimi qayta shakllanish jarayonlari va klinik-funksional ko'rsatkichlarni baholash, shuningdek, kompleks patogenetik davolash samaradorligini aniqlash.

Materiallar va usullar: 41–70 yoshdagi 42 nafar bemor ishtirokida prospektiv tadqiqot o'tkazildi. Yurak-qon tomir tizimi holati EKG, Xolter monitoringi, exokardiografiya, SMAD hamda laboratoriya tekshiruvlari yordamida baholandi. Davolash protokoliga Empagliflozin (Farojard), Perindopril va Allapinin preparatlari kiritildi.

Natijalar: Davolash yakunida bemorlarning 78,6 % ida arterial bosim nazoratga olindi, chap qorincha gipertrofiyasi pasaydi, ejeaksiya fraksiyasi sezilarli darajada oshdi. Bundan tashqari, yurak ritmi buzilishlari va buyrak faoliyati buzilishlari kamaygani kuzatildi.

Xulosa: AG va QD2 ning birgalikda kechishi yurak-qon tomir tizimidagi qayta shakllanish jarayonlarini kuchaytiradi. Kompleks patogenetik davolash yurak-qon tomir asoratlari xavfini kamaytirishda yuqori samaradorlik ko'rsatadi.

Kalit so'zlar: arterial gipertenziya, 2-tip qandli diabet, yurak-qon tomir tizimi, qayta shakllanish, empagliflozin, perindopril.

СОВРЕМЕННЫЕ ПОДХОДЫ К ТЕРАПИИ СЕРДЕЧНО-СОСУДИСТОГО РЕМОДЕЛИРОВАНИЯ У ПАЦИЕНТОВ С ГИПЕРТОНИЕЙ И САХАРНЫМ ДИАБЕТОМ 2 ТИПА.

Исломов Иномжон Исломович,

PhD, Старший преподаватель кафедры внутренних болезней.

Ургенский государственный медицинский институт.

Файзуллаев Бахром Рустамович,

к.м.н., доцент кафедры внутренних болезней.

Ургенский государственный медицинский институт.

Хусайнов Адхам Шухратович

Врач-эндокринолог Ургенского РМО.

Юлдашев Отабек Сабирович,

PhD, доцент кафедры пропедевтики

внутренних болезней и эндокринологии.

Ургенский государственный медицинский институт.

Норматова Умида Йўлдош қизи,

Магистрант – кардиолог кафедры внутренних болезней

Ургенский государственный медицинский институт.



АННОТАЦИЯ

Введение: Артериальная гипертензия (АГ) в сочетании с сахарным диабетом 2 типа (СД2) существенно усиливает риск сердечно-сосудистых осложнений. Данная проблема особенно значима для регионов с неблагоприятной экологической и социально-экономической обстановкой, таких как Хорезмская область Узбекистана.

Цель: Изучить механизмы сердечно-сосудистого ремоделирования, определить клинико-функциональные показатели и оценить эффективность патогенетически обоснованной комплексной терапии у пациентов с АГ и СД2.

Материалы и методы: В проспективное исследование были включены 42 пациента в возрасте от 41 до 70 лет. Оценка состояния сердечно-сосудистой системы проводилась с использованием ЭКГ, суточного мониторирования по Холтеру, эхокардиографии, СМАД и лабораторных исследований. В терапевтическую схему были включены эмпаглифлозин (Фарождар), периндоприл и Аллапинин.

Результаты: Проведение терапии позволило достичь контроля АД у 78,6% пациентов, наблюдалось уменьшение гипертрофии левого желудочка, повышение фракции выброса, снижение частоты нарушений ритма и улучшение показателей функции почек.

Заключение: Коморбидное течение АГ и СД2 сопровождается выраженными изменениями сердечно-сосудистой системы. Применение патогенетически обоснованной комбинированной терапии способствует снижению риска сердечно-сосудистых осложнений и улучшает клинические исходы.

Ключевые слова: артериальная гипертензия, сахарный диабет 2 типа, сердечно-сосудистое ремоделирование, эмпаглифлозин (Фарождар), периндоприл.

MODERN APPROACHES TO THE THERAPY OF CARDIOVASCULAR REMODELING IN PATIENTS WITH HYPERTENSION AND TYPE 2 DIABETES MELLITUS.

Islomov Inomjon Islomovich,

PhD, senior lecturer of the Department of Internal Medicine,
Urgench State Medical Institute

Fayzullaev Bahrom Rustamovich,

PhD, docent of department of Internal Medicine.
Urgench State Medical Institute

Djumaniyazova Zulxumor Farxadovna,

PhD, chief of department of Internal Medicine.
Urgench State Medical Institute

Xusainov Adham Shuhratovich,

Endocrinologist of Urganch district multidisciplinary central polyclinic

Yuldashev Otabek Sabirovich,

PhD, docent of department of Propaedeutics
of Internal Diseases and Endocrinology

Urgench State Medical Institute

Normatova Umida Yo'ldosh qizi,

Master of cardiology of department of Internal Diseases
Urgench State Medical Institute

ANNOTATION

Introduction: The coexistence of arterial hypertension (AH) and type 2 diabetes mellitus (T2D) markedly increases the risk of cardiovascular complications, particularly in ecologically and



socioeconomically disadvantaged regions such as Khorezm, Uzbekistan. **Objective:** To investigate the mechanisms of cardiovascular remodeling, evaluate clinical and functional markers, and determine the efficacy of pathogenetically justified combination therapy in patients with AH and T2D.

Materials and Methods: A prospective study was conducted involving 42 patients aged 41–70 years. Cardiovascular assessment included electrocardiography (ECG), Holter monitoring, echocardiography, ambulatory blood pressure monitoring (ABPM), and laboratory investigations. The therapeutic regimen comprised Diampa, Prestarium, and Allapinin.

Results: Following therapy, blood pressure control was achieved in 78.6% of patients, left ventricular hypertrophy was reduced, left ventricular ejection fraction significantly improved, rhythm disturbances decreased, and renal function parameters showed improvement.

Conclusion: The comorbid course of AH and T2D exacerbates cardiovascular remodeling. Pathogenetically based combination therapy demonstrates high efficacy in reducing cardiovascular alterations and lowering the risk of related complications.

Keywords: arterial hypertension, type 2 diabetes mellitus, cardiovascular remodeling, empagliflozin, perindopril.

Introduction. The comorbid combination of arterial hypertension (AH) and type 2 diabetes mellitus (T2DM) represents one of the most complex and socially significant challenges in modern medicine. Both conditions are highly prevalent worldwide and are leading causes of cardiovascular morbidity and mortality. According to the World Health Organization (WHO, 2023), the global prevalence of hypertension among adults exceeds 30%, while diabetes mellitus affects more than 460 million individuals, with projections suggesting a rise to 700 million by 2045. The comorbidity of AH and T2DM creates a particularly adverse clinical scenario due to mutual potentiation of risk factors, accelerated cardiovascular remodeling, and a heightened probability of fatal complications, including myocardial infarction, stroke, heart failure, and sudden cardiac death.

In Uzbekistan, the problem is further aggravated by environmental and socioeconomic determinants. The Khorezm region, characterized by a low-mountainous terrain, salinization of soil and water resources, and chronic environmental stress associated with the Aral Sea ecological catastrophe, represents a model territory where the combined impact of hypertension and T2DM is especially severe. The high sodium content in drinking water, poor dietary diversity with low intake of antioxidants, and limited access to specialized high-tech cardiometabolic care increase the burden of disease. Epidemiological surveys conducted by the Ministry of Health of Uzbekistan (2022) reported that up to 40% of adults in Khorezm suffer from hypertension, and approximately 15% have T2DM, with comorbidity rates approaching 10–12%.

From a pathophysiological perspective, AH and T2DM mutually accelerate the process of cardiovascular remodeling. Hyperglycemia induces oxidative stress, endothelial dysfunction, and glycation of vascular proteins, while chronic hypertension increases left ventricular afterload, leading to hypertrophy and impaired relaxation. Insulin resistance contributes to systemic inflammation and the activation of profibrotic cascades, promoting myocardial fibrosis and diastolic dysfunction. Ultimately, these mechanisms converge on the development of heart failure with preserved ejection fraction (HFpEF) and increased susceptibility to arrhythmias.

International guidelines, including the ESC/ESH 2023, ADA 2024, and AHA/ACC 2022, emphasize the importance of strict blood pressure and glycemic control in comorbid patients. Target levels are defined as systolic blood pressure <130 mmHg, diastolic blood pressure <80 mmHg, and glycated hemoglobin (HbA1c) <7%. Pharmacological strategies with proven organoprotective properties, including renin–angiotensin–aldosterone system (RAAS) blockers, sodium-glucose cotransporter-2 (SGLT2) inhibitors, glucagon-like peptide-1 (GLP-1) receptor agonists, and statins, form the cornerstone of therapy. Combination regimens that address both hemodynamic and



metabolic pathways are considered optimal, as they simultaneously reduce cardiovascular and renal risks.

Clinical evidence from large multicenter trials supports this integrated approach. For example, the UKPDS and ADVANCE studies demonstrated that intensive blood pressure control significantly reduces the risk of macrovascular and microvascular complications in patients with diabetes. The EMPA-REG OUTCOME and CANVAS trials revealed that SGLT2 inhibitors (empagliflozin, canagliflozin) lower hospitalization rates for heart failure and slow the progression of diabetic kidney disease. GLP-1 receptor agonists such as semaglutide and liraglutide were shown to reduce stroke risk and favorably influence body weight, lipid metabolism, and systemic inflammation.

Nevertheless, the translation of these findings into everyday clinical practice in resource-limited regions remains challenging. Socioeconomic constraints, limited availability of novel medications, and patient non-adherence due to low awareness necessitate the development of adapted regional protocols. These should include affordable pharmacological options, structured patient education programs, lifestyle interventions emphasizing dietary sodium restriction, and regular monitoring of cardiovascular and renal status using cost-effective diagnostic methods.

The present study aimed to investigate the mechanisms of cardiovascular remodeling in patients with comorbid AH and T2DM in the Khorezm region, to identify clinical and functional markers of disease progression, and to evaluate the effectiveness of comprehensive pathogenetically oriented therapy incorporating modern antihypertensive and metabolically active agents.

Materials and Methods. This prospective observational study was conducted at the Cardiology Department of the Elit Clinic, Urgench State Medical Institute. A total of 42 patients with confirmed diagnoses of arterial hypertension (stage I–III according to ESC/ESH 2018 criteria) and type 2 diabetes mellitus (based on ADA 2023 diagnostic standards) were enrolled between January and December 2023.

Inclusion criteria:

- Age between 41 and 70 years;
- Verified diagnoses of both AH and T2DM;
- Stable clinical course without acute decompensation;
- Informed consent for participation.

Exclusion criteria:

- Severe concomitant somatic diseases (advanced chronic kidney disease, chronic liver failure, malignancies);
- Decompensated heart failure (NYHA class III–IV);
- Cognitive impairment or inability to comply with study procedures.

The mean age of patients was 56 ± 10 years; 19 were female and 23 were male. Patients were stratified into two groups according to metabolic and hemodynamic compensation:

- Group I: mild hypertension with compensated diabetes (n=20);
- Group II: moderate hypertension with subcompensated diabetes (n=22).

Diagnostic program:

- Standard 12-lead electrocardiography (ECG) to assess rhythm disturbances and left ventricular hypertrophy;
- 24-hour Holter ECG monitoring to detect paroxysmal arrhythmias and variability of heart rate;
- Transthoracic echocardiography (ECHO) with calculation of left ventricular mass index, ejection fraction, and diastolic function parameters (E/A ratio, E/e');;
- 24-hour ambulatory blood pressure monitoring (ABPM) to evaluate circadian variability, nocturnal dipping, and blood pressure load;



- Laboratory studies: fasting plasma glucose, 2-hour postprandial glucose, HbA1c, serum lipid profile (total cholesterol, LDL-C, HDL-C, triglycerides), creatinine, estimated glomerular filtration rate (eGFR), and urinary albumin excretion;
- Zimnitsky's test for assessment of renal concentration capacity.

Therapeutic protocol:

Pharmacological therapy was selected according to current guidelines and included:

- Empagliflozin (10 mg/day) as the main metabolic modulator with nephro- and cardioprotective effects;
- ACE inhibitor (perindopril 5–10 mg/day) for blood pressure control and attenuation of cardiac remodeling;
- Allapinin (25 mg t.i.d.) in patients with documented arrhythmias;
- Additional correction with calcium channel blockers or ARBs in patients not achieving target blood pressure.

Lifestyle interventions such as dietary sodium restriction (<5 g/day), increased consumption of fruits and vegetables rich in antioxidants, weight reduction strategies, and structured physical activity (30 minutes of moderate aerobic exercise at least 5 times per week) were also implemented.

Statistical analysis was performed using SPSS v.26. Continuous variables were expressed as mean $\pm$ standard deviation (SD). Between-group comparisons were performed with Student's t-test, and categorical variables with chi-square test. A p-value <0.05 was considered statistically significant.

Results. Baseline clinical and hemodynamic characteristics showed significant differences between groups. Systolic arterial pressure (SAP) averaged 151 ± 2.0 mmHg in Group I and 169 ± 3.2 mmHg in Group II ($p < 0.01$). Diastolic blood pressure (DAP) was 91 ± 1.5 mmHg vs. 97 ± 2.1 mmHg, respectively. Glycemic control was also worse in Group II, with mean HbA1c of $8.1 \pm 0.6\%$ compared to $6.8 \pm 0.4\%$ in Group I.

Echocardiographic evaluation revealed left ventricular hypertrophy (LVH) in 62% of patients overall, more frequent in Group II (77%) compared to Group I (45%). The mean ejection fraction (EF) was significantly reduced in Group II ($51.2 \pm 2.1\%$) versus Group I ($58.2 \pm 1.1\%$; $p < 0.01$). Diastolic dysfunction of grade I–II was documented in 71% of patients, particularly prevalent among those with subcompensated diabetes.

Arrhythmia burden assessed by Holter monitoring included paroxysmal supraventricular tachycardia in 16 patients, atrial fibrillation in 2 patients, and frequent ventricular ectopy (>30/hour) in 6 patients. Arrhythmia occurrence strongly correlated with nocturnal non-dipping pattern and reduced heart rate variability indices, highlighting autonomic dysfunction as a central mechanism.

Renal function tests demonstrated early signs of nephropathy: 35% of patients showed impaired concentration capacity in Zimnitsky's test, and microalbuminuria (>30 mg/24h) was detected in 29% of cases. Notably, blood pressure variability was inversely associated with eGFR values, particularly in patients with poor glycemic control ($r = -0.41$; $p < 0.05$).

Effect of therapy: After 4 weeks of combined therapy, 33 patients (78.6%) achieved target blood pressure (<140/90 mmHg). Additional ACE inhibitor titration was required in 9 patients. Significant improvement in EF was observed in both groups: from 58.2% to 60.2% in Group I and from 51.2% to 58% in Group II ($p < 0.05$). Diastolic function indices also improved, with an increase in E/A ratio and reduction of E/e' values.

Empagliflozin therapy led to a mean reduction of HbA1c by 0.7% and body weight by 2.1 kg over the study period. Lipid profile showed modest but favorable changes, with increased HDL-C (+5.2%) and reduced triglycerides (–12.4%). No serious adverse effects were reported, and tolerability was high.

Allapinin effectively suppressed arrhythmias, reducing the frequency of supraventricular tachycardia episodes by 68%. No proarrhythmic complications were observed.



Discussion. Our study confirmed that the coexistence of hypertension and T2DM exerts a synergistic detrimental effect on the cardiovascular system, resulting in structural remodeling, impaired systolic and diastolic function, increased arrhythmogenicity, and renal dysfunction. The findings are consistent with international evidence, including data from Framingham Heart Study and UKPDS, which highlighted the dramatic rise in cardiovascular risk associated with this comorbidity.

Pathophysiologically, the interplay of hemodynamic overload, hyperglycemia, oxidative stress, and neurohormonal activation creates a vicious cycle leading to myocardial hypertrophy, fibrosis, and electrophysiological instability. The strong correlation between blood pressure variability, reduced heart rate variability, and arrhythmia incidence underscores the role of autonomic imbalance. This supports the need for ABPM and Holter monitoring as essential diagnostic tools in this patient population.

The therapeutic protocol applied in our study—empagliflozin combined with ACE inhibitors—demonstrated significant benefits, consistent with outcomes of EMPA-REG OUTCOME and DAPA-HF trials. The ability of SGLT2 inhibitors to lower hospitalization for heart failure by approximately 30–35% was reflected in improved functional parameters and reduced arrhythmia burden in our patients. The metabolic benefits of empagliflozin, including modest weight reduction and improved lipid metabolism, are particularly relevant in regions with high prevalence of obesity and metabolic syndrome.

The antiarrhythmic effect of Allapinin in our cohort is noteworthy. Although less widely studied compared to other antiarrhythmics, its favorable safety profile and efficacy in suppressing supraventricular tachyarrhythmias make it an attractive option in resource-limited settings.

From a regional perspective, the results highlight the urgent need for adapted protocols in Uzbekistan and similar regions. Factors such as high dietary sodium intake, limited access to GLP-1 receptor agonists, and socioeconomic barriers to continuous monitoring necessitate pragmatic approaches: prioritizing affordable medications, scaling up community-based education programs, and integrating low-cost diagnostics.

Future studies should expand sample size, incorporate longer follow-up periods, and evaluate hard endpoints such as hospitalization rates and cardiovascular mortality. Moreover, molecular biomarkers of inflammation and fibrosis could provide deeper insights into disease mechanisms and help personalize therapy.

Conclusions:

1. The comorbid course of arterial hypertension and type 2 diabetes mellitus is associated with significant structural and functional alterations of the cardiovascular system, including left ventricular hypertrophy, impaired contractile function, arrhythmias, and renal dysfunction.
2. Blood pressure variability and glycemic decompensation are key drivers of these pathological changes.
3. Comprehensive therapy incorporating SGLT2 inhibitors (empagliflozin), ACE inhibitors, and antiarrhythmics (allapinin) provides significant improvement in hemodynamic parameters, echocardiographic indices, metabolic control, and arrhythmia suppression.
4. ABPM and Holter monitoring are essential for individualized patient management, enabling detection of hidden arrhythmias and nocturnal hypertension.
5. Regional adaptation of international guidelines is necessary in the Khorezm region, emphasizing affordable pharmacological choices, dietary sodium restriction, antioxidant-rich nutrition, patient education, and systematic follow-up.
6. Future research should focus on long-term outcomes, broader patient populations, and integration of novel biomarkers to refine risk stratification and optimize therapy.

Considering the climatogeographic and demographic characteristics of individual regions (for example, the Khorezm region). It is urgent to introduce adapted regional protocols for the



management of patients with comorbid pathology, including modern diagnostic approaches and pharmacotherapy algorithms.

References:

1. Williams B., Mancia G., Spiering W., et al. 2023 ESC/ESH Guidelines for the management of arterial hypertension // *European Heart Journal*. – 2023. – Vol. 44 (19). – P. 1735–1852.
2. American Diabetes Association. Standards of Care in Diabetes — 2024 // *Diabetes Care*. – 2024. – Vol. 47, Suppl. 1. – P. S1–S188.
3. Whelton P.K., Carey R.M., Aronow W.S., et al. 2022 AHA/ACC Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults // *Journal of the American College of Cardiology*. – 2022. – Vol. 79 (20). – P. e101–e199.
4. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes // *Lancet*. – 1998. – Vol. 352 (9131). – P. 837–853.
5. ADVANCE Collaborative Group. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes // *New England Journal of Medicine*. – 2008. – Vol. 358 (24). – P. 2560–2572.
6. Action to Control Cardiovascular Risk in Diabetes (ACCORD) Study Group. Effects of intensive blood-pressure control in type 2 diabetes mellitus // *New England Journal of Medicine*. – 2010. – Vol. 362 (17). – P. 1575–1585.
7. Zinman B., Wanner C., Lachin J.M., et al. Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes // *New England Journal of Medicine*. – 2015. – Vol. 373 (22). – P. 2117–2128.
8. Neal B., Perkovic V., Mahaffey K.W., et al. Canagliflozin and cardiovascular and renal events in type 2 diabetes // *New England Journal of Medicine*. – 2017. – Vol. 377 (7). – P. 644–657.
9. Marso S.P., Daniels G.H., Brown-Frandsen K., et al. Liraglutide and cardiovascular outcomes in type 2 diabetes // *New England Journal of Medicine*. – 2016. – Vol. 375 (4). – P. 311–322.
10. Gerstein H.C., Colhoun H.M., Dagenais G.R., et al. Dulaglutide and cardiovascular outcomes in type 2 diabetes (REWIND trial) // *Lancet*. – 2019. – Vol. 394 (10193). – P. 121–130.
11. World Health Organization. Global report on hypertension. – Geneva: WHO, 2023. – 115 p.
12. O'zbekiston Respublikasi Sog'liqni saqlash vazirligi. Surunkali kasalliklarning tarqalishi bo'yicha epidemiologik kuzatuvlar. – Toshkent: SSV nashriyoti, 2022. – 84 b.
13. Глобальная инициатива по хронической обструктивной болезни легких (GOLD). Глобальная стратегия диагностики, лечения и профилактики ХОБЛ: отчет 2023. – Женева: ВОЗ, 2023. – 168 с.
14. Чучалин А.Г. Хроническая обструктивная болезнь легких: современное состояние проблемы // *Терапевтический архив*. – 2020. – Т. 92, № 8. – С. 4–12.
15. Vogelmeier C.F., Criner G.J., Martinez F.J., et al. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease 2023 Report // *American Journal of Respiratory and Critical Care Medicine*. – 2023. – Vol. 207, No. 10. – P. 1197–1223.
16. European Society of Cardiology (ESC). 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice // *European Heart Journal*. – 2021. – Vol. 42, No. 34. – P. 3227–3337.
17. Barnes P.J. Inflammatory mechanisms in patients with chronic obstructive pulmonary disease // *Journal of Allergy and Clinical Immunology*. – 2016. – Vol. 138, No. 1. – P. 16–27.
18. Wedzicha J.A., Seemungal T.A. COPD exacerbations: defining their cause and prevention // *Lancet*. – 2007. – Vol. 370, No. 9589. – P. 786–796.