GEORGIAN MEDICAL NEWS

ISSN 1512-0112

No 12 (309) Декабрь 2020

ТБИЛИСИ - NEW YORK

ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

No 12 (309) 2020

Published in cooperation with and under the patronage
of the Tbilisi State Medical University

Издается в сотрудничестве и под патронажем
Тбилисского государственного медицинского университета

გამოიცემა თბილისის სახელმწიფო სამედიცინო უნივერსიტეტთან
თანამშრომლობითა და მისი პატრონაჟით

ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

ТБИЛИСИ - НЬЮ-ЙОРК

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 and The International Academy of Sciences, Education, Industry and Arts (U.S.A.) 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 и Международной академией наук, образования, искусств и естествознания (IASEIA) США 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.

МЕДИЦИНСКИЕ НОВОСТИ ГРУЗИИ

Ежемесячный совместный грузино-американский научный электронно-печатный журнал
Агентства медицинской информации Ассоциации деловой прессы Грузии,
Академии медицинских наук Грузии, Международной академии наук, индустрии,
образования и искусств США.
Издается с 1994 г., распространяется в СНГ, ЕС и США

Website:
www.geomednews.org

The International Academy of Sciences, Education, Industry & Arts. P.O.Box 390177,
Mountain View, CA, 94039-0177, USA. Tel/Fax: (650) 967-4733

Версия: печатная. **Цена:** свободная.
Условия подписки: подписка принимается на 6 и 12 месяцев.
По вопросам подписки обращаться по тел.: 293 66 78.
Контактный адрес: Грузия, 0177, Тбилиси, ул. Асатиани 7, IV этаж, комната 408
тел.: 995(32) 254 24 91, 5(55) 75 65 99
Fax: +995(32) 253 70 58, e-mail: ninomikaber@geomednews.com; nikopir@geomednews.com

По вопросам размещения рекламы обращаться по тел.: 5(99) 97 95 93

GEORGIAN MEDICAL NEWS
Monthly Georgia-US joint scientific journal published both in electronic and paper formats of the Agency of Medical Information of the Georgian Association of Business Press; Georgian Academy of Medical Sciences; International Academy of Sciences, Education, Industry and Arts (USA).
Published since 1994. Distributed in NIS, EU and USA.

CONTACT ADDRESS IN TBILISI

GMN Editorial Board
7 Asatiani Street, 4th Floor
Tbilisi, Georgia 0177

Phone: 995 (32) 254-24-91
995 (32) 253-70-58
Fax: 995 (32) 253-70-58

CONTACT ADDRESS IN NEW YORK

NINITEX INTERNATIONAL, INC.
3 PINE DRIVE SOUTH
ROSLYN, NY 11576 U.S.A.

Phone: +1 (917) 327-7732

WEBSITE
www.geomednews.org

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.

Содержание:

EFFICACY OF SPIRONOLACTONE IN ANTIHYPERTENSIVE THERAPY IN PATIENTS WITH RESISTANT HYPERTENSION IN COMBINATION WITH RHEUMATOID ARTHRITIS

Kondratiuk V., Stakhova A., Hai O., Karmazina O., Karmazin Y.

Bogomolets National Medical University, Ukraine

The influence of concomitant pathology on the development and progression of hypertension (H) in recent years has attracted researchers` attention. H is found twice as often and is characterized by poorer control and frequent combination with resistant hypertension (RH) in patients with rheumatoid arthritis (RA) [35]. 51% of patients with RA have a significant increase in cardiovascular risk even in the absence of concomitant cardiovascular pathology. The risk of ischemic cardiac events is comparable to that of diabetes mellitus [3].

Increased inflammatory activity is associated with the development of diastolic heart failure (HF) in patients with H [13, 27]. T cells play an important role in the pathogenesis of H and HF, with various stimuli leading to the formation of effector T cells, which together with monocytes and macrophages penetrate into arterial walls. Increased levels of a number of cytokines (interleukin-6, interleukin-17, interleukin-10, tumor necrosis factor-α, and interferon-γ) contribute to the damage and aging of blood vessels and cardiomyocytes, which causes their fibrosis and hypertrophy. Cross-reactions between natural killer cells, adaptive immune cells, and innate immune cells contribute to myocardial damage and dysfunction [25]. On the other hand, the activation of the renin-angiotensin-aldosterone system and the increase in the level of transforming growth factor-β stimulate the deposition of the extracellular matrix in patients with H, which causes perivascular fibrosis of the heart [5].

The treatment of patients with H remains a difficult issue in cardiology. According to the latest data, only half of the patients with H in the general population reach the target levels of blood pressure (BP) [10]. However, the achievement of the target level of BP occurs only in 42% in patients with RA [35]. There are no data on the frequency and features of RH in patients with RA in different populations.

A decrease in sodium levels and an increase in potassium levels have a positive effect on the level and profile of BP in patients with H [6, 32]. As many as a third of patients with H were diagnosed with primary hyperaldosteronism, which makes the use of aldosterone blockers pathogenetically justified. A differentiated treatment approach occurs in the presence of RH [23]. Experimental studies have shown that chronic administration of aldosterone to rats induced myocardial fibrosis in the hypertrophied left ventricle (LV), even under conditions of normotension. Administration of spironolactone (aldosterone antagonist) has an antifibrotic effect [7, 8, 33]. Spironolactone together with the other antihypertensive drugs can prevent or reduce myocardial fibrosis [38], improve cardiovascular prognosis [17], which requires comprehensive studies in a cohort of patients with coexistence of RH with RA.

The aim of the study was to investigate the antihypertensive efficacy, structural and functional remodeling of the heart in patients with RH in combination with RA after 12-month combination therapy, including angiotensin-converting enzyme (ACE) inhibitor, calcium channel blocker, diuretics, aldosterone receptor blocker (spironolactone) and immunosuppressive drug (methotrexate).

Materials and methods. The analysis of medical documentation (outpatient medical cards and medical histories) was performed, patients who met the inclusion criteria and were able to provide informed consent were selected. Possible causes of secondary H were excluded. Initially, the study involved 101 patients with RA and H, whom at a pre-screening visit were adjusted the dose of the basic disease-modifying drug (all RA patients received methotrexate 15 mg per week), when necessary. Doses of antihypertensive drugs (ACE inhibitors, calcium channel blocker and/or diuretic) were added or increased as required. 60 patients were selected after 1 month. They were on the triple antihypertensive drug therapy (with mandatory inclusion of diuretics) in maximal and submaximal doses, did not reach the target BP levels, and met the criteria for RH. According to the prescribed treatment, patients were divided into two groups: the main group and the comparison group, randomly. 12.5 mg of spironolactone was added to the existing triple therapy once daily with an increase in dose after 1 month to 25 mg (group 1, n=30). Treatment or left unchanged (without spironolactone) in group 2 (n=30). The duration of therapy was 12 months. The strategy for the diagnosis and treatment of RA was determined according to EULAR 2019 criteria [29]. The diagnosis of H was established on the basis of the 2018 ESC/ESH recommendations. Target levels of office BP was established (for systolic BP (SBP) <140 mm Hg and or diastolic BP (DBP) <90 mm Hg). The goal of SBP should be <130 mm Hg and/or DBP <80 mm Hg according to the results of 24-Hour Ambulatory Blood Pressure Monitoring (ABPM) [34, 37]. RH was diagnosed as uncontrolled despite optimal doses of 3 classes of antihypertensive drugs, including thiazide diuretics, or if 4 or more antihypertensive drugs of different classes are required for adequate BP control [2].

A randomized, parallel-group prospective study was conducted to investigate the clinical effectiveness of spironolactone in 60 patients (mean age 61.9±9.1 years; 84.6% women) patients with RA and RH.

Inclusion criteria: age 45-74 years, patients with stage II RH and RA, receiving disease-modifying therapy - methotrexate, chronic kidney disease (CKD) not higher than stage II (GFR not less than 60 ml/min/1.73 m^2), K + serum level from 3.0 to 5.0 mmol/l, informed consent to participate in the study.

Exclusion criteria: stage 3 H, history of CKD III-V, acute renal damage, endocrine pathology (diabetes mellitus, Addison's disease, etc.), clinical signs of hypovolemia, office SBP <115 mm Hg or DBP <55 mm Hg, atrial fibrillation, and flutter, AV blocks 2nd and 3rd degree when performing an ECG, classes III and IV of chronic HF according to NYHA, decreased LV ejection fraction (<40%) or valvular heart disease, acute myocardial infarction or other cardiovascular events (Q wave myocardial infarction, non-Q wave myocardial infarction, unstable angina), myocardial revascularization, stroke, transient ischemic attack) in the anamnesis, alcoholism, drug or mental disorders, infectious diseases, active chronic diarrhea, oncological and hematological diseases, active phases of diseases of the gastrointestinal tract, gout, liver, K^+ serum> 5.0 mmol/l, Na^+ serum <130 mmol/l, inability to give informed consent to participate in the study.

All patients were evaluated by general clinical, laboratory, and instrumental methods of examination. Complete blood count, urinalysis, blood glucose, lipid profile, K+, Na+, Cl-, creatinine, urea, AST, bilirubin, total protein, C-reactive protein (CRP), and

electrocardiography (ECG) were performed. All patients signed an informed consent to participate in the study. The Helsinki Declaration (2000) and international standards for research were taken into account.

All patients underwent office blood pressure (BP) measurement. 24-Hour Ambulatory Blood Pressure Monitoring (ABPM) was performed using ABPM50 (Heaco, Great Britain) with an oscillometric measurement method to assess BP levels. SBP, DBP, and pulse blood pressure (PBP) were determined. Doppler echocardiography was performed with an Arietta S60 devise (Aloka-Hitachi) and a 2.5 - 3.5 MHz transducer. The main indicators of the structure and geometry of the heart were determined: left atrial volume (LAV), left atrial volume index (LAVI) by the formula: LAVI= LAV /BSA (where BSA is the body surface area and was calculated by the modified Dubois-Dubois formula (BSA = 0,007184 * Weight (kg) 0,425 * Height (cm) 0,725), the thickness of an interventricular septum (IVS), a posterior wall of LV (PW), LV end-diastolic dimension (LVEDD), LV end-systolic dimension (LVESD), LV end-diastolic volume (LVEDV), LV end-systolic volume (LVESV), LV stroke volume (LVSV). LV mass (LVM) was calculated by the modified formula of R. Devereux: LVM = 0.8 * (1.04 * (LVEDD + IVS + PW)^3-LVEDD^3))) + 0.6, LVM index (LVMI) according to the formula: LVMI = LVM/ BSA, relative wall thickness (RWT) according to the formula: RWT= 2 * PW / LVEDD, LV fractional shortening (FS), LV midwall fractional shortening (mFS), LV chamber dilatation (LVEDV/BSA).

We categorized patients into 4 groups based on LAVI: without LA dilatation (16-28 ml/m^2), slight increase (29-33 ml/m^2), moderate increase (34-39 ml/m^2) and severe increase (≥40 ml/m^2). The types of LV geometry were assessed from RWT, LVMI and LVEDV/ BSA values [4]: concentric LV hypertrophy (LVH) with dilatation (RWT≥0.42, LVMI ≥115 g/m^2 in men and ≥95 g/m^2 in women, LVEDV /BSA ≥74 ml/m^2 in men, LVEDV /BSA ≥ 68 ml/m^2 in women); concentric LVH without dilatation (RWT ≥0.42, LVMI ≥115 g/m^2 in men and ≥95 g/m^2 in women, LVEDV /BSA <74 ml/m^2 in men, LVEDV /BSA <68 ml/m^2 in women); eccentric LVH with dilatation (RWT <0.42, LVMI ≥115 g/m^2 in men and ≥95 g/m^2 in women, LVEDV /BSA ≥74 ml/m^2 in men, LVEDV /BSA ≥68 ml/m^2 in women); eccentric LVH without dilatation (RWT<0.42, LVMI ≥115 g/m^2 in men and ≥95 g/m^2 in women, LVEDV /BSA <74 ml/m^2 in men, LVEDV /BSA <68 ml/m^2 in women); normal LV geometry (RWT <0.42, LVMI <115 g/m^2 in men and <95 g/m^2 in women, LVEDV /BSA <74 ml/m^2 in men, LVEDV /BSA <68 ml/m^2 in women).

Evaluation of left ventricular diastolic function (LVDF) and right ventricle (RV) was performed according to the assessment of transmitral blood flow from the apical 4-chamber position on the mitral and tricuspid valves, respectively, using pulsed-wave Doppler and Continuous-Wave Doppler. The peak modal velocity in early diastole (peak E, cm sec) and the peak modal velocity in late diastole (peak A, cm/sec), the ratio of early to late transmitral diastolic velocity (E/A), the deceleration time of E (DT, msec), and time of LV isovolumetric relaxation time (IVRT, msec) were determined. Peak systolic mitral annular velocity at the lateral and medial parts of the mitral annulus (s ‘lat and s’ med, respectively, cm/sec), as well as early diastolic myocardial velocity at the lateral and medial parts of the mitral annulus (e ‘lat and e’ med, respectively, cm/sec) and late diastolic myocardial velocity at the lateral and medial parts of mitral annulus (a ‘lat and a’ med, respectively, cm/sec) were determined using tissue Doppler to better assess diastolic function. The average values of these indicators were calculated as their half-sum (S ‘, E’, and A’ respectively). Tricuspid regurgitation (TR) was also taken into account [19, 24, 28, 31].

The primary endpoints were highlighted as improved BP control, better diastolic function (E/A, DT, E/e’), and myocardial remodeling (decline of LVMI, LVEDV/ BSA, LAVI) in Doppler echocardiography after 12 months. The groups of patients with RA and RH were comparable in age, sex, duration of RA and H, RA activity by CRP level and DAS28-CRP scale, which corresponded to high disease activity in both cases, Steinbrocker radiological stage, stage of functional impairment (FI), smoking status, the necessity to take nonsteroidal anti-inflammatory drugs (NSAIDs) and glucocorticosteroids (GCs), Table1.

Statistical processing of the results was performed with the

Table 1. Clinical characteristics of patients with RH in combination with RA

	Group 1 (n=30)	**Group 2** (n=30)
Mean Age, years, M ± σ	60,5 ± 8,5	63,4 ± 9,6
Gender (female), n (%)	26 (86,7)	24 (80,0)
Seropositive RA, n (%)	26 (86,7)	22 (73,3)
DAS28-CRP, M ± σ	5,3 ± 1,0	5,5 ± 0,9
X-ray stage II, n (%)	9 (30,0)	8 (26,7)
X-ray stage III, n (%)	15 (50,0)	17 (56,7)
X-ray stage IV, n (%)	6 (20,0)	5 (16,7)
FI stage I, n(%)	8 (26,7)	7 (23,3)
FI stage II, n (%)	17 (56,7)	19 (63,3)
FI stage III, n (%)	5 (16,7)	4 (13,3)
NSAIDs, n (%)	24 (80,0)	22 (73,3)
GCs, n (%)	10 (33,3)	12 (40,0)
RA duration, years, M ± σ	10,9 ± 6,6	8,4 ± 6,1
H duration, years, M ± σ	9,8 ± 6,7	11,3 ± 7,5
I stage of H, n (%)	27 (90,0)	28 (93,3)
II stage of H, n (%)	3 (10,0)	2 (6,7)
Smoking status, n (%)	5 (16,3)	6 (20,0)

Table 2. Systemic hemodynamic parameters in patients of the main and comparison groups before and after 12 months of therapy, M±σ

	Group 1 (n = 30)		Group 2 (n = 30)	
	before treatment	after treatment	before treatment	after treatment
Office SBP, mm Hg	143,0±6,4	125,9±6,1**	140,8±7,6	132,6±4,4**
Office DBP, mm Hg.	84,4±5,1	72,8±4,0***	84,0±6,5	80,0±6,3**
Office PBP, mm Hg	58,5±6,6	53,1±5,6**	56,8±8,0	52,6±7,5***
SBP by ABPM, mm Hg	140,8±8,7	123,9±3,9**	141,7±6,4	133,2±4,6*
DBP by ABPM, mm Hg	83,1±6,7	73,8±4,5**	81,9±9,7	76,4±7,6
PBP by ABPM, mm Hg	57,7±7,1	50,1±4,3*	59,8±11,0	56,8±7,8

*notes (here and in tables 4, 5): * - P <0,05, ** - P <0,01, *** - P <0,001 in comparison with values of data before treatment*

help of Statistics SPSS 22. The normality of the distribution was assessed using the Shapiro-Wilk test. Under the condition of the normal distribution of the studied trait in the sample, parametric statistical methods were used. The mean value of the indicator (M), standard deviation (σ), standard error (SE), and 95% confidence interval for the mean (95% CI) were determined for descriptive statistics. The t-test for related samples was used to compare the mean values. When distributing of the trait was different from normal, nonparametric statistics was used. We choose the values of the median (Me), 25 and 75 quartiles (Q25 - Q75) for the descriptive part. Variables were expressed as a percentage (%) for categorical part. The Mann-Whitney U-test was used to compare the two independent groups. A comparison of groups on qualitative binary data was performed using Pearson's chi-squared (χ^2) test (corrected by Yates) and Fisher's exact test.

Results and discussion. Prior to inclusion in the study, the groups were comparable in terms of BP. The target level of office BP was achieved in 26 (86.7%) patients versus 12 (40.0%) patients (χ^2 = 12.6, p <0.001) in the group of 12-month antihypertensive therapy with spironolactone compared with treatment without it. This could be due to the corresponding changes in the office BP. Office SBP, DBP and PBP were significantly reduced by 11.9%, 13.7%, and 8.7%, in patients of group 1 respectively (in group 2 - by 5.7%, 4.6%, and 4.0%). Therefore, there was a more pronounced decrease in SBP and DBP in 2.1 and 2.9 times in patients who additionally took spironolactone compared with the group of patients who did not take it (Table 2). Taking into account "harder" indicators of ABPM, the target BP was recorded in 26 (86.7%) and 9 (30.0%) patients after treatment, respectively groups 1 and 2. After spironolactone therapy, the mean SBP, DBP, and PBP were likely dwindled by 11.8%, 17.8%, and 5.4% against the less significant dynamics of group 2, while only SBP reduced statistically significantly - by 8.8%. The findings were confirmed in a study by Roongsritong C., 2005, where SBP remained unchanged in the placebo group, while in the spironolactone group it was reduced from 144 ± 22 to 138±15 mm Hg after 4 months of treatment [28].

Thus, in patients with RH in combination with RA, the addition of spironolactone to standard antihypertensive therapy for 12 months leaded to a significant reduction in BP and reaching its target level in 86.7% of cases, which improved cardiovascular prognosis.

It should be noted that in the group with spironolactone no electrolyte disturbances were obtained. In patients of group 1, the level of potassium did not exceed the reference ranges. It was slightly increased from 4.7 (4.2-5.0) to 4.8 (4.4-5.2) mmol/l (p=0.02), which corresponded to the results of another study, that showed an increase in potassium levels by 0.2 mmol/l (p <0.001) in patients with diastolic type of HF [9]. The level of sodium on spironolactone therapy remained unchanged: 145.0 (141.0-146.0) mmol/l against 145.0 (141.0-147.0) mmol/l (p = 0.8). In patients of group 2 there was a constant level of potassium: 4.5 (4.2-5.0) mmol/l against 4.5 (4.2-5.0) mmol/l (p = 0.3), but the sodium level increaseed from 143.0 (140.0-145.0) mmol/l to 146.0 (142.5-150.0) mmol/l (p = 0.01), indicating a potential prohypertensive effect caused by sodium retention.

The next stage of the work was the assessment of changes in the structural and functional state of the heart on different treatment options in patients with RH in combination with RA. According to recent studies, the size of the left atrium (LA) is an independent factor in predicting cardiovascular disease and heart failure. That`s why, determining the dynamics of the frequency and stage of LA dilatation is strategic during the treatment [1, 21, 22]. LA dilatation at the beginning of research was defined at 26 (86.7%) patients in group 1, as well as in group 2. Patients with moderate LA dilatation (11 (36.7%) cases) and severe increase (10 (33.3%) patients) were the majority of all. A slight increase of LA was registered less often - in 5 (16.7%) people. There was a decrease in the number of patients with LA dilatation after 12 months of treatment in group 1: it was determined in 19 (63.3%) people (χ^2 = 4.4, p = 0.037). There was a drop in a number of patients with severe and moderate stages of LA dilatation (1.5 (22.2%) and 2.8 times (13.3%) respectively), and an increase in the mild stage of LA dilatation - 1.8 times (30.0%) of patients. A positive dynamics was not observed in group 2. LA dilatation was defined in 25 (83.3%) of patients. Given that LAVI indirectly reflects the state of LV diastolic function, a significant decrease in its value in group 1 by 18.3% against the absence of shifts in group 2, maight indicate a significant contribution of spironolactone in improving LV relaxation function in patients with RH and RA. It should be noted that the RV dimension of on long-term therapy in both groups of patients did not change.

At the time of inclusion in the study in groups 1 and 2, LVH was detected in 27 (90.0%) and 26 (86.7%) patients, respectively. Severe LVH was dominated in the structure of LVH in both groups (Table 3). The frequency of LVH detection declined by 10% (χ^2=3.9, p=0.048) in patients of group 1 due to a 1.8-fold reduction in the frequency of detection of severe LVH. The most common was eccentric LVH with LV dilatation in group 1 before the treatment, which indicated a worse prognosis for patients with the development of HF [20, 36]. The frequency of its reduced by 2.2 times after 12 months of therapy. Aa number of patients with concentric LVH with LV dilatation diminished by 2.5 times. Opposite changes were observed in group 2. Despite the lowering of BP, hypertensive LV remodeling continued its progression: the distribution of detection of concentric LV without dilatation of the LV increased (χ^2=3.3, p=0.04) (Table 3).

Changes in the parameters of the geometry and frequency of

Table 3. Distribution in patients of the main and comparison groups before and after 12 months of therapy according to the stage of LVH and the type of LV remodeling, n (%)

	Group 1 (n=30)		Group 2 (n=30)	
	before treatment	after treatment	before treatment	after treatment
Mild LVH, n (%)	2 (6,7%)	2 (6,7%)	4 (13,3%)	5 (16,7%)
Moderate LVH, n (%)	1 (3,3%)	9 (30,0%)***	6 (20,0%)	4 (13,3%)
Severe LVH, n (%)	24 (80,0%)	13 (43,3%)***	16 (53,3%)	20 (66,7%)
No LVH, n (%)	3 (10,0%)	6 (20,0%)*	4 (13,3%)	1 (3,3%)
Eccentric LVH with dilatation, n (%)	11 (36,7%)	5 (16,7%)***	9 (30,0%)	7 (23,3%)
Concentric LVH without dilatation, n (%)	8 (26,7%)	(23,3%)	8 (26,7%)	13 (43,3%)**
Concentric LVH with dilatation, n (%)	5 (16,7%)	2 (6,7%)**	5 (16,7%)	4 (13,3%)
Eccentric LVH without dilatation, n (%)	3 (10,0%)	10 (33,3%)***	4 (13,3%)	5 (16,7%)

*notes: * - P <0,05, ** - P <0,01, *** - P <0,001 in comparison with values of data before treatment*

Table 4. Parameters of the structural and functional state of the heart in patients of the main and comparable groups before and after 12 months of therapy, Me (25% - 75%)

	Group 1 (n=30)		**Group 2 (n=30)**	
	before treatment	**after treatment**	**before treatment**	**after treatment**
LAVI, ml/m^2	39,4 (31,9-45,1)	32,3 (24,2-39,4)**	40,6 (32,8-46,2)	40,2 (31,8-49,6)
IVS, mm	12,0 (11,0-13,0)	11,0 (9,0-11,0)**	11,1 (10,0-12,5)	11,0 (10,0-12,0)
PW, mm	10,4 (9,0-11,0)	9,7 (9,0-11,0)**	10,3 (9,0-11,0)	10,2 (10,0-11,0)
LVM, g	266,7 (206,0-307,0)	227,9 (175,0-278,0)**	238,0 (192,5-269,5)	235,1 (210,5-266,5)
LVMI, g/m^2	141,7 (122,2-157,6)	122,8 (98,0-149,0)**	127,9 (104,4-149,0)	128,3 (119,8-143,8)
LVEDV/BSA, ml/m^2	69,9 (58,8-78,4)	64,1 (53,2-71,2)**	67,6 (57,7-76,6)	68,2 (56,5-76,0)
FS, %	31,6 (28,4-35,6)	36,5 (33,0-39,3)**	36,5 (29,9-41,9)	33,7 (30,1-36,6)
mFS, %	17,1 (14,0-20,1)	20,7 (18,0-24,3)**	16,7 (12,7-21,5)	18,2 (14,6-21,4)
LV EF, %	59,3 (58,4-63,1)	64,0 (60,4-67,9)**	60,3 (54,9-65,0)	61,0 (55,8-64,9)

LVH were reflected in the dynamics of the values of LV structural and functional parameters. Analysis of the dynamics of data representing the stage of LVH showed concordance with the antihypertensive efficacy of the combined treatment of patients in both groups. There was a decrease in LVM and LVMI by 13.9% (-38.7 g) and 13.0% (-18.9 g / m^2, both p <0.01) in patients of group 1 in the absence of probable changes in patients of group 2. A lowering in the thickness of its walls (respectively IVS and PW by 2.3 mm (17.3%) and 1.75 mm (15.2%), both p <0.01)) was detected in group 1 at torpidity these indicators in group 2 (Table 4).

The values of the LV contractile were within the reference range in patients of both groups. However, the data that reflects the regional contractility (FS and mFS) were likely to increase by 15.5% and 21%, respectively, and the global LV contractility (EF) - by 7.9% (all p <0, 01) after 12 months of therapy in patients of group 1 in the absence of the dynamics of these figures in group 2.

ALDO-DHF, a randomized, prospective study, involving 422 elderly outpatients, the vast majority of whom had H, showed that the addition of spironolactone to antihypertensive therapy for 12 month leaded to a regression of LVH (decrease in LVMI by 6 g / m^2, p = 0.009), but did not improve the quality of life and did not reduce the frequency of hospitalizations [9]. The informativeness of\ the LV relaxation index (E / e') had been proven even in masked uncontrolled H. The value of E / e' diminished from 12.7 to 12.1 (p <0.01), which indicated an improvement in LVDF [14]. The lower antihypertrophic efficacy of treatment in this study may be due to a lower dose of spironolactone (25 mg/day without titration), a lower baseline LVH, and the fact that not all patients had RH.

Similar results were obtained in another study, which included 34 patients with RH and studied the effect of spironolactone at a dose of 25 mg with a titration of up to 50 mg per day for 6 months [12]. It was found that the pronounced antihypertrophic efficacy of spironolactone did not depend on the level of aldosterone. However, there was no improvement in LVDF and the dynamics of connective tissue markers, which could be explained by a shorter duration of treatment and fewer patients involved.

In another study, patients with RH received spironolactone for 6 months [11]. Regardless of the concentration of aldosterone, a decrease in BP and a decline in the stage of LVH have been demonstrated. However, in patients with hyperaldosteronism, in addition to a pronounced diuretic effect, the reversal of LVH was identified mainly by reducing the stage of LV dilatation, while in patients with normal aldosterone concentration - by reducing wall thickness as well as stronger vasorelaxation.

Given that patients with H suffered the most from LV diastolic dysfunction (LVDD), it was interesting to analyze the effect of combination antihypertensive therapy on the LV relaxation in patients with RH and RA. The frequency of LVDD reduced from 25 (83.3%) to 12 (40.0%) (χ^2 = 11.9, p <0.001) in patients of the spironolactone group, which was accompanied by changes in its structure: decline in a number of patients with impaired LV relaxation, pseudonormal and restrictive types, respectively, from 18 (60.0%) to 11 (36.7%), from 6 (20.0%) to 1 (3.3%) and from 1 (3.3%) to its absence. LVDD was detected in 28 (93.3%) patients of group 2 before the treatment, impaired LV relaxation, pseudonormal and restrictive types - in 19 (63.3%), 8 (26.7%)

and 1 (3, 3%) patients, then after 12 months- in 26 (85.8%), 13 (42.9%), 11 (36.7%) 2 (6.6%) patients respectively, which indicated the lack of improvement of LVDF without the addition of an aldosterone antagonist.

These data were confirmed by analyzing the parameters of Doppler echocardiography that characterize LVDF. There was an increase in peak E and the ratio of E / A by 14.7% and 24.9%, respectively (both p <0,01), a drop in peak A, the value of DT, and TR by 6.9%, 15.1%, and 16.7%, respectively (all p <0.01) after 12 months of treatment in patients receiving spironolactone, which indicated an improvement of LVDF. No significant changes in the data characterizing LVDF in patients of group 2 were found. There were no statistical differences in the dynamics of diastolic function of the RV in both groups.

Tissue Doppler echocardiography (a more sensitive method of assessing LVDF) was used. Significant positive changes in LV relaxation function on spironolactone therapy in the 1 group were confirmed and characterized by an increasing in e' med, e' lat and E' by 26.7%, 23.1 % and 23.8%, respectively (all p <0.01), and decreasing E / e' med, E / e' lat and E / E' by 8.6%, 6.0% and 7.3%, respectively (all p <0,01). No significant improvement in LV DF was found in group 2. The characteristics of systolic and early diastolic myocardial velocities in the area of the mitral annulus did not differ in both groups and were compared with pre- and post-treatment (Table 5).

Spironolactone at a dose of 25 mg/day, even with a short course of administration (for 4 months), improved LVDF in elderly people with isolated LVDD. The value of E / A was increased (from 0.71 +/- 0.08 to 0.84 +/- 0.19, p = 0.025) and DT was decreased (from 285.5 +/- 73.1 to 230.0 +/- 54.7, p = 0.035) in the group of spironolactone treatment, which corresponded to the data obtained in another study [26]. Other researchers analyzed the results of 80 patients with a metabolic syndrome who took spironolactone 25 mg per day for 6 months. A decrease in E / e' (β = -0.21, p <0.03) and an increase in the peak E (β = -0.44, p <0.001) were noted, but E / A and DT remained unchanged [15, 16]. A German study evaluated the efficacy of spironolactone in 213 patients with H at a dose of 25 mg/day with treatment for 12 months. It has been determined that such a period of therapy was sufficient to improve LVDF, which coincided with our results [9].

The results of 7 studies involving 4147 participants were analyzed in PubMed, EMBASE, and COCHRANE databases. Treatment of patients with H using spironolactone compared with placebo led to a lessening in E / e' (SD -1.38; 95% CI, -2.03 to -0.73; p <0.001) and an increase in E / A' (SD -0, 05; 95% CI, -0.10 to - 0.00; p = 0.03), which coincided with the data of our study. The fact that DT remained unchanged was interesting (SD 1.04; 95% CI, -8.27 to 10.35; p = 1.83). Improvement of LV relaxation may be associated with the additional antifibrotic effect of the aldosterone antagonist, which is especially inherent for patients with a combination of H and RA. The question of the duration of therapy with this diuretic to correct LVDD remains important. It was shown that for patients with H an improvement of LVDF (according to shifts in the E / A ratio) was observed on spironolactone therapy for > 6 months (SD -0.06; 95% CI, −0.11 to -0.00, p = 0.03) against its absence during therapy ≤ 6 months (SD -0.04; 95% CI, -0.18-0.10; p = 0.61) [18]. This was consistent with our results.

Along with the study of antihypertensive and antihypertrophic effects, the analysis of the effect of spironolactone on the clinical and laboratory activity of RA in patients with RH was performed. There was a decrease in RA activity: a decline in CRP from 6.4 (4.0-20.1) mg / l to 4.2 (2.0-11.6) mg / l (p = 0.04) and reduction in the DAS28-CRP from 5.6 (4.9-6.4) to 4.0 (3.4-5.0) (p <0.0001) in patients of group 1. In contrast, patients in group 2 did not have the dynamics of RA activity: CRP changed from 8.2 (3.2-16.6) mg / l to 10.9 (2.5-27.6) mg / l (p = 0.3) and the DAS28-CRP was 5.7 (5.0-6.1) against 5.6 (5.0-6.5) (p = 0.6). This may indicate an increase in the anti-inflammatory effect of long-term use of aldosterone antagonists. Our data were comparable with data from another study involving 24 RA patients (mean age 49 ± 1.8 years; disease duration 8.5 ± 5.8 years) with high RA activity on 12-week spironolactone 2 mg/kg /day therapy. The reduction of both the level of CRP from 15.2 ± 3.8 to 9.4 ± 2.6 mg / dl (p = 0.019) and the DAS28-CRP from 6.9 ± 0.25 to 4.1 ± 0.31 (p <0.05) was proved [30].

The number of patients with pericardial separation decreased

Table 5. Parameters of LV diastolic function in patients of the main and comparable groups before and after 12 months of therapy, Me (25% - 75%)

	Group 1 (n=30)		Group 2 (n=30)	
	before treatment	**after treatment**	**before treatment**	**after treatment**
LV E, cm / sec	66,9 (53,0-75,7)	75,4 (62,9-83,6)**	70,1 (54,2-85,1)	68,6 (54,2-77,4)
LV A, cm / sec	80,2 (64,6-95,4)	73,5 (61,0-83,0)**	75,2 (64,0-84,9)	75,0 (63,2-90,2)
LV E/A	0,9 (0,7-1,1)	1,1 (0,8-1,2)**	1,0 (0,7-1,2)	0,9 (0,7-1,1)
LV DT, msec	192,2 (160,0-220,0)	161,0 (136,0-180,0)**	184,4 (151,0-211,0)	183,6 (145,0-234,0)
LV IVRT, msec	92,8 (84,0-104,0)	90,7 (84,0-88,0)	89,8 (75,5-100,0)	88,0 (84,0-94,0)
e' med, cm / sec	9,1 (7,0-11,0)	11,3 (9,7-12,9)**	9,1 (7,1-10,7)	8,3 (6,6-10,0)
e' lat, cm / sec	10,0 (8,4-11,1)	12,1 (9,9-13,9)**	9,5 (7,6-10,7)	9,6 (8,3-10,8)
E', cm / sec	9,5 (8,5-10,5)	11,7 (10,3-12,9)**	9,3 (8,1-10,8)	9,0 (7,8-9,7)
E/ e' med	7,8 (5,8-8,6)	7,1 (5,3-7,5)**	8,8 (6,5-8,4)	8,3 (6,8-9,7)
E/e' lat	7,1 (5,3-8,4)	6,6 (5,2-7,7)**	7,6 (6,2-8,6)	7,7 (5,3-9,2)
E/E'	7,3 (5,9-8,1)	6,7 (5,6-7,3)**	7,7 (6,3-8,5)	7,8 (5,9-8,7)
TR, cm / sec	2,7 (2,4-3,0)	2,3 (2,2-2,7)**	2,5 (2,1-3,0)	2,5 (2,2-3,1)
S', cm / sec	7,4 (6,4-7,7)	7,0 (6,6-7,4)	7,6 (6,3-8,4)	7,1 (6,4-7,8)
A', cm / sec	9,0 (7,1-10,5)	8,9 (7,6-9,9)	9,6 (7,5-11,7)	8,9 (7,5-10,1)

from 11 (36.7%) to 3 (10.0%) ($\chi^2 = 8.0$, $p < 0.05$) in patients of group 1 after treatment. Dynamics of pericarditis was absent in patients of group 2 ($\chi^2 = 2.2$, $p = 0.137$). The more pronounced anti-inflammatory and diuretic effects of combined antihypertensive and immunosuppressive treatment with the addition of spironolactone were confirmed clinically and instrumentally in patients with RH in combination with RA.

Conclusions. Additional administration of an aldosterone blocker to standard triple antihypertensive therapy in patients with RH and RA is characterized by high antihypertensive efficacy - the target blood pressure is reached three times more often than in the comparison group, and safety - it is not accompanied by hyperkalemia and/or hypotension. Therapy with the inclusion of spironolactone shows a probable decrease in the mean SBP and DBP by 11.8% and 17.8%, respectively. The addition of spironolactone to therapy leads to a decline in the number of patients with LA dilatation by 23.4% ($\chi^2 = 4.4$, $p = 0.037$) and LVH by 10% ($\chi^2 = 3.9$, $p = 0.048$), which is combined with a decline in eccentric and concentric LV dilatation 2.2 and 2.5 times, respectively, with the progression of LV hypertensive remodeling in patients without spironolactone treatment: detection of concentric LVH without LV dilatation is increased by 16.7% ($\chi^2 = 3.3$, $p = 0.04$). Spironolactone leads to a lessening of LVH (by 13.0%, $p < 0.01$) by reducing the stage of LV dilatation (by 7.3%, $p < 0.01$) and wall thickness (IVS by 17.3% and PW by 15.2%, both $p < 0,01$). LVH regression is associated with an improvement in LV contractility, both regional (FS) and global (EF) - by 15.5% and 7.9%, respectively (both $p < 0.01$). There is a diminution in the incidence of LLDD by 43.0% ($\chi^2 = 11.9$, $p < 0.001$) and changes in its structure on spironolactone treatment: a lowering in the ratio of patients with impaired LV relaxation and pseudonormal LVDD by 23.3% and 16.7%, respectively (both $p < 0.05$). This is accompanied by a decline in E / e' med, E / e' lat and E / E' by 8.6%, 6.0% and 7.3%, respectively ($p < 0,01$), which indicates an improvement in LVDF. Potent antihypertensive and antihypertrophic effects of spironolactone are combined with increased anti-inflammatory action in patients with RH and RA. It is expressed by a decrease in clinical and laboratory activity of RA: the DAS28-CRP lessens from 5.6 (4.9-6.4) to 4.0 (3.4-5.0) ($p < 0.001$).

We consider that it is appropriate to conduct further studies with a larger sample of patients and a wider range of laboratory markers to clarify the relationship between aldosterone receptor blockade and mechanisms of the antihypertensive effect in patients with RA and RH, given the positive effect of spironolactone on hypertrophy, dilatation, and diastolic dysfunction.

REFERENCES

1. Antit S, Zakhama L, Amri A, et al. Assessment of left atrial mechanical function by two-dimensional echocardiography in hypertensive patients. // Tunis Med. 2019;97(7):882-890.
2. Aronow W.S. Approaches for the Management of Resistant Hypertension in 2020. Current Hypertension Reports, 2020. 22(1), 3.
3. Balsa A, Lojo-Oliveira L, Alperi-López M, et al. Prevalence of comorbidities in rheumatoid arthritis and evaluation of their monitoring in clinical practice: the spanish cohort of the COMORA study. // Reumatol Clin. 2019;15(2):102-108.
4. Bang CN, Gerdts E, Aurigemma GP, et al. Systolic left ventricular function according to left ventricular concentricity and dilatation in hypertensive patients: the Losartan Intervention For Endpoint reduction in hypertension study [published correction appears in J Hypertens. 2014 Jul;32(7):1548]. // J Hypertens. 2013;31(10):2060-2068.
5. van den Berg TN, Rongen GA, Fröhlich GM, et al. The cardioprotective effects of mineralocorticoid receptor antagonists. // Pharmacol Ther 2014;142:72–87.
6. Bernabe-Ortiz A, Sal Y, Rosas VG, et al. Effect of salt substitution on community-wide blood pressure and hypertension incidence. // Nat Med. 2020;26(3):374-378.
7. Brilla CG. Aldosterone and myocardial fibrosis in heart failure. Herz 2000; 25: 299–306
8. Brilla C.G., Weber K.T. Mineralocorticoid excess, dietary sodium, and myocardial fibrosis. // J Lab Clin Med 1992;120:893–901.
9. Edelmann F, Wachter R, Schmidt AG, et al. Effect of spironolactone on diastolic function and exercise capacity in patients with heart failure with preserved ejection fraction: the Aldo-DHF randomized controlled trial. // *Jama*, 2013;309(8), 781-791.
10. Ekström M, Hellman A, Hasselström J, et al. The transition from hypertension to hypertensive heart disease and heart failure: the PREFERS Hypertension study. // ESC Heart Fail. 2020;7(2):737-746.
11. Gaddam K, Corros C, Pimenta E, et al. Rapid reversal of left ventricular hypertrophy and intracardiac volume overload in patients with resistant hypertension and hyperaldosteronism: a prospective clinical study. // Hypertension 2010;55:1137–1142.
12. Gupta A, Schiros CG, Gaddam KK, et al. Effect of spironolactone on diastolic function in hypertensive left ventricular hypertrophy. // J Hum Hypertens. 2015;29(4):241-6.
13. Kessler EL, Oerlemans MIFJ, van den Hoogen P, et al. Immunomodulation in Heart Failure with Preserved Ejection Fraction: Current State and Future Perspectives [published online ahead of print, 2020 May 22]. // J Cardiovasc Transl Res. 2020;10.1007/s12265-020-10026-3.
14. Komori T, Eguchi K, Kabutoya T, et al. Left ventricular diastolic function evaluated by the E/e› ratio is impaired in patients with masked uncontrolled hypertension. // Clin Exp Hypertens. 2014;36(8):538-544.
15. Kosmala W, Przewlocka-Kosmala M, Szczepanik-Osadnik H, et al. A randomized study of the beneficial effects of aldosterone antagonism on LV function, structure, and fibrosis markers in metabolic syndrome. // JACC Cardiovasc Imaging. 2011;4(12):1239-49.
16. Kosmala W, Przewlocka-Kosmala M, Szczepanik-Osadnik H, et al. Fibrosis and cardiac function in obesity: a randomised controlled trial of aldosterone blockade. // Heart. 2013;99(5):320-6.
17. Li F, Xu M, Fan Y, et al. Diffuse myocardial fibrosis and the prognosis of heart failure with reduced ejection fraction in Chinese patients: a cohort study. // Int J Cardiovasc Imaging. 2020;36(4):671-689.
18. Li S, Zhang X, Dong M, et al.. Effects of spironolactone in heart failure with preserved ejection fraction: A meta-analysis of randomized controlled trials. // Medicine (Baltimore). 2018;97(35):e11942. doi: 10.1097/MD.0000000000011942.
19. Mordi IR, Singh S, Rudd A, et al. Comprehensive Echocardiographic and Cardiac Magnetic Resonance Evaluation Differentiates Among Heart Failure With Preserved Ejection Fraction Patients, Hypertensive Patients, and Healthy Control Subjects [published correction appears in JACC Cardiovasc Imaging. 2019 Mar;12(3):576]. // JACC Cardiovasc Imaging. 2018;11(4):577-585.
20. Nadruz W. Myocardial remodeling in hypertension. // J Hum Hypertens. 2015;29(1):1-6.
21. Ocaranza MP, Bambs C, Salinas M, et al. Early left atrial

dysfunction is associated with suboptimal cardiovascular health. // Echocardiography. 2020;37(1):47-54.
22. Parajuli P, Ahmed AA. Left Atrial Enlargement. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2020.
23. Parasiliti-Caprino M, Lopez C, Prencipe N, et al. Prevalence of primary aldosteronism and association with cardiovascular complications in patients with resistant and refractory hypertension [published online ahead of print, 2020 May 7]. // J Hypertens. 2020;10.1097/HJH.0000000000002441.
24. Pieske B, Tschöpe C, de Boer RA, et al. How to diagnose heart failure with preserved ejection fraction: the HFA-PEFF diagnostic algorithm: a consensus recommendation from the Heart Failure Association (HFA) of the European Society of Cardiology (ESC). // Eur J Heart Fail. 2020;22(3):391-412.
25. Rai A, Narisawa M, Li P, et al. Adaptive immune disorders in hypertension and heart failure: focusing on T-cell subset activation and clinical implications [published online ahead of print, 2020 Apr 6]. // J Hypertens. 2020;10.1097/HJH.0000000000002456.
26. Roongsritong C, Sutthiwan P, Bradley J, et al. Spironolactone improves diastolic function in the elderly. // Clin Cardiol. 2005;28(10):484-7.
27. Sava RI, Pepine CJ, March KL. Immune Dysregulation in HFpEF: A Target for Mesenchymal Stem/Stromal Cell Therapy. // J Clin Med. 2020;9(1):241.
28. Shehata IE, Eldamanhory AS, Shaker A. Early predictors of left ventricular dysfunction in hypertensive patients: comparative cross-section study. // Int J Cardiovasc Imaging. 2020;36(6):1031-1040.
29. Smolen JS, Landewé R B, Bijlsma JW, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2019 update. // Annals of the rheumatic diseases, 2020;79(6),685-699.
30. Syngle A, Vohra K, Kaur L, Sharma S. Effect of spironolactone on endothelial dysfunction in rheumatoid arthritis. // Scand J Rheumatol. 2009;38(1):15-22.
31. Tadic M, Cuspidi C, Calicchio F, et al. Diagnostic algorithm for HFpEF: how much is the recent consensus applicable in clinical practice? [published online ahead of print, 2020 Apr 28]. // Heart Fail Rev. 2020;10.1007/s10741-020-09966-4.
32. Targoński R, Sadowski J, Price S, Targoński R. Sodium-induced inflammation-an invisible player in resistant hypertension [published online ahead of print, 2020 Mar 19].// Hypertens Res. 2020;10.1038/s41440-020-0428-y.
33. Tu W, Pratt JH. Autonomous Aldosterone Production and Left Ventricular Hypertrophy. // Hypertension. 2020;75(6):1409-1411.
34. Unger T, Borghi C, Charchar F, et al. 2020 International Society of Hypertension global hypertension practice guidelines. // Hypertension, 2020; *75*(6), 1334-1357.
35. Velmakin S, Troitskaya, E, Kobalava, Z. Hypertensive patients with rheumatoid arthritis are characterized by higher levels of the office blood pressure and worse control of central blood pressure compared to controls. // Journal of Hypertension, 2019; 37, e317.
36. Verdecchia P, Angeli F, Mazzotta G, et al. Impact of Chamber Dilatation on the Prognostic Value of Left Ventricular Geometry in Hypertension. // J Am Heart Assoc. 2017;6(6):e005948.
37. Williams B, Giuseppe M, Spiering W, et al. ESC/ESH Guidelines for the management of arterial hypertension. // European Heart Journal, 2018.;39(33),3021-3104.
38. Zhao H, Gu DW, Li HT, et al. Inhibitory effects of spironolactone on myocardial fibrosis in spontaneously hypertensive rats. // Genet Mol Res. 2015;14(3):10315-21.

SUMMARY

EFFICACY OF SPIRONOLACTONE IN ANTIHYPERTENSIVE THERAPY IN PATIENTS WITH RESISTANT HYPERTENSION IN COMBINATION WITH RHEUMATOID ARTHRITIS

Kondratiuk V., Stakhova A., Hai O., Karmazina O., Karmazin Y.

Bogomolets National Medical University, Ukraine

The aim of the study is to investigate the antihypertensive efficacy, structural and functional remodeling of the heart in patients with resistant hypertension (RH) and rheumatoid arthritis (RA) after 12-month of therapy.

The treatment includes angiotensin-converting enzyme inhibitor, calcium channel blocker, diuretics, aldosterone receptor blocker (spironolactone), and immunosuppressive drug (methotrexate). 101 patients with hypertension (H) and RA were examined at the screening visit. 60 patients (mean age 61.9±9.1 years; 84.6% of women) meeting the criteria for RH were selected after 1 month. A randomized, controlled, parallel-group prospective study was conducted. Patients underwent general clinical, laboratory, and Doppler echocardiography investigations. They were divided into 2 groups: the main group, which represented patients whom to the basic antihypertensive therapy were added spironolactone 25 mg/day (group 1, n=30), and the comparison group, which represented patients who continued antihypertensive treatment without the addition of spironolactone (group 2, n=30) with 12- monthly observation. Groups of patients are comparable in age, sex, duration of RA and H, RA activity. The target blood pressure was achieved in 86.7% against 30.0% of patients ($p < 0.001$) on spironolactone treatment compared to the inclusion of it. Therapy with spironolactone shown a probable decrease in the mean systolic blood pressure, diastolic blood pressure, and pulse blood pressure by 11.8%, 17.8%, and 5.4%, respectively. There was a reduction in the number of patients with left atrium dilatation from 86.7% to 63.3% ($\chi^2=4.4$, $p=0.037$) in group 1. The frequency of left ventricular hypertrophy (LVH) dropped by 10% ($\chi^2=3.9$, $p=0.048$) in patients of group 1. The incidence of eccentric LVH with left ventricular (LV) dilatation decreased by 2.2 times, concentric LVH with LV dilatation declined by 2.5 times after treatment in group 1. There was a further LV hypertensive remodeling in group 2: detection of concentric LVH without LV dilatation ($\chi^2=3.3$, $p=0.04$) was increased. There was a reduction of LV mass index (by 13.0%, $p<0.01$) due to a decrease in the stage of LV dilatation (by 7.3%, $p<0.01$), and the thickness of its walls (respectively interventricular septum and posterior wall by 17.3% and 15.2%, both $p<0.01$) in spironolactone group with the absence of probable changes in group 2. The LV contractile capacity, both regional fractional shortening and global ejection fraction improved (decline by 15.5% and 7.9% (both $p<0.01$)) in group 1 in the absence of dynamics in group 2. The incidence of LV diastolic dysfunction subsided from 83.3% to 40.0% ($\chi^2=11.9$, $p<0.001$) in patients of the spironolactone group, mainly due to a probable lessening in a number of patients with an abnormal LV relaxation from 60.0% to 36.7%. There was a lowering in E/e' med, E/e' lat and E/E' by 8.6%, 6.0% and 7.3%, respectively (all p

<0.01) in patients on spironolactone therapy, which reflected the improvement of LV diastolic function. Patients of group 1 demonstrated a de-escalation of RA activity: a dropping of the DAS28-CRP from 5.6 (4.9-6.4) to 4.0 (3.4-5.0) (p<0,0001) in the absence of its dynamics in patients of group 2 (from 5.7 (5.0-6.1) to 5.6 (5.0-6.5) (p=0.6)).

The addition of spironolactone to basic therapy demonstrates increased antihypertensive efficacy and potent antihypertrophic efficacy. These effects are combined with improved systolic and diastolic LV function and a decrease of clinical and laboratory activity of RA in elderly patients with RH in combination with RA.

Keywords: resistant arterial hypertension, rheumatoid arthritis, spironolactone, left ventricular diastolic dysfunction.

РЕЗЮМЕ

ЭФФЕКТИВНОСТЬ СПИРОНОЛАКТОНА В СОСТАВЕ КОМБИНИРОВАННОЙ АНТИГИПЕРТЕНЗИВНОЙ ТЕРАПИИ У БОЛЬНЫХ РЕЗИСТЕНТНОЙ АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИЕЙ В СОЧЕТАНИИ С РЕВМАТОИДНЫМ АРТРИТОМ

Кондратюк В.Е., Стахова А.П., Гай О.И., Кармазина Е.М., Кармазин Я.Е.

Национальный медицинский университет им. А.А. Богомольца, Киев, Украина

Целью исследования является изучение антигипертензивной эффективности и структурно-функциональной перестройки сердца у больных резистентной артериальной гипертензией и ревматоидным артритом (РА) на фоне 12-месячной комбинированной терапии, включающей: ингибитор ангиотензин превращающего фактора, блокатор кальциевых каналов, диуретик, антагонист альдостерона (спиронолактон) и иммуносупрессор (метотрексат). На скрининговом визите обследован 101 пациент с артериальной гипертензией (АГ) и ревматоидным артритом (РА). Спустя 1 мес. отобраны 60 пациентов, средний возраст 61,9±9,1 г., 51 (84,6%) женщина и 9 (15,4%) мужчин, соответствующие критериям резистентной артериальной гипертензии (РАГ). Проспективное, рандомизированное исследование проведено в параллельных группах. Пациентам проведены обще-клиническое, лабораторное и допплерэхокардиографическое исследования. Больные разделены на 2 группы: I группа (основная) (n=30) – пациенты, к базисной антигипертензивной терапии которых добавлялся спиронолактон 25 мг/сут, II группа (сравнения, n=30), - пациенты, продолжившие антигипертензивное лечение без добавления спиронолактона с 12-месячным наблюдением. Группы больных сопоставимы по возрасту, полу, варианту РА, продолжительности РА и АГ, активности РА. На фоне терапии с включением спиронолактона в сравнении с лечением без него целевой уровень АД достигнут у 26 (86,7%) больных против 9 (30,0%) больных, (p<0,001). Терапия с включением спиронолактона демонстрирует достоверное снижение среднесуточных систолического, диастолического и пульсового артериального давления на 11,8%, 17,8% и 5,4%, соответственно. В I группе наблюдалось уменьшение числа больных с дилатацией левого предсердия с 86,7% до 63,3% (χ^2=4,4, p=0,037). У больных I группы частота гипертрофии левого желудочка (ГЛЖ) уменьшилась на 10% (χ^2=3,9, p=0,048). После лечения в I группе уменьшились частота выявления эксцентричной ГЛЖ с дилатацией левого желудочка (ЛЖ) в 2,2 раза и концентрической ГЛЖ с дилатацией ЛЖ в 2,5 раза. У пациентов II группы отмечается дальнейшее гипертензивное ремоделирование ЛЖ: увеличивается выявление концентрической ГЛЖ без дилатации ЛЖ (χ^2=3,3, p=0,04). У пациентов группы спиронолактона отмечается уменьшение индекса массы миокарда ЛЖ на 13,0%, (p<0,01) за счет уменьшения степени дилатации ЛЖ (на 7,3%, p<0,01), и толщины его стенок (согласно межжелудочковой перегородке и задней стенке ЛЖ на 17,3% и 15,2%, в обеих случаях p<0,01) при отсутствии достоверных сдвигов у больных II группы. У больных I группы улучшилась сократительная способность ЛЖ: регионарное фракционное укорочение и глобальная фракция выброса - на 15,5% и 7,9%, соответственно, (p<0,01) при отсутствии динамики во II группе. На фоне лечения у больных группы спиронолактона частота выявления диастолической дисфункции ЛЖ уменьшается с 83,3% до 40,0% (χ^2=11,9, p<0,001) преимущественно за счет возможного уменьшения доли аномального расслабления ЛЖ с 60,0% до 36,7%. На фоне терапии спиронолактоном отмечается уменьшение E/e' med, E/e' lat и E/E', соответственно, на 8,6%, на 6,0% и 7,3% (p<0,01), что отражает улучшение диастолической функции ЛЖ. На фоне лечения у больных I группы наблюдается уменьшение активности РА: снижение значения индекса DAS28-СРБ с 5,6 (4,9-6,4) баллов до 4,0 (3,4-5,0) баллов (p<0,0001) при отсутствии его динамики у больных II группы - с 5,7 (5,0-6,1) до 5,6 (5,0-6,5) баллов (p=0,6).

У больных старшего возраста с РАГ в сочетании с РА добавление к базисной терапии спиронолактона демонстрирует усиление антигипертензивной эффективности, мощную антигипертрофическую эффективность, что сочетается с улучшением систоло-диастолической функции ЛЖ и снижением клинико-лабораторной активности РА.

რეზიუმე

სპირონოლაქტონის ეფექტურობა კომბინირებულ ანტიჰიპერტეზიულ თერაპიაში პაციენტებში რევმატოიდულ ართრიტთან შერწყმული რეზისტენტული არტერიული ჰიპერტენზიით

ვ.კონდრატიუკი, ა.სტახოვა, ო.გაი, ე.კარმაზინა, ი.კარმაზინი

ა.ბოგომოლეცის სახელობის ეროვნული სამედიცინო უნივერსიტეტი, კიევი, უკრაინა

კვლევის მიზანს წარმოადგენდა ანტიჰიპერტენზიული ეფექტურობის და გულის სტრუქტურულ-ფუნქციური გარდაქმნების შეფასება პაციენტებში რეზისტენტული არტერიული ჰიპერტენზიით და რევმატოიდული ართრიტით 12-თვიანი კომბინირებული თერაპიის ფონზე, რაც მოიცავდა: ანგიოტენზინგარდამქმნელი ფაქტორის ინჰიბიტორს, კალციუმის არხების ბლოკატორს, დიურეტიკს, ალდოსტერონის ანტაგონისტს (სპირონოლაქტონი) და იმუნოსუპრესორს (მეტოტრექსატი). სკრინინგულ ვიზიტზე გამოკვლეული იყო 101 პაციენტი არტერიული ჰიპერტენზიით და რევმატოიდული ართრიტით. 1 თვის შემდეგ შერჩეული იყო 60 პაციენტი (საშუალო ასაკი - 61,9±9,1 წელი, 51 (84,6%) ქალი და 9 (15,4%) მამაკაცი), რომლებიც შეესაბამებოდა რეზისტენტული არტერიული ჰიპერ-

ტენზიის კრიტერიუმებს. პროსპექტული, რანდომიზებული კვლევა ჩატარდა ორ პარალელურ ჯგუფში. პაციენტებს ჩაუტარდა საერთო კლინიკური, ლაბორატორიული და დოპლერექოკარდიოგრაფიული კვლევა. პაციენტები დაიყო ორ ჯგუფად: I ჯგუფი (ძირითადი, n=30) – პაციენტები, რომელთა ბაზისურ თერაპიას დამატებული ჰქონდა სპირონოლაქტონი – 25 მგ/დღეში, II ჯგუფი (შედარების, n=30) – პაციენტები, რომლებიც აგრძელებდნენ ანტიჰიპერტენზიულ მკურნალობას სპირონოლაქტონის დამატების გარეშე 12-თვიანი დაკვირვების პერიოდში.

თერაპიაში სპირონოლაქტონის ჩართვის ფონზე არტერიული წნევის სამიზნე დონე მიღწეული იქნა 26 პაციენტში (86,7%) (*vs* 9 (30%); p<0,001). სპირონოლაქტონის ჩართვა განსაზღვრავს სისტოლური, დიასტოლური და პულსური არტერიული წნევის საშუალო დღეღამური მაჩვენებლების სარწმუნო შემცირებას 11,8%-ით, 17,8%-ით და 5,4%-ით, შესაბამისად. I ჯგუფში აღინიშნა პაციენტების რაოდენობის შემცირება მარცხენა წინაგულის დილატაციით 86,7%-დან 63,3%-მდე (χ^2=4,4, p=0,037). ამავე ჯგუფში მარცხენა პარკუჭის ჰიპერტროფიის სიხშირე შემცირდა 10%-ით (χ^2=3,9, p=0,048). მკურნალობის შემდეგ I ჯგუფში შემცირდა მარცხენა პარკუჭის ექსცენტრული ჰიპერტროფიის, მარცხენა პარკუჭის დილატაციით, გამოვლენის სიხშირე 2,2-ჯერ, მარცხენა პარკუჭის კონცენტრული ჰიპერტროფიის, მარცხენა პარკუჭის დილატაციით, გამოვლენის სიხშირე კი - 2,5-ჯერ. II ჯგუფის პაციენტებში აღინიშნება შემდგომი ჰიპერტენზიული რემოდელირება: იმატებს მარცხენა პარკუჭის კონცენტრული ჰიპერტროფიის გამოვლინება მარცხენა პარკუჭის დილატაციის გარეშე (χ^2=3,3, p=0,04). სპირონოლაქტონის ჯგუფის პაციენტებში აღინიშნება მარცხენა პარკუჭის მიოკარდიუმის მასის ინდექსის შემცირება 13,0%-ით (p<0,01) მარცხენა პარკუჭის დილატაციის ხარისხის შემცირების (7,3%-ით, p<0,01) და მისი კედლების სისქის (პარკუჭთშორისი ძგიდის და მარცხენა პარკუჭის უკანა კედლის მიხედვით, 17,3%-ით და 15,2%-ით, ორივე შემთხვევაში p<0,01) ხარჯზე. I ჯგუფის პაციენტებს გაუმჯობესდათ მარცხენა პარკუჭის კუმშვადი აქტივობა: რეგიონული ფრაქციული დამოკლება და განდევნის გლობალური ფრაქცია – 15,5%-ით და 7,9%-ით (p<0,01), შესაბამისად, II ჯგუფში დინამიკის არარსებობის ფონზე. სპირონოლაქტონით მკურნალობის ფონზე აღინიშნება E/e' med-ის, E/e' lat-ის და E/E'-ის შემცირება, შესაბამისად, 8,6%-ით, 6,0%-ით და 7,3%-ით (p<0,01), რაც ასახავს მარცხენა პარკუჭის დიასტოლური ფუნქციის გაუმჯობესებას. I ჯგუფის პაციენტებში მკურნალობის ფონზე აღინიშნება რევმატოიდული ართრიტის აქტივობის შემცირება (5,6 ქულიდან 4,0 ქულამდე) ამ მაჩვენებლის დინამიკის არარსებობისას II ჯგუფის პაციენტებში (5,7 ქულიდან 5,6 ქულამდე) (p=0,6).

უფროსი ასაკის პაციენტებში რეზისტენტული არტერიული ჰიპერტენზიით და რევმატოიდული ართრიტით ბაზისურ თერაპიაში სპირონოლაქტონის ჩართვა ზრდის ანტიჰიპერტენზიულ ეფექტურობას, ავლენს მძლავრ ანტიჰიპერტროფიულ ეფექტურობას, რაც შერწყმულია მარცხენა პარკუჭის სისტოლურ-დიასტოლური ფუნქციის გაუმჯობესებასთან და რევმატოიდული ართრიტის კლინიკურ-ლაბორატორიული აქტივობის შემცირებასთან.

COMORBID CONDITION – DIABETES MELLITUS WITH CO-EXISTENT RAYNAUD'S SYNDROME IN PATIENTS WITH RHEUMATOID ARTHRITIS

Hotiur O., Boichuk V., Skoropad K., Vandzhura Y., Bacur M.

Ivano-Frankivsk National Medical University, Ukraine

Comorbidity (from Latin "co" – along with, "morbus" – disease) is defined as the co-existence of two and/or more syndromes (trans-syndromal comorbidity) or diseases (trans-nosological comorbidity), which are pathogenically interrelated or simultaneous (chronological comorbidity), in a single patient. The most common comorbidities in patients with rheumatic diseases include cardiovascular diseases (CVD), liver and biliary tract infection, lung diseases, amyloidosis, fractures of different localizations, malignant neoplasms, metabolic disorders and diabetes mellitus (DM) [11].

According to the Ministry of Health of Ukraine, rheumatoid arthritis (RA) affected an estimated 112,960 individuals (49,420 people of working age) in 2016 [16]. In other words, the prevalence of RA in Ukraine is 340 cases per 100,000 adult population. Women are 3-4 times more likely to develop RA than men; however, in seropositive patients (rheumatoid factor (RF)+) and elderly people, these gender differences are less obvious [15].

On one hand, the inflammatory process is accompanied by the formation of a great number of cytokines, including tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6), that induce the synthesis of C-reactive protein (CRP) which increases the expression of cell adhesion molecules in endothelial cells and promotes attachment of leukocytes to the endothelium [20]. On the other hand, there is a correlation between the presence and activity level of non-specific inflammation and the development of metabolic syndrome (MS) (obesity, arterial hypertension, dyslipidemia and DM) [15].

According to Ivanytskyi I.V., patients with RA present with higher plasma levels of cholesterol and blood glucose as compared to those with deforming osteoarthritis, reactive arthritis [13,15].