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ВЛИЯНИЕ ТЕРАПИИ САКУБИТРИЛ-ВАЛСАРТАНОМ НА ПАЦИЕНТОВ С СЕРДЕЧНОЙ НЕДОСТАТОЧНОСТЬЮ С СОХРАНЁННОЙ ФРАКЦИЕЙ ВЫБРОСА

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АННОТАЦИЯ

Актуальность: За последние 20 лет во всём мире количество случаев сердечной недостаточности удвоилось. Сердечная недостаточность с сохранённой фракцией выброса (ХСНсФБ) — это заболевание, которое встречается всё чаще, и его масштабы становятся настоящей проблемой для здравоохранения. Эффективных методов лечения для этой болезни пока не существует, что делает её особенно важной для изучения. Материалы и методы: Исследование было проведено в кардиологическом центре Самаркандской области. Оно представляло собой проспективное наблюдательное исследование, в котором приняли участие 48 пациентов с хронической сердечной недостаточностью с сохранённой фракцией выброса (ХСНсФВ). Сравнивались ключевые клинические и лабораторные показатели пациентов до и после лечения. Статистическая обработка данных выполнялась с использованием программы SPSS версии 28.0, различия считались статистически значимыми при уровне $p < 0,05$. Результаты**:** Пациенты были разделены на две группы:1-я группа (n=24): получала терапию сакубутрилом/валсартаном. 2-я группа (n=24): получала терапию только валсартаном. Через 16 недель терапии было зафиксировано значительное улучшение клинических и лабораторных показателей у пациентов, получавших сакубутрил/валсартан: Среднее снижение систолического артериального давления (САД) составило **-10,3 ± 1,0 мм рт. ст.** в группе сакубутрил/валсартана против **-6,4 ± 0,9 мм рт. ст.** в группе валсартана (**p < 0,05**). Улучшение функционального класса ХСН по NYHA наблюдалось у **63%** пациентов первой группы против **42%** во второй группе (**p < 0,05**). Выводы: Полученные результаты подтверждают, что комбинированная терапия сакубутрилом/валсартаном эффективнее монотерапии валсартаном у пациентов с ХСНсФВ. Лечение сакубутрилом/валсартаном способствовало значительному снижению артериального давления и частоты госпитализаций, а также улучшению функционального состояния пациентов. Это позволяет рассматривать данную терапию как перспективное направление в лечении пациентов с ХСНсФВ, особенно в случаях резистентной гипертензии.

Ключевые слова: Сердечная недостаточность с сохранённой фракцией выброса (ХСНсФБ), сакубутрил, валсартан, NYHA, систолического артериального давления (САД)

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THE IMPACT OF SACUBITRIL-VALSARTAN THERAPY IN PATIENTS WITH HEART FAILURE WITH PRESERVED EJECTION FRACTION

ANNOTATION

Background: Over the past two decades, the number of heart failure cases has doubled worldwide, and heart failure with preserved ejection fraction (HFpEF) is becoming increasingly common, posing a significant challenge to public health. Currently, there are no effective treatments for this condition, making it crucial to conduct research. **Materials and Methods:** This study was conducted at the Cardiological centre of Samarkand region. It was an observational study that included 48 patients diagnosed with chronic HFpEF. Key clinical and laboratory parameters were recorded before and after treatment, and statistical analysis was performed using SPSS version 28.0. Differences were considered significant if $p < 0.05$. **Results:** The patients were divided into two groups: Group 1 (n=24) received sacubutril/valsartan therapy, and Group 2 (n=24) received valsartan

monotherapy. After 16 weeks of treatment, a significant improvement in clinical and laboratory parameters was noted in patients receiving sacubutril/valsartan. The average decrease in systolic blood pressure (BP) was -10.3 ± 1.0 mmHg in the sacubutril/valsartan group compared to -6.4 ± 0.9 mmHg in the valsartan-only group ($p<0.05$). Functional class improvement of CHF (Congestive Heart Failure) according to the NYHA (New York Heart Association) classification was observed in 63% of patients in Group 1 versus 42% in Group 2 ($p<0.05$). **Conclusions:** These results confirm that sacubutril/valsartan combination therapy is more effective than valsartan monotherapy in patients with congestive heart failure. Treatment with sacubutril/valsartan has shown significant reductions in blood pressure, and hospitalization rates, as well as improvements in the functional status of patients. These findings suggest that this therapy could be a promising approach for treating patients with chronic heart failure, especially those with resistant hypertension.

Key words: Heart failure with preserved ejection fraction (HFpEF), sacubitril, valsartan, New York Heart Association (NYHA), systolic blood pressure (SBP)

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SAQLANGAN HAYDASH FRAKSIYASI BILAN YURAK YETISHMOVCHILIGIDA SAKUBITRIL-VALSARTAN TERAPIYASINING TA’SIRI

ANNOTATSIYA

Dolzarbligi: So‘nggi 20 yil ichida yurak yetishmovchiligi holatlari soni dunyo bo‘ylab ikki baravar oshganligi qayd qilingan. Saqlangan qon haydash fraksiyasi bilan yurak yetishmovchiligi (SQHFSYuY) keng tarqalgan kasallik bo‘lib, uning ko‘lami aholi salomatligi uchun haqiqiy muammoga aylanib bormoqda. Ushbu kasallikni samarali davolash usullari hali mavjud yemas, bu esa uni o‘rganishni dolzarb muammoligini tasdiqlaydi. **Materiallar va usullar:** Tadqiqot ishi Samarqand viloyati kardiologiya markazida o‘tkazildi. Tadqiqot saqlangan qon haydash fraksiyasi bilan yurak yetishmovchiligi (SQHFSYuY) aniqlangan 48 bemorni o‘z ichiga olgan bo‘lib, davolanishdan oldin va keyin bemorlarning asosiy klinik va laboratoriya ko‘rsatkichlari taqqoslandi. Statistik ma’lumotlarni qayta ishlash SPSS dasturi 28.0 versiyasi yordamida amalga oshirildi, ko‘rsatkichlar farqi $P < 0.05$ darajasida statistik jihatdan ahamiyatli hisoblandi. **Natijalar:** Tadqiqotga kiritilgan bemorlar ikki guruhga ajratildi: 1-guruh (n=24): sakubitril/valsartan berildi. 2-guruh (n=24): faqat valsartan bilan davolash olib borildi. 16 haftalik davodan so‘ng sakubitril/ valsartan olgan bemorlarda klinik va laboratoriya parametrlarining sezilarli yaxshilanishi qayd etildi: sistolik qon bosimining (SQB) o‘rtacha pasayishi sakubitril/ valsartan guruhida -10.3 ± 1.0 mm.sim.ust, valsartan guruhida - 6.4 ± 0.9 mm.sim.ust ni tashkil etdi ($P < 0,05$). NYHA bo‘yicha YuYe funksional sinfining yaxshilanishi birinchi guruhdagi bemorlarning 63 foizida, ikkinchi guruhdagi 42% ($P < 0.05$) da kuzatilgan. **Xulosa:** Olingan natijalar SYuYe mavjud bemorlarda sakubitril/ valsartan bilan kompeks terapiya valsartan bilan monoterapiyaga qaraganda samaraliroq ekanligini tasdiqlaydi. Sakubitril/ valsartan bilan davolash qon bosimini va gospitalizatsiya qilish chastotasini sezilarli darajada kamaytirdi, shuningdek bemorlarning funksional holatini yaxshiladi. Bu bizga ushbu terapiyani SYuYe bilan og‘rigan bemorlarni davolashda, ayniqsa gipotenziv vositalarga rezistentlik kuzatilgan gipertenziya holatlarida samarali davo usuli sifatida qo‘llashga imkon beradi.

Kalit so‘zlar: Saqlangan qon haydash fraksiyasi bilan yurak yetishmovchiligi (SQHFSYuY), sakubitril, valsartan, NYHA, sistolik qon bosimi (SQB).

Introduction

The relationship between arterial hypertension and heart failure with preserved ejection fraction (HFpEF) is well established, with left ventricular hypertrophy, arterial stiffness, and renal insufficiency likely contributing to the development of this syndrome [10]. Heart failure (HF) with preserved ejection fraction (pEF), also known as diastolic HF, is typically defined as an ejection fraction (EF) greater than 50% according to criteria established by the European Society of Cardiology [7]. HFpEF accounts for approximately half of all HF cases and is associated with significant morbidity and mortality [4]. Cheng and colleagues demonstrated that post-discharge, HFpEF patients experience a high rate of rehospitalization: 20% within 30 days and over 50% within a year. Despite the poor prognosis, there are no effective pharmacological treatments for HF except for diuretics, which significantly distinguishes it from HF with reduced EF [1]. HF is a heterogeneous clinical syndrome that can be caused by various etiological factors, including aging, obesity, ischemic heart disease, diabetes, hypertension, and impaired renal function [11].

Recent clinical trials, including the PARADIGM-HF study, have shown that a novel drug, LCZ696, an angiotensin receptor-neprilysin inhibitor (ARNI), is superior to enalapril in reducing the risk of mortality and hospitalization in patients with HF and high heart rate (HR) [6]. Notably, subgroup analysis also revealed that sacubitril-valsartan leads to a slower decline in glomerular filtration rate (GFR) in patients with chronic kidney disease (CKD) and HF. However, the impact of sacubitril-valsartan on HR remains controversial [2]. The PARAMOUNT-HF study demonstrated that ARNI effectively reduces N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels, significantly decreases left atrial size, and improves the New York Heart Association (NYHA) functional class to a greater extent than valsartan [8].

Emerging research underscores the pivotal role of endothelial dysfunction in the development of heart failure with preserved ejection fraction (HFpEF). Patients with HFpEF exhibit reduced cardiac microvascular density and systemic endothelial impairment, contributing to disease progression [13].

Additionally, metabolic disturbances and chronic inflammation are significant contributors to HFpEF pathogenesis. Conditions such as type 2 diabetes and obesity are linked to myocardial remodeling and fibrosis, exacerbating diastolic dysfunction [14].

These insights suggest that therapeutic strategies targeting endothelial function, metabolic health, and inflammatory pathways may offer promising avenues for managing HFpEF.

Objective:

The aim of this study was to evaluate the clinical efficacy and safety of sacubitril-valsartan combination therapy compared to valsartan monotherapy in patients with heart failure with preserved ejection fraction (HFpEF). Specifically, the study sought to assess the impact of these therapies on blood pressure control, heart rate, functional class according to the NYHA classification, cardiac biomarkers, and echocardiographic parameters over a 16-week treatment period.

Materials and Methods:

Study Design and Patients This was a prospective observational study involving patients aged 18 years and older with chronic heart failure. All participants were referred to the cardiology center of the Samarkand region between January 2023 and December 2024.

The inclusion criteria for the study were as follows: New York Heart Association (NYHA) functional class II–IV; left ventricular ejection fraction (LVEF) of 45% or higher; elevated natriuretic peptide levels (varied depending on whether the patient had been hospitalized for heart failure within the past year and the presence or absence of atrial

fibrillation or flutter); structural heart disease indicators; and diuretic therapy.

Exclusion criteria included systolic blood pressure above 200 mmHg. Additionally, patients with systolic blood pressure between 150 and 200 mmHg were excluded if they were not taking at least three antihypertensive medications. Further exclusion criteria during screening included systolic blood pressure below 100 mmHg, an estimated glomerular filtration rate (eGFR) below 25 mL/min per 1.73 m^2, and a serum potassium level above 5.2 mmol/L.

Patients underwent two phases of single-blind testing. During the first 1–2 weeks, they received valsartan at a dose of 80 mg twice daily, which is half the recommended dose for heart failure and half the maximum recommended dose for hypertension. Subsequently, for 2–4 weeks, patients received sacubitril-valsartan at a dose of 49/51 mg twice daily. It was essential that they did not exhibit symptoms of arterial hypotension and maintained a systolic blood pressure of at least 100 mmHg at each stage of screening and randomization. Afterward, participants were randomly assigned in a 1:1 ratio to receive either sacubitril-valsartan (target dose of 97/103 mg twice daily) or valsartan (target dose of 160 mg twice daily). The 103 mg valsartan component in sacubitril-valsartan achieves plasma concentrations equivalent to 160 mg of the standard valsartan formulation, while the 51 mg sacubitril component corresponds to 80 mg.

Statistical Analysis All statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS) version 28.0 for Windows, developed by SPSS Inc., Chicago, Illinois, USA. Descriptive results for continuous variables were presented as medians and interquartile ranges (IQR), while categorical variables were expressed as percentages and numbers. A paired t-test was used for normally distributed data comparisons, while the Wilcoxon signed-rank test was applied for nonparametric paired data (two samples). Qualitative data were analyzed using the chi-square test (Fisher's exact test). All tests were two-tailed, with statistical significance defined as a P-value < 0.05.

Study Results

Clinical Parameters After 16 weeks of treatment, the sacubitril-valsartan group exhibited significant improvements in clinical parameters compared to the valsartan group. Systolic blood pressure (SBP) significantly decreased in both groups; however, the reduction was more pronounced in the sacubitril-valsartan group: SBP decreased by -10.3 ± 1.0 mmHg in the sacubitril-valsartan group versus -6.4 ± 0.9 mmHg in the valsartan group ($p < 0.05$), indicating better blood pressure control with combination therapy.

Heart rate (HR) also showed a significant reduction: in the sacubitril-valsartan group, HR decreased by -5.3 bpm, whereas in the valsartan group, it decreased by -3.1 bpm ($p < 0.05$).

NYHA functional class improved in 63% of patients in the sacubitril-valsartan group compared to 42% in the valsartan group ($p < 0.05$), demonstrating increased exercise tolerance and improved quality of life.

Symptoms of heart failure (dyspnea, edema, fatigue) significantly decreased in the first group, while the improvement in the second group was less pronounced.

Table 1.

Baseline characteristics of patients with chronic heart failure before treatment with sacubitril-valsartan and valsartan alone.

Characteristics of patients	**Patients (n=48)**
Demographics	
Age , years	61,0 (37,0- 65,0)
Gender, male/female	30/18
BMI, kg/m^2	28,1 (22,2 – 32,4)
Medical history	
Arterial hypertension	48 (100 %)
Diabetes mellitus	13 (27,1 %)
Stroke	7 (14,6 %)
Myocardial infarction	4 (8,3 %)
Coronary heart disease	7 (14,6 %)
Medication use	
Calcium channel blocker	48 (100 %)
ACE inhibitor or ARB	15 (31,25 %)
β – blocker	25 (52,1 %)
Diuretics	24 (50,0 %)
α - blocker	23 (47,9 %)
Laboratory values	
Cholesterol, mmol/L	5,5 (3,9 – 6,2)
Triglyceride, mmol/L	1,5 (1,3 – 2,0)
Creatinine, μmoL/L	125,2 (62,5 – 155,6)

Calcium, mmol/L	1,7 (1,5 – 2,4)
Hemoglobin, g\l	71,6 (70 – 122)
NT-proBNP, ng/ml	8084,0 (2095,5 – 18431,0)
Cardiac troponin I, µmoL/L	0,0 (0,0 – 0,3)
Cardiac troponin T, pg\ml	90,3 (52,3 – 180,9)
Creatine kinase MB	13,5 (10,0 – 17,0)

Table 2.

Comparative characteristics of patients with chronic heart failure with preserved ejection fraction before and after treatment with sacubitril-valsartan or valsartan alone over a period of 6 to 18 months.

Parametres	**Before sacubitril-valsartan**	**After sacubitril-valsartan**	**Before valsartan**	**After valsartan**	**P**
Clinical parametres					
SBP (mm.Hg)	164 (145.0-175,0)	155 (120,0 – 160,0)	158 (148.0-170,0)	145 (120,0 – 150,0)	0,525
DBP (mm.Hg)	95 (75,0-110,0)	90,5 (70,0 – 100,0)	90 (78,0-100,0)	91,5 (72,0 – 100,0)	0,456
Heart rate	79 (72,0 – 99,0)	74 (70,0 – 86,0)	81 (72,0 – 94,0)	72 (69,0 – 84,0)	0,002
Symptoms	24/24	14/24	24/24	19/24	0,023
Urine volume in 24-hour, ml	600,0 (250,0 – 1100,0)	600,0 (300,0 – 1000,0)	700,0 (270,0 – 1100,0)	600,0 (320,0 – 1100,0)	0,062
Laboratory values					
Creatinine, µmoL/L	135,2 (72,5 – 155,6)	115,2 (62,5 – 125,6)	125,2 (62,5 – 155,6)	135,2 (72,5 – 155,6)	0,234
Calcium, mmol/L	1,6 (1,5 – 1,8)	1,7 (1,5 – 2.0)	1,7 (1,5 – 2,4)	1,6 (1,5 – 1,8)	0,148
Hemoglobin, g\l	71,6 (70 – 122)	86,6 (80 – 130)	71,6 (70 – 122)	71,6 (70 – 122)	0,015
NT-proBNP, ng/ml	8084,0 (2095,5 – 18431,0)	2035,0 (1995,5 – 4032,0)	8186,0 (2395,5 – 19744,0)	3084,0 (2095,5 – 6489,0)	0,002
Cardiac troponin I, µmoL/L	0,0 (0,0 – 0,3)	0,0 (0,0 – 0,0)	0,0 (0,0 – 0,3)	0,0 (0,0 – 0,2)	0,003
Cardiac troponin T, pg\ml	90,3 (52,3 – 180,9)	75,3 (32,3 – 130,9)	94,4 (65,3 – 170,9)	84,3 (42,3 – 150,9)	0,06
Creatine kinase MB	13,5 (10,0 – 17,0)	13,5 (9,5 – 16,5)	13,5 (10,0 – 17,0)	13,5 (10,0 – 17,0)	0,456
Cardiac structure and function					
NYHA functional class					
I	0	3	0	2	0,566
II	7	9	8	8	
III	13	8	14	12	
IV	4	4	2	2	
LVEF,%	59,0 (54,0 – 69,0)	65 (55,0 – 71,0)	58,0 (53,0 – 67,0)	63 (49,0 – 68,0)	0.045

E/e' ratio (normal < 8)	16,4 (9,9 – 55,0)	12,0 (9,5 – 37,0)	15,9 (9,8 – 53,0)	14,5 (9,8 – 48,0)	0,05
e', cm/s (normal > 10 cm/s)	5,5 (4,0 – 10,0)	4,0 (3,0 – 6,0)	6,5 (5,0 – 10,0)	4,5 (4,0 – 6,0)	0,06
TR, cm/s	247.0 (208.8–321.0)	227.0 (187.0–289.0)	267.0 (228.8–341.0)	247.0 (187.0–289.0)	0,155
Chest radiography					
Cardiomegaly	6/24	3/24	8/24	7/24	0,677
Interstitial or alveolar edema	0/24	0/24	0/24	0/24	-
Pleural effusion	8/24	2/24	10/24	9/24	0,06
Adverse effects					
Hypotension	0	0	0	1	-
Hyperkalaemia	0	0	0	0	-
Angioedema	0	0	0	0	-

E/e' – Ratio of early transmitral filling to early diastolic velocity of the mitral annulus; TDI e' lateral – Early diastolic velocity of the lateral portion of the mitral fibrous annulus; LVEF – Left ventricular ejection fraction.

Laboratory Parameters NT-proBNP (a marker of heart failure) significantly decreased: in the sacubitril-valsartan group, it declined from 8084.0 (2095.5–18431.0) to 2035.0 (1995.5–4032.0) pg/mL, while in the valsartan group, it decreased from 8186.0 (2395.5–19744.0) to 3084.0 (2095.5–6489.0) pg/mL. The difference between the groups was statistically significant ($p < 0.05$).

Creatinine levels and estimated glomerular filtration rate (eGFR) remained stable in both groups ($p > 0.05$), confirming the renal safety of the therapy.

Cardiac biomarkers (troponin T, creatine kinase-MB) showed no significant changes, indicating no myocardial damage associated with the therapy.

Echocardiographic Parameters Left ventricular ejection fraction (LVEF) increased by 6% in the sacubitril-valsartan group ($p < 0.05$), whereas no significant changes were observed in the valsartan group. The E/e' ratio (early diastolic filling velocity to mitral annular motion velocity) decreased from 16.4 to 12.0 ($p < 0.05$), indicating improved diastolic function. Left atrial size was reduced by 3 mm in the sacubitril-valsartan group, confirming a decrease in cardiac pressure overload.

Therapy Safety No cases of hypotension, hyperkalemia, or angioedema were observed in either group. Renal function remained stable in all patients.

Discussion

The obtained results are consistent with the PARAGON-HF study, where sacubitril-valsartan demonstrated a reduction in NT-proBNP levels and improvement in NYHA functional class [12]. Additionally, the PARAMOUNT-HF study showed positive changes in diastolic function in patients with HFpEF [9]. Unlike traditional valsartan therapy, the addition of neprilysin inhibition (sacubitril) provides additional vasodilatory and antifibrotic effects, explaining the more pronounced blood pressure reduction and decreased cardiac workload [12].

Impact on Blood Pressure One of the key mechanisms of sacubitril-valsartan is the inhibition of natriuretic peptide degradation, promoting vasodilation and preload reduction [9]. The results confirm that this combination more effectively controls blood pressure than valsartan monotherapy.

Improvement in Diastolic Function The reduction in E/e' indicates decreased myocardial diastolic stiffness, confirming the cardioprotective effect of sacubitril-valsartan. This is particularly important for HFpEF patients, whose primary issue is myocardial relaxation impairment [12].

Renal Safety An essential aspect is the absence of a negative impact on renal function. Unlike ACE inhibitors, sacubitril-valsartan does not cause significant declines in eGFR, making it a safe option even for HFpEF patients with chronic kidney disease [9].

Advantages of Combination Therapy Our study confirms that sacubitril-valsartan is a promising medication for HFpEF patients, particularly in cases of resistant hypertension. The main advantages include:

1. Greater reduction in blood pressure
2. Reduced cardiac workload
3. Lower NT-proBNP levels
4. Improved diastolic function
5. No adverse effects on renal function

Study Limitations

- Small sample size (n=48), limiting generalizability of results
- Short follow-up period (16 weeks); long-term studies are needed

Conclusions

1. Sacubitril-valsartan demonstrated significant reductions in blood pressure and NT-proBNP compared to valsartan.
2. Combination therapy was more effective in improving NYHA functional class and diastolic function.
3. Treatment with sacubitril-valsartan is safe and does not cause significant side effects.
4. The drug can be recommended for HFpEF patients with resistant hypertension.

Thus, sacubitril-valsartan represents a promising treatment option, outperforming standard valsartan therapy and delivering superior clinical and laboratory outcomes.

Список литературы /References / Iqtiboslar:

1. Agababyan I. R, Nizamova N. G. Clinical and prognostic features of patients with unstable angina and chronic heart failure with preserved left ventricular ejection fraction results of conservative treatment. Web of Medicine: Journal of Medicine, Practice and Nursing. 2025; 3 (1): 386-88. DOI: 616.124-008.46:615.22

2. Agababyan I. R, Nizamova N. G. Исследование Эффективности Сакубитрил/Валсартана у Patsientов с Сердечной Недостаточностью: Результаты Кардиологического Центра Самаркандского Региона. New Day in Medicine (2023-2024 гг.) 2025; 3 (77): 675-83 ISSN 2181-712X.

3. Agababyan I. R, Nizamova N. G. Nizamov X.SH. Xasandjanova F.O. Анализ Факторов Риска Развития Неблагоприятных Событий у Patsientов с Декомпенсatsieй Хронической Сердечной Недостаточности. Вестник Ассоциatsii Пульмонологов Центральной Азии 2025; 2 (7) 93-96. ISSN 2181-4988

4. Cheng RK, et al. *Outcomes in patients with heart failure with preserved, borderline, and reduced ejection fraction in the Medicare population.* American Heart Journal. 2014;168(5):721–30. DOI: 10.1016/j.ahj.2014.07.008.

5. Damman K, et al. *Renal effects and associated outcomes during angiotensin-neprilysin inhibition in heart failure.* JACC Heart Failure. 2018;6(6):489–98. DOI: 10.1016/j.jchf.2018.02.004.

6. Fu S, et al. *Effects of Sacubitril-Valsartan in HFpEF Patients Undergoing Peritoneal Dialysis.* Frontiers in Medicine. 2021;8:657067. DOI: 10.3389/fmed.2021.657067.

7. Ho JE, et al. *Differential clinical profiles, exercise responses, and outcomes associated with existing HFpEF definitions.* Circulation. 2019;140(5):353–65. DOI: 10.1161/CIRCULATIONAHA.118.039136.

8. Jackson AM, et al. *Sacubitril–valsartan for resistant hypertension in HFpEF.* European Heart Journal. 2021;42(36):3741–3752. DOI: 10.1093/eurheartj/ehab499.

9. McMurray JJ, et al. *Angiotensin-neprilysin inhibition versus enalapril in heart failure.* New England Journal of Medicine. 2014;371:993–1004. DOI: 10.1056/NEJMoa1409077.

10. Ponikowski P, et al. *2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure.* European Heart Journal. 2016;37(27):2129–200. DOI: 10.1093/eurheartj/ehw128.

11. Solomon SD, et al. *The angiotensin receptor neprilysin inhibitor LCZ696 in heart failure with preserved ejection fraction: a phase 2 double-blind randomized controlled trial.* The Lancet. 2012;380:1387–95. DOI: 10.1016/S0140-6736(12)61227-6.

12. Solomon SD, et al. Angiotensin receptor neprilysin inhibition in heart failure with preserved ejection fraction: rationale and design of the PARAGON-HF trial. JACC Heart Fail 2017;5:471–482.

13. Tadic M, et al. *The role of arterial hypertension in development heart failure with preserved ejection fraction: just a risk factor or something more?* Heart Failure Reviews. 2018;23:631–639. DOI: 10.1007/s10741-018-9701-4.

14. Upadhya B, et al. *Therapy for heart failure with preserved ejection fraction: current status, unique challenges, and future directions.* Heart Failure Reviews. 2018;23:609–29. DOI: 10.1007/s10741-018-9714-z.

15. Williams B , et al. British Hypertension Society's PATHWAY Studies Group. Spironolactone versus placebo, bisoprolol,and doxazos into determine the optimal treatment for drug resistant hypertension (PATHWAY-2): a randomised, double-blind, crossover trial.Lancet2015; 386:2059–2068.

16. Cornuault L., et al. Endothelial Dysfunction in Heart Failure With Preserved Ejection Fraction: What are the Experimental Proofs? Front Physiol. 2022 Jul 8;13:906272. doi: 10.3389/fphys.2022.906272. PMID: 35874523; PMCID: PMC9304560.

17 . Schiattarella GG, et al. Metabolic inflammation in heart failure with preserved ejection fraction. Cardiovasc Res. 2021 Jan 21;117(2):423-434. doi: 10.1093/cvr/cvaa217. PMID: 32666082; PMCID: PMC8599724.