Literature review

PERINDOPRIL IN PATIENTS WITH HEART FAILURE REDUCED EJECTION FRACTION - HFrEF

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Heart failure (HF) has been known since ancient times. The first cases were described in Egypt, and later Avicenna and other leading historical figures discussed this pathology. William Harvey made a significant contribution to defining the physiological foundations of heart function and blood circulation, and in the 20th century, E.H. Starling formulated the "law of the heart", which became the basis for the hemodynamic understanding of heart function.

HF is a growing global problem, the second most common cardiovascular disease, and the leading cause of hospitalization. Properly selected drug treatment for patients is the cornerstone of the management of this nosology. Studies show that after 6 months of drug discontinuation, most patients relapse, contractile function decreases, and hospitalization is required . This emphasizes the importance of properly selected and continuous therapy.

The sympathetic nervous system and renin-angiotensin-aldosterone system (RAAS) play a leading role in heart failure. Their activation causes hemodynamic disturbances, cardiac remodeling, and chronic dysfunction.

According to the classification, heart failure is distinguished according to the ejection fraction:

- **HFrEF** – reduced (EF < 40%);
- **HFmrEF** – moderately reduced (EF 41–49%);
- **HFpEF** – preserved (EF ≥ 50%).

Heart failure with reduced ejection fraction is characterized by frequent exacerbations and high mortality. The main goals of treatment are: reducing mortality, reducing hospitalizations, and improving quality of life.

According to the therapeutic standard, first-line medications for HfrEF include ACE inhibitors, ARNI, beta-blockers, spironolactone, SGLT2 inhibitors, and diuretics.

Perindopril – an ACE inhibitor characterized by long-lasting action and relatively low side effects (e.g., dry cough). It has proven efficacy in various cardiovascular nosologies in clinical trials: ASCOT, EUROPA, PROGRESS, PREAMI, and ADVANCE.

However, it is important to clarify that, to date, no specific, high-quality study has demonstrated the direct efficacy of perindopril in patients with HFrEF. Analysis of the available data suggests a potential benefit, but targeted studies are necessary to meet evidence-based medicine standards.

Key words: Heart Failure; Reduced Ejection Fraction; HFrEF

HISTORICAL FACTS

The oldest known case of decompensated heart failure is a 3,500-year-old Egyptian nobleman named Nebiri, discovered in a looted tomb in the Valley of the Queens by Egyptologist Ernesto Schiaparelli. Now housed in the Egyptian Museum in Turin, Nebiri lived during the reign of 18th Dynasty pharaoh Thutmose III. Pathologist Andreas Nerlich examined the lung tissue, finding evidence of pulmonary edema presumably due to heart failure, after ruling out other causes such as tuberculosis, granulomas, or mycobacterial infections [1].

The medieval Arab scholar Ibn Sina, known in the West as Avicenna (980–1037), was renowned as a specialist in heart disease. His treatise Kitab al-Adviyt-al-Qalbiye, or "Book of Medicines for the Heart", discusses the treatment of dyspnea, palpitations, and syncope [2]. The turning point came in 1628, when William Harvey clearly described the circulation of blood and laid the foundation for understanding the hemodynamic abnormalities in heart failure. A few years later, descriptions of heart failure caused by tamponade and mitral stenosis became available. In the mid-18th century, Lancisi noted that valvular regurgitation causes ventricular dilatation, but he noted that the ventricular cavity does not dilate in aortic stenosis. He also hypothesized that dilation weakens the heart [3].

The Romans were known to use digitalis as a "cure." Bloodletting and leeches were used for centuries. In 1785, William Withering published his work on the benefits of digitalis [4]. In the 19th and early 20th centuries, Southey's tubes were inserted into swollen limbs to drain fluid in heart failure. The discovery of X-rays by Roentgen and of electrocardiography by Einthoven in the 1890s improved understanding of heart failure. Later, echocardiography, cardiac catheterization, and nuclear medicine advanced diagnostic and investigative capabilities. By the 20th century, distinguishing types of cardiac enlargement became especially important. In 1918, E.H. Starling published his "Law of the Heart." His demonstration that increasing diastolic volume strengthens the heart surprised many, as

it went against the 19th-century view that dilation weakened the heart [5].

The study conducted in India was significant; it contributed to a new understanding and treatment of heart failure, leading to its recognition as a neuroendocrine disease rather than a heart disease. As a result, angiotensin-converting enzyme inhibitors (ACE inhibitors) and beta-blockers were successfully introduced for the treatment of heart failure. ACE inhibitors reduce the risk of death and hospitalization in all patients with heart failure who have a reduced ejection fraction (HFrEF), regardless of the severity of symptoms [6].

Heart failure is the final stage of most heart diseases and is one of the main causes of morbidity and mortality. In clinical practice, heart failure presents with symptoms such as shortness of breath, fatigue, and fluid retention, leading to frequent hospitalizations. As the population ages, the prevalence of heart failure will continue to rise, further straining healthcare systems through increased morbidity, mortality, and healthcare costs [7].

THE ESSENCE OF HEART FAILURE: EPIDEMIOLOGY, PATHOGENESIS, AND DEVELOPMENT MECHANISMS

The epidemiology of heart failure has been a subject of interest since 1997, when it was called a new pandemic. Today, the total number of patients is increasing alongside the world's population. At present, 64.3 million patients have been diagnosed with heart failure. In developed countries, 1-2% of adults suffer from heart failure, and this figure increases to 11.8% over the age of 65 [8].

By 2021, 6 million people in the United States had heart failure. It is the most common cause of hospitalization in people over 40 [9]. 40% of patients will be hospitalized 4 or more times in their lifetimes. The risk of rehospitalization is high, and mortality within 30 days is significant. In Europe [10], 1-2% of the population has heart failure, and the rate rises to 10-15% for those over 70.

Frequent and prolonged hospitalization imposes a significant financial burden on the country and the patient. It also causes stress for the patient and their family or caregiver.

With proper, timely treatment, it is possible to prevent and delay the development of heart failure and reduce hospitalization frequency.

Heart failure is not a specific pathological diagnosis but rather a clinical syndrome characterized by certain symptoms (shortness of breath, easy fatigue, etc.) and signs (swelling of the lower extremities, wet wheezing in the lungs, etc.). The pathogenesis of the disease involves structural and/or functional damage to the heart, leading to increased intracardiac pressures and/or decreased cardiac output. Heart failure most often occurs as the final stage of various cardiovascular nosologies. It is necessary to determine the cause of heart failure because the underlying disease dictates the appropriate course of treatment [11].

Heart failure is a progressive disease. Any acute damage to the heart's structure - whether caused by genetic mutation, infiltration of cardiac tissue, ischemia, valvular disease, myocarditis, or acute myocardial injury - can trigger compensatory mechanisms that, after exhaustion, lead to maladaptation. In the early stages of heart failure, several compensatory mechanisms attempt to maintain cardiac output and meet systemic demands. Chronic activation of the sympathetic nervous system leads to decreased beta-receptor sensitivity and reduced adrenaline stores. This leads to alterations in myocyte regeneration, myocardial hypertrophy, and myocardial hypercontractility [12].

Increased sympathetic stimulation also activates the renin-angiotensin-aldosterone system (RAAS). This causes systemic vasoconstriction and sodium retention. RAAS releases angiotensin II, which increases myocardial cell hypertrophy and interstitial fibrosis. These changes promote myocardial remodeling [13].

The reduction in cardiac output stimulates the neuroendocrine system to release epinephrine, norepinephrine, endothelin-1 (ET-1), and vasopressin. These mediators cause vasoconstriction, thereby increasing afterload. Cyclic adenosine monophosphate (cAMP) increases, which leads to an increase in cytosolic calcium in myocytes. This increases myocardial contractility and further impairs myocardial relaxation. The increase in afterload and myocardial contractility, together with the impairment of myocardial relaxation, increases myocardial oxygen demand. This paradoxical need for increased cardiac output to meet myocardial demand ultimately leads to myocardial cell death and apoptosis. As apoptosis continues, the reduction in cardiac output with increased demand leads to a prolonged cycle of increased neurohumoral stimulation and maladaptive hemodynamic and myocardial responses [14].

THE RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM (RAAS) AND ITS ROLE IN THE PATHOGENESIS OF HFrEF

The renin-angiotensin-aldosterone system (RAAS) is an important mediator of cardiac, vascular, and renal physiology by regulating vascular tone and salt and water homeostasis. In addition to its basic physiological functions, the RAAS plays an important role in the pathophysiology of hypertension, heart failure, other cardiovascular diseases, and renal disease [15]. Blockade of renin-angiotensin-aldosterone hyperactivation with various medications improves the outcome of various cardiovascular and renal diseases [16].

Juxtaglomerular cells in the afferent arterioles of the kidney contain prorenin. Activation of juxtaglomerular cells results in the breakdown of prorenin to renin. Activation of prorenin occurs in the kidney by enzymes such as proconvertase 1 and cathepsin B. Mature renin is stored in the granules of juxtaglomerular cells and is released into the circulation by four main stimuli [17]:

1. Changes in renal perfusion, which are sensed by pressure transduction mechanisms in the afferent arterioles (reflecting stretch from mechanoreceptors in the arteriolar wall);

2. Sodium and chloride delivery to the distal convoluted tubule, which is perceived by the macula densa;
3. Increased beta-sympathetic flow, which acts through beta-1 adrenergic receptors, especially in the upright position;
4. Negative feedback from humoral factors such as angiotensin I, potassium (renin release increases with hypokalemia and decreases with hyperkalemia), and ANP (atrial natriuretic peptide) [18].

Accordingly, conditions that reduce renal perfusion and trigger tubular sodium retention stimulate renin release. The half-life of renin activity in the circulation is 10–15 minutes [19].

Angiotensinogen

This molecule is primarily synthesized and constitutively secreted by the liver. Renin cleaves the N-terminus of angiotensinogen, forming angiotensin I.

Angiotensin I

This peptide lacks known biological activity.

Angiotensin-converting enzyme (ACE)

This enzyme is expressed on the plasma membranes of vascular endothelial cells, mainly in the pulmonary circulation. It cleaves the C-terminal 2 amino acids of angiotensin I to form the peptide angiotensin II.

Angiotensin II

ACE produces angiotensin II by cleaving 2 amino acids from the C-terminus of angiotensin I. Angiotensin II is the principal mediator of the physiological effects of the renin-angiotensin-aldosterone system, including blood pressure, fluid volume regulation, and aldosterone secretion. The half-life of angiotensin II in the circulation is very short, less than 60 seconds. It is cleaved by peptidases to angiotensin III and IV. Angiotensin III has 100% of the aldosterone-stimulating effect of angiotensin II but only 40% of the pressor effects.

The physiological effects of angiotensin II on the regulation of extracellular volume and blood pressure are mediated through 5 pathways:

1. Vasoconstriction by contraction of vascular smooth muscle in arterioles [20];
2. Aldosterone secretion from the adrenal cortex into the zona glomerulosa, via transcription of CYP11B2 (aldosterone synthase);
3. Increase sodium reabsorption by increasing the activity of the Na-H antiporter in the proximal convoluted tubule;
4. Increase sympathetic outflow from the central nervous system;
5. Release of vasopressin from the hypothalamus [21].

Angiotensin II is also involved in many pathophysiological mechanisms and is known to induce oxidative stress, vascular smooth muscle contraction, endothelial dysfunction, fibrosis, and hypertrophic, antiapoptotic, and promitogenic effects. Through these effects, angiotensin II plays a fundamental role in the pathogenesis of hypertension, atherosclerotic disease, heart failure, and renal disease [22].

The most important role in the pathogenic mechanism of heart failure with reduced ejection fraction is played by pathological activation of the renin-angiotensin-aldosterone system, which leads to fluid retention, remodeling of the heart muscle, activation of the sympathetic nervous system, etc. Accordingly, it is not surprising that in both European and American heart failure guidelines [23], RAAS system inhibitors, in particular angiotensin-converting enzyme inhibitors (hereinafter ACE) are the foundation of treatment and first-line drugs, followed by β-blockers, mineralocorticoid antagonists, and SGLT2 inhibitors.

In 1987, the CONSENSUS-I trial first demonstrated a clear survival benefit of angiotensin-converting enzyme inhibitors in severe heart failure [13].

CLASSIFICATION AND TREATMENT PRINCIPLES OF HEART FAILURE

Heart failure is classified by various parameters; the most important is the division based on contractile function. Based on ejection fraction, heart failure is classified as reduced (<40%), moderate (41-49%), or preserved (>50%). The percentage distribution is as follows: 60% HFrEF, 24% HFmrEF, and 16% HFpEF. In Western and developed countries, the most common causes of heart failure are coronary artery disease and arterial hypertension. They are followed by valvular pathologies, arrhythmias, cardiomyopathies, and other conditions. In addition to the typical division, the American Heart Association and Cardiology Association suggest a division into stages:

Stage A: At risk of heart failure. There are no current or past symptoms, structural heart disease, or elevated cardiac biomarkers, but there are risk factors. Risk factors include hypertension, diabetes, metabolic syndrome, cardiotoxic medications, or having a genetic variant of cardiomyopathy.

Stage B: Pre-heart failure. Patients do not have signs or symptoms of heart failure but have risk factors and structural heart disease, evidence of increased filling pressures (invasively or noninvasively assessed), or persistently elevated cardiac markers in the absence of other causes of elevated markers, such as chronic kidney disease or myocarditis.

Stage C: Symptomatic heart failure stage. Patients with a current or past history of heart failure symptoms.

Stage D: Advanced heart failure. Patients with refractory symptoms that interfere with daily life or have repeated hospitalizations despite targeted guideline-based medical therapy [24].

Heart failure is classified into different severity categories based on clinical manifestations and natriuretic peptide levels. For example, one person with a 35% contractility may not be able to function at home, while another may be able to perform daily activities without symptoms. Clinical history, examination, and laboratory analysis de-

termine the clinical status and physiological level of left ventricular failure, allowing comparison with baseline parameters after treatment and the level of improvement.

The diagnosis of heart failure requires the presence of specific symptoms, signs, and evidence of cardiac dysfunction.

Heart failure with reduced ejection fraction is diagnosed by a combination of symptoms and signs, along with echocardiographic evidence of reduced ejection fraction. The natriuretic peptide NT-proBNP is an important tool for diagnosing the disease and assessing its severity, prognosis, and treatment effectiveness.

Medical treatment of heart failure is the cornerstone of the management of this disease. It must be included before and after the use of any instrumental method. The goals of treatment can be divided into three large groups:

1. Reducing mortality
2. Reduction in recurrent hospitalizations due to worsening heart failure
3. mprovement of clinical status, functional capacity, and quality of life.

There are various methods for assessing the effectiveness of drug treatment in HFrEF , including the increase in ejection fraction and the reduction in the size of the heart chambers, as well as the determination and normalization of intracardiac pressures, which are markers of effective treatment and correlate with both the decrease in NT-pro-BNP and the improvement in functional status. Determination of the NT-pro-BNP index is recommended for the diagnosis of HFrEF, which is responsible for determining the severity of the disease, and, on the background of treatment, for assessing the level of functional and prognostic improvement, as well as the need for treatment intensification [11].

The primary markers of treatment effectiveness for the patient are symptom reduction and improvement in quality of life, as measured by KCCQ questionnaire scores and NYHA functional class.

It is important to note that only in the case of heart failure with reduced ejection fraction does evidence-based medicine suggest therapeutic treatment that improves prognosis , morbidity, and mortality. The guideline calls for treating patients with moderately reduced contractility as if they had a reduced fraction [25]. Accordingly, the evidence for treating reduced ejection fraction extends to the second large group, which accounts for 2/3 of heart failure cases.

Modulation of the RAAS and sympathetic nervous systems with angiotensin-converting enzyme inhibitors (ACE-I) or angiotensin receptor neprilysin inhibitor (ARNI), beta-blockers, and mineralocorticoid receptor antagonists (MRAs) improves survival, reduces the risk of hospitalization for heart failure, and reduces symptoms in patients with heart failure with HFrEF. These drugs are the mainstay of pharmacotherapy for patients with HfrEF. The ACE-I/ARNI, beta-blocker, and MRA triad is recommended as the main therapy for these patients, and should be titrated to the doses used in clinical trials (or to the maximum tolerated dose if this is not possible).

The sodium-glucose co-transporter 2 (SGLT2) inhibitors dapagliflozin and empagliflozin, added to ACE-I/ARNI/beta-blocker/MRA therapy, reduce the risk of cardiovascular death and worsening of heart failure in patients with HFrEF.

Dapagliflozin or empagliflozin is recommended for all patients with HFrEF who are already receiving an ACE-I/ARNI, a beta-blocker, and an MRA, regardless of diabetes status [11]. (Figure 1).

ACE inhibitors are recommended as first-line medications for patients with heart failure with reduced ejection fraction to reduce the risk of heart failure hospitalization and death.

In 1995, the European Society of Cardiology published guidelines for the diagnosis of heart failure. ACE inhibitors have been consistently proven in numerous studies to reduce mortality. They are the drugs of choice for the entire spectrum of cardiovascular diseases - heart failure, myocardial infarction, stroke, arterial hypertension, diabetes mellitus, stable angina, etc.

The list of angiotensin-converting enzyme inhibitors included in the European Society of Cardiology's heart failure guidelines has not changed for many years; it is as follows: captopril, enalapril, lisinopril, ramipril, trandolapril.

Perindopril

A prominent representative of ACE inhibitors is perindopril. Perindopril was developed in 1980 and received its first patent in 1981, with 4 additional patents since 1988. It has been used in clinical practice for 35 years. The most common side effect of ACE inhibitors - dry cough induced by bradykinin accumulation - is least common with perindopril. The incidence of cough associated with ACE inhibitors is as follows: perindopril - 5.4%, ramipril - 6.89%, and lisinopril - 8.82%. The overall incidence of dry cough when using three different ACE inhibitors was 7.0% [26].

Perindopril - a non-sulfhydryl group angiotensin-converting enzyme inhibitor, like enalapril, is a prodrug and is rapidly metabolized in the liver to the active substance perindoprilat. It is characterized by potent, long-lasting ACE inhibition, a 24-hour duration of action [27], and its effectiveness has been confirmed by numerous large-scale studies in various cardiovascular diseases, such as:

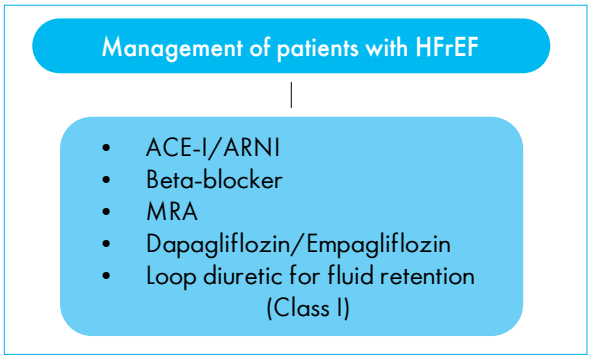

Figure 1. Algorithm for medical management of patients with HFrEF

1. **ASCOT11 -Anglo-Scandinavian Cardiac Outcomes Trial** [28]. 19,257 patients were included in the study, with a mean follow-up of 5.4 years; the aim of the study was to determine the effectiveness of treatment with a new combination of a calcium antagonist and an ACE inhibitor compared with an older combination of a beta-blocker and a diuretic; the study demonstrated the proven superiority of perindopril-amlodipine over the combination of atenolol-hydrochlorothiazide in arterial hypertension.
2. **EUROPA12 -The EURopean trial on reduction of Cardiac Events with Perindopril in Stable Coronary Artery disease** [29]. 12,218 patients were included in the study; mean follow-up period 3.7 years; Inclusion criteria and study cohort: myocardial infarction, PCI/CABG >6 months, angiographically determined stenosis ≥70%, patients with chest pain and a positive stress test; The aim of the study was to compare the efficacy of perindopril with placebo in groups of patients with coronary artery disease; The study found a reduced mortality compared to placebo in the perindopril group in stable coronary angina (figure 2).
3. **PROGRESS13 Perindopril protection Against Recurrent Stroke Study** [30]. 6105 patients from 172 centers worldwide participated in the study. The study design compared placebo and active treatment (perindopril + indapamide) in patients with stroke or transient ischemic attack, with the primary endpoint being the incidence of recurrent stroke in these groups; over a 4-year follow-up period, recurrent neurological events occurred in 307 (10%) patients in the active treatment group and 420 (14%) patients in the placebo group (95% confidence interval 17-38), P < 0.0001]. Active treatment also reduced the risk of MACE [26% (16-34)]., non-fatal myocardial infarction [38% (14-55)]., severe cognitive impairment [19% (4-32)]., stroke-associated dementia [34% (3-55)]., and disability [18% (8-28)]. The perindopril-indapamide combination reduced blood pressure by 12/5 mmHg and stroke risk by 43%.
4. **PREAMI28 Perindopril and Re-modelling in Elderly with Acute Myocardial Infarction study** [30].1252 patients participated, observation period 1 year, patients over 65 years of age with acute myocardial infarction participated in the study; primary endpoints were obtained - reduction in mortality, morbidity, hospitalization in the post-myocardial infarction period in the perindopril group, compared with placebo.
5. **ADVANCE6 Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation Trial** [31]. 11,140 patients participated; primary endpoints were reduced mortality, morbidity, type II diabetes mellitus, and arterial hypertension.

According to Georgian statistics for 2021-2022 (pharmacy.moh.gov.ge), perindopril is the undisputed leader among imported ACE inhibitors, with 15% more perindopril and its combinations imported in 2021 than enalapril and its combinations (which ranked second in terms of quantity imported), and 31% more in 2022. This indicates the high frequency of use of perindopril in the country compared to other ACE inhibitors. In addition, perindopril is included on the state list of free medicines, further increasing its availability and prescribing [32] (Picture 3).

Based on all of the above, the role of perindopril in the management of cardiovascular diseases is clear, and it is worth noting its particular popularity in Georgia, driven by its effectiveness, price, and availability.

However, one issue remains open in the evidence for perindopril. To date, no study has specifically investigated its efficacy in patients with heart failure and reduced ejection fraction, and this is a very large cohort. As noted above, heart failure with reduced ejection fraction is a syndromic disease and is a complication of other cardiovascular diseases. The efficacy of perindopril in this cardiovascular disease suggests that, in appropriate study settings, the drug should reduce the primary endpoints—mortality, morbidity, and hospitalization—in patients with HFrEF.

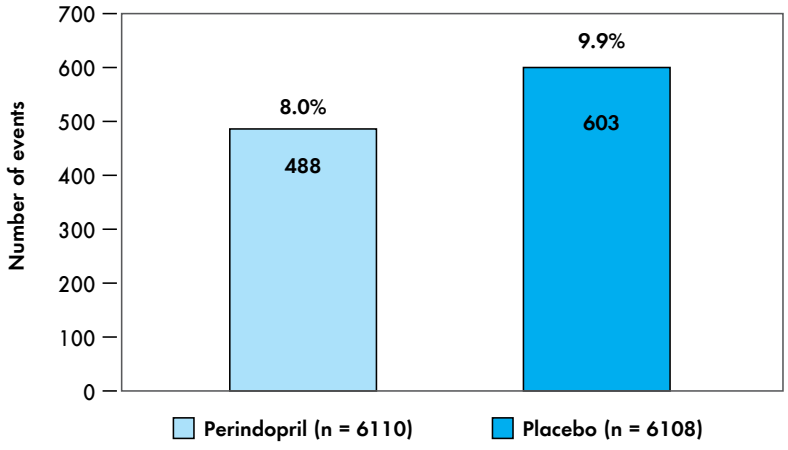

Figure 2. EUROPA: primary endpoint (cardiovascular death, MI, or cardiac arrest). RRR: 20% [95% CI, 9-29].

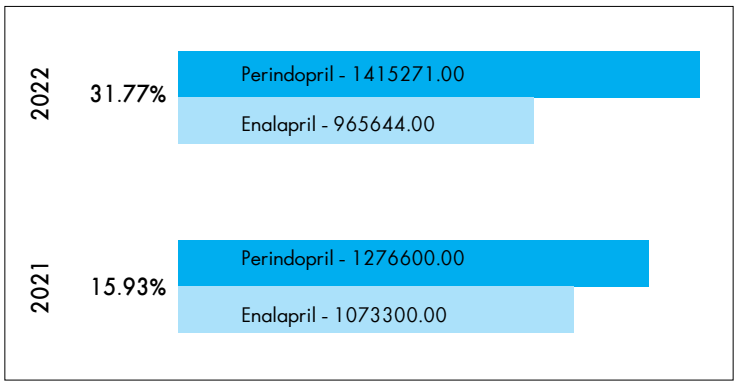

Figure 3. Imported medicines 2020-2022 years

DISCUSSION

Chronic heart failure has not lost its relevance for years; moreover, it is increasingly becoming a subject of research, it is a growing nosology, the second most common among cardiovascular diseases, and the first in terms of hospitalization. Properly selected drug treatment for patients is the cornerstone of managing this nosology. Studies show that in the event of discontinuation of drugs for 6 months, most patients developed a relapse, decreased contractile function, and required inpatient treatment [33]. That is why the 2021 European and 2022 American guidelines for heart failure urge us to continue the medications that led to improvement, even in cases of heart failure that have improved with treatment [14, 24].

Heart failure requires increased awareness among the patient, their family members, and those around them, and the doctor is obliged to develop an appropriate medication regimen for each patient after making a timely, accurate diagnosis to achieve the best possible results.

Chronic heart failure is often associated with other non-cardiological diseases [34] - chronic kidney failure, chronic lung diseases, anemia, etc. - therefore, collaboration between cardiologists and doctors from other fields is very important in the management of heart failure.

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პერინდოპრილი გულის უკმარისობის მქონე პაციენტებში შემცირებული განდევნის ფრაქციით - HFrEF

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რეზიუმე

გულის უკმარისობა (გუ) მზარდი გლობალური პრობლემაა, გულ-სისხლძარღვთა დაავადებებს შორის სიხშირით მეორე ადგილზეა და ჰოსპიტალიზაციის მთავარ მიზეზს წარმოადგენს. პაციენტებისთვის სწორად შერჩეული მედიკამენტური მკურნალობა ამ ნოზოლოგიის მართვის ქვაკუთხედია — კვლევები აჩვენებს, რომ მედიკამენტების მიღების შეწყვეტიდან 6 თვის შემდეგ პაციენტთა უმრავლესობაში ვლინდება რეციდივი, მცირდება კუმშვითი ფუნქცია, და საჭირო ხდება ჰოსპიტალიზაცია. ეს, კიდევ ერთხელ, ხაზს უსვამს მართებულად შერჩეული და უწყვეტი თერაპიის მნიშვნელობას.

სიმპათიკური ნერვული და რენინ-ანგიოტენზინ-ალდოსტერონის სისტემები წამყვან როლს ასრულებენ გუ-ს პათოგენეზში, მათი აქტივაცია ხელს უწყობს ჰემოდინამიკურ დარღვევებს, გულის რემოდელირებას და ქრონიკულ დისფუნქციას. კლასიფიკაციის მიხედვით, გულის უკმარისობა განდევნის ფრაქციის მიხედვით იყოფა:

HFrEF - შემცირებული (EF < 40%); **HFmrEF** - ზომიერად შემცირებული (EF 41–49%); **HFpEF** - შენარჩუნებული (EF ≥ 50%). შემცირებული განდევნის ფრაქციის დროს გულის უკმარისობა ხასიათდება ხშირი გამწვავებებით და მაღალი სიკვდილობით. მკურნალობის მთავარი მიზნებია: სიკვდილობის შემცირება, ჰოსპიტალიზაციების შემცირება და ცხოვრების ხარისხის გაუმჯობესება.

თერაპიული სტანდარტის თანახმად, HFrEF-ის პირველი რიგის მედიკამენტებს მიეკუთვნება აგფ ინჰიბიტორები, ARNI, ბეტა-ბლოკერებთან, სპირონოლაქტონთან, SGLT2 ინჰიბიტორებთან და დიურეტიკებთან ერთად.

პერინდოპრილი — აგფ ინჰიბიტორი, რომელიც ხასიათდება ხანგრძლივი მოქმედებით და შედარებით დაბალი გვერდითი მოვლენებით (მაგ., მშრალი ხველა). მის ეფექტურობა დამტკიცებულია კლინიკური კვლევებში: ASCOT, EUROPA, PROGRESS, PREAMI, ADVANCE.

აღსანიშნავია, რომ დღეის მდგომარეობით არ არსებობს სპეციფიკური, მაღალი ხარისხის კვლევა, რომელიც შეაფასებდა პერინდოპრილის პირდაპირ ეფექტურობას მხოლოდ HFrEF-ის მქონე პაციენტებში. არსებული მონაცემების ანალიზი მიუთითებს მის პოტენციურ სარგებელზე ამ ჯგუფშიც, თუმცა, მტკიცებულებებზე დაფუძნებული მედიცინის მოთხოვნების გათვალისწინებით, საჭიროა მიზნობრივი კვლევები.

საკვანძო სიტყვები: გულის უკმარისობა; შემცირებული განდევნის ფრაქცია; HFrEF