

1.2 Features of modern management patients with heart failure

The heart is a hollow fibromuscular organ of the cardiovascular system, thanks to which blood circulates throughout the body, which provides all the metabolic needs of our body. In order for there to be adequate metabolism, a full cardiac output is required, which is calculated by multiplying the stroke volume by the number of contractions per minute [7].

There are many factors that affect the dysfunction of cardiomyocytes, which causes systolic dysfunction, cardiac overload, diastolic dysfunction, which actually affect the deterioration of cardiac output and subsequently lead to heart failure. Such factors include: excess fat accumulation, aging, heredity, diabetes, hypertension, myocardial infarction, ischemic heart disease, kidney disease and others [8].

Heart failure (HF) is a set of symptoms, i.e. a syndrome that occurs due to insufficient functioning of the ventricles of the heart, which do not provide normal filling and ejection of blood [9]. At the moment when cardiac output is disturbed, compensatory mechanisms begin to work. Normally, compensatory mechanisms work to eliminate temporary disturbances in the functioning of the cardiovascular system, such mechanisms include: the Frank- Starling mechanism , neurohumoral activation, sympathetic nervous system, renin -angiotensin - aldosterone system, natriuretic peptides. In the presence of reasons that complicate the work of the heart muscle, the above-described mechanisms are unable to maintain adequate perfusion, which leads to disruption of their functioning, and this in turn will lead to the development of HF [10].

Acute heart failure is a clinical syndrome that has a sudden and rapid onset in the form of impaired pumping function of the heart and occurs due to a number of causes, including: acute myocardial infarction, hypertensive crisis, cardiac tamponade, pneumothorax, life-threatening rhythm disturbances, etc. In contrast, chronic heart failure (CHF) develops as a result of long-term impaired cardiac output and is usually

diagnosed in a patient with an existing chronic disease of the cardiovascular system[11].

According to 2019 data from the UK's National Institute for Health and Care Excellence (NICE), the main reason for hospital admissions in people over 65 years of age is HF, and only about 21% of such patients are able to return home within a month [12].

In 2019, the Heart Failure Association of the European Society of Cardiology developed the "Heart Failure Association Atlas", which surveyed the number of Europeans with CHF. Almost all European countries participated in the study (42 out of 44 countries that were invited). The average prevalence of this pathology was 17.20 cases per 1000 people [13].

As for Ukraine, the Center for Demography and Human Ecology of the Academy of Sciences has considered several scenarios of population aging in the country. According to the "slow aging" scenario, by 2050, people of retirement age will account for up to 33% of the population, which in absolute terms is more than 8 million, among whom the share of people with CHF will be about 63% [14].

At the same time, it is worth considering the polymorbidity of patients, in particular the appearance or progression of heart failure in patients with diabetes. In particular, according to WHO, the number of patients with diabetes increased from 108 million in 1980 to 422 million in 2014. In addition, due to the fact that the global increase in the prevalence of diabetes has not decreased, but has increased at least twice, this will lead to a significant deterioration of the epidemiological situation in terms of cardiovascular complications, in particular, the number of patients with HF will increase [15].

The exact relationship between type 2 diabetes and HF is not yet fully understood, but there are assumptions about the mechanisms involved, which include: macro-, microvasculopathy, perfusion disorders independent of vasculopathy. myocardial dysfunction [16]. In patients with diabetes, macrovascularization increases the release of reactive oxygen species, which activates protein kinase C and leads to low levels of NO and endothelial dysfunction, and this further contributes

to the development of a thrombotic state, leading to atherothrombosis. With microvascularization, pathological changes occur in the capillaries, leading to hypoperfusion. If we consider vasculopathy-independent myocardial dysfunction, then in this case, the following processes are involved: hyperglycemia, which causes an increase in the amount of glycation end products, which subsequently leads to their binding to extracellular matrix proteins, increased fibrosis and impaired diastole; impaired mitochondrial uncoupling, due to an excessive amount of reactive oxygen species, with subsequent energy deficiency, will lead to impaired calcium uptake, since this is an energy-dependent process, and this in turn leads to abnormalities in cardiac contraction and relaxation [17].

The relevance of the issue of HF lies not only in the paradigm of prevalence and impact on life expectancy, but also in the significant importance of the quality of life of patients with this pathology. Thus, in 2023, Hryhorets D. K. and her team assessed the quality of life and activity status of patients with CHF in the Bukovina region of Ukraine. During the study, 70 patients aged 30–85 years with a diagnosis of HF stage II-A (40%-28 patients), stage II-B (32.8%-23 patients) and stage I (27.1%-19 patients), who were undergoing inpatient treatment in the “Chernivtsi Regional Clinical Cardiological Center”, were interviewed. According to the results of the study, it was determined that 56 patients out of 70, while in satisfactory material and living conditions, had a high indicator of low quality of life (70.8 points) and a low test indicator of physical and emotional activity (less than 20%). [18].

In 2021, Khanyukov O. O. and Smolyanova O. V. developed a predictive model for predicting hospitalizations within 6 months in elderly patients with CHF to reduce the number of hospital admissions and improve quality of life. The study criteria were the age of patients (from 60 to 74 years), the presence of CHF stage II, arterial hypertension stage II and chronic kidney disease stage II- IIIa. According to the results of multiple logistic analysis, adherence to treatment, a decrease in glomerular filtration rate below 59.9 ml/min/1.73m², the presence of wheezing in the lungs, as well as NYHA FC are statistically significant predictors of hospitalization for CHF in elderly patients [19].

Classification of HF plays an important role in the subsequent management of the patient. There are different types and several ways of dividing, but the most common classification is the division into left- or right-ventricular HF [20].

According to the degree of left ventricular contractile function impairment and left ventricular ejection fraction (EF) indicators, the following types are distinguished: with reduced left ventricular EF (less than 40%), with moderately reduced EF (41-49%), and with preserved ejection fraction (more than 50%) [21].

In addition, there is a classification of the New York Heart Association, where patients can be divided into 4 types depending on the reaction and appearance of symptoms to physical exertion:

Grade 1: no complaints during rest and moderate physical activity.

Grade 2: There are no complaints at rest, but shortness of breath and fatigue are detected during physical activity, which prevents exercise.

Grade 3: Moderate discomfort and fatigue occur at rest, shortness of breath, fatigue, and tachycardia occur during minor physical activity.

Grade 4: obvious signs of HF at rest, no physical activity possible [22].

The new classification is important for predicting the development of HF.

In stage A, also called increased risk of developing HF, there are no objective / subjective signs of HF, including laboratory ones, but risk factors are present.

Stage B, called preCH, has objective signs of heart damage or function changes or a positive natriuretic peptide result, but no symptoms of HF are present at the time of examination or in the anamnesis.

Present HF is designated as stage C, which is characterized by both objective and subjective symptoms of HF.

Severe HF (stage D) is characterized by severe symptoms at rest and frequent hospitalizations despite modern treatment approaches. Patients with this stage should consider major interventions such as heart transplantation, mechanical circulatory support, or palliative care [23].

There is no pathognomonic symptomatology for heart failure. The most typical symptoms that we include during diagnosis are: shortness of breath, orthopnea,

paroxysmal nocturnal dyspnea, fatigue, edema of the lower legs and other parts of the body, and difficulty with physical activity. Typical signs that occur in HF include increased pressure in the jugular vein, cardiomegaly, lateral displacement of the apical impulse, Cheyne-Stokes breathing, a third heart sound, a total gallop between the third and fourth heart sounds. It is possible to suspect the presence of HF if the patient has risk factors, symptoms and signs of impaired heart function, and changes on the electrocardiogram [24].

If a patient is suspected of having HF, according to the ESC 2021 recommendations, the following tests should be performed [25]:

1. Electrocardiogram (if not previously performed) to identify the cause of the development of functional heart disorders. However, it is worth noting that it is impossible to diagnose HF with only an ECG.

2. Measurement of natriuretic peptides is one of the “gold standards” for diagnosing a patient with suspected HF. Concentration of B-type natriuretic peptide (BNP) <35 pg /mL, N-terminal pro-B-type natriuretic peptide (NT -proBNP) <125 pg /mL, or mid-regional proatrial natriuretic peptide (MP - proANP) <40 pmol / l makes the diagnosis of HF unlikely. It is worth noting that the number of natriuretic peptides can increase with age, as well as due to non- cardiac diseases and conditions: renal dysfunction, burns, subarachnoid hemorrhage, thyrotoxicosis, anemia, COPD, paraneoplastic syndrome, ischemic stroke. Therefore, this indicator should be evaluated in conjunction with the clinical picture as a whole.

3. Echocardiography is recommended as a key investigation for assessing cardiac function. In addition to determining left ventricular ejection fraction, it also provides information on chamber size, left ventricular myocardial and interventricular septal thickness, regional wall motion abnormalities (which may indicate etiological causes such as ischemic heart disease, Takotsubo syndrome, or myocarditis), right ventricular function, pulmonary hypertension, valvular function, and markers of diastolic function.

4. Basic investigations such as serum urea and electrolytes, creatinine, complete blood count, cholesterol metabolism, liver and thyroid function tests to

differentiate HF from other conditions, provide prognostic information, and guide potential therapy.

5. A chest x-ray is recommended to investigate other possible causes of dyspnea (e.g., pulmonary disease). It may also provide confirmatory evidence of HF (e.g., pulmonary congestion or cardiomegaly).

In case of confirmation of the diagnosis of HF, it is considered mandatory to indicate the degree of ventricular damage and the value of EF. If heart failure was not confirmed by tests and examinations, other causes of symptoms should be considered [26].

Before starting treatment, it is important to determine the cause of the occurrence in order to further select adequate therapeutic options. After all, the approach to treatment is not only limited to pharmacological treatment, but also possible surgical interventions on the heart valves, interventional approach in case of rhythm disturbances, as well as endovascular techniques in case of proven atherosclerotic lesions of the coronary arteries [27].

According to the updated recommendations of the European Society of Cardiology [25], new concepts have emerged for the treatment of CHF, including:

1. A new simplified algorithm for treating patients with reduced EF.
2. Adding a treatment algorithm with reduced EF according to phenotypes.
3. Updated treatment methods for most non-cardiovascular vascular diseases, including diabetes mellitus, hyperkalemia , iron deficiency , and oncological conditions.
4. Updates in cardiomyopathies sections , including the role of genetic testing and new treatments.

In addition, new drugs of choice have appeared for the treatment of CHF with reduced EF, which include: dapagliflozin and empagliflozin Dapagliflozin is a sodium-glucose cotransporter 2 inhibitor that was previously only used to treat type 2 diabetes. Dapagliflozin has now been shown to be effective in the treatment of HF and chronic kidney disease [28] .

Scott D. Solomon, MD, and others from the DELIVER trial conducted a study in which patients with HF and EF >40% received dapagliflozin or a matching placebo in addition to their usual care. Over 2.3 years, the primary outcome was observed in 512 of 3131 patients (16.4%) in the dapagliflozin group and in 610 of 3132 patients (19.5%) in the placebo group. Dapagliflozin reduced the combined risk of progression to HF or cardiovascular death in these patients, even if EF was preserved. Adverse events leading to discontinuation of dapagliflozin or placebo were reported in 182 patients (5.8%) in the dapagliflozin group and 181 patients (5.8%) in the placebo group. However, it is worth noting that fatal outcomes were also described, which were registered in 1361 patients (43.5%) in the dapagliflozin group and in 1423 patients (45.5%) in the placebo group, without a significant difference between them [29].

Kieran F. Docherty and his team conducted a study on the efficacy of dapagliflozin in patients with HF. In the study, the team showed that dapagliflozin not only improved outcomes when added to background therapy, but also had a consistent benefit regardless of whether the background therapy included ivabradine or sacubitril / valsartan . In summary, the researchers found a consistent advantage of dapagliflozin over placebo, regardless of background drug therapy. These results suggest that the effects of dapagliflozin are gradual and complementary to conventional therapy, especially in patients with reduced left ventricular ejection fraction [30].

An American study reviewed and demonstrated that the effectiveness of dapagliflozin was worth the cost, with the cost of the drug ranging from \$953/year to \$6,188/year depending on the dosage of the drug and the bulk purchase, the amount of the drug for patients [31].

In Ukraine, this drug is not included in the list of state purchases and the patient will not be able to get it for free. On average, the price of 1-month treatment with dapagliflozin costs an average of 1,148 UAH for 30 tablets, that is, a patient needs to spend approximately 14,000 UAH per year to reduce the risk of hospitalization and complications in existing CHF. This information should be taken into account by primary care physicians at the stage of communication with the patient [8 12].

Empagliflozin also belongs to the group of sodium-glucose cotransporter 2 inhibitors, which increases the excretion of glucose in the urine, and was used specifically for the treatment of diabetes mellitus, and now also in patients with cardiovascular diseases and kidney diseases [33].

Milton Packer and his team evaluated the effect of empagliflozin in their study . In the study, the combined risk of cardiovascular death or hospitalization for HF was 25% lower among patients receiving empagliflozin than among those receiving placebo, a difference that was mainly due to a 31% lower risk of hospitalization for HF. These benefits were observed in patients receiving any of the currently recommended HF medications, including sacubitril-valsartan , and were observed regardless of the presence or absence of diabetes [34].

Matthew Griffin and his team investigated the effects of empagliflozin on heart failure and its mechanism of action. They found that empagliflozin causes significant natriuresis , especially when combined with loop diuretics. diuretics , which results in a reduction in cardiac preload from circulating blood volume. This favorable diuretic profile may offer a significant advantage in managing volume status in patients with HF and may be a mechanism contributing to the better long-term outcomes observed with these drugs [35].

The EMPULSE trial also reported positive results for empagliflozin in reducing hospitalizations for CHF exacerbations. However, the study also reported negative results, including mortality, complications in 20% of subjects, and the need for dose adjustments for the heart failure drug [36].

If a patient is diagnosed with HF with moderately reduced EF, well-known drugs such as ACE inhibitors, angiotensin receptor blockers , beta -blockers , mineralocorticoid receptor antagonists , sacubitril / valsartan can be used for pharmacological treatment [27].

For example, Rui's research Zhang et al . showed that sacubitril / valsartan can improve cardiac function and exercise capacity, reduce cardiac remodeling , and reduce the risk of cardiovascular mortality and hospitalization in patients with HF. Meta-analyses and observational studies have shown that sacubitril / valsartan also has

benefits in lowering HF biomarkers , improving quality of life and antiarrhythmic effects , improving renal dysfunction , and regulating metabolism in patients with HF [37] .

Thus, HF is a complex symptom complex that arises from a number of cardiac causes and in the context of the patient's polymorbidity . Establishing the diagnosis of HF is of key importance, as each of the classification points requires an individual monitoring and treatment strategy, including determining the risk of developing HF/existing symptoms of the disease, functional and structural state of the heart muscle, tolerance to physical exertion and the possibility of daily activity.

When treating a patient with HF, it is worth using not only “classical” therapeutic approaches (in particular, ACE inhibitors, diuretics , beta-blockers), but also modern drugs that, in addition to cardioprotective properties, also have a positive effect on the kidneys and metabolic metabolism, taking into account the patient's frequent comorbid pathology.