MANAGEMENT OF PATIENTS WITH CHRONIC HEART FAILURE

MODERN PRACTICE OF INTERNAL MEDICINE WITH EMERGENCY CONDITIONS

Guidelines for students and interns

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
Харківський національний медичний університет

MANAGEMENT OF PATIENTS WITH CHRONIC HEART FAILURE

MODERN PRACTICE OF INTERNAL MEDICINE WITH EMERGENCY CONDITIONS

Guidelines for students and interns

ВЕДЕННЯ ПАЦІЄНТІВ З ХРОНІЧНОЮ СЕРЦЕВОЮ НЕДОСТАТНІСТЮ

СУЧАСНА ПРАКТИКА ВНУТРІШНЬОЇ МЕДИЦИНИ З НЕВІДКЛАДНИМИ СТАНАМИ

Методичні вказівки для студентів та лікарів-інтернів

Затверджено
Вченою радою ХНМУ.
Протокол № 3 від 25.02.2021.

ХАРКІВ
ХНМУ
2021

Management of patients with chronic heart failure. Modern practice of internal medicine with emergency conditions : guidelines for students and interns / compil. O. Ya. Babak, M. O. Vizir, N. M. Zheleznyakova et al. – Kharkiv : KhNMU, 2021. – 20 p.

Compilers O. Ya. Babak
M. O. Vizir
N. M. Zheleznyakova
A. S. Shalimova
K. A. Lapshyna
G. Yu. Panchenko
V. I. Molodan
L. I. Ovcharenko
M. I. Klimenko
O. Ye. Zaychenko
I. I. Karpenko
K. O. Prosolenko
E. Yu. Frolova-Romaniuk
A. O. Rozhdestvenskaya

Ведення пацієнтів з хронічною серцевою недостатністю. Сучасна практика внутрішньої медицини з невідкладними станами : метод. вказ. для студентів та лікарів-інтернів / упоряд. О. Я. Бабак, М. О. Візір, Н. М. Железнякова та ін. – Харків : ХНМУ, 2021. – 20 с.

Упорядники О. Я. Бабак,
М. О. Візір,
Н. М. Железнякова,
А. С. Шалімова
К. А. Лапшина
Г. Ю. Панченко
В. І. Молодан
Л. І. Овчаренко
М. І. Кліменко
О. Є. Зайченко
І. І. Карпенко
К. О. Просоленко
Е. Ю. Фролова
А. О. Рождественська

Management of patients with chronic heart failure

Number of hours: Classroom work – 5:00, independent work – 3:00

Material and methodological support of the theme: table, multimedia presentation, laboratory data and instrumental methods of investigation.

Justification threads. Chronic heart failure (CHF) remains a pressing medical and social problem worldwide, including in Ukraine. According to national registries of European countries and epidemiological studies, the prevalence of CHF in the adult population is 25 % and increases in proportion to age, in people over 70 years it is from 10 to 20 %. The severity of the prognosis of clinically manifested CHF is indicated by the fact that approximately half of such patients die within four years, and among patients with severe CHF mortality within the next year is 50 %. Up to 40 % of patients admitted to the hospital for symptoms of heart failure (HF) die or are re-hospitalized within the next year.

The purpose of the activity:

- General: The students should be able to describe main links of pathogenesis, clinical features, diagnostic and treatment of chronic heart failure.
- Specific: Provide a basic overview of the pathophysiology, diagnosis, and classification of chronic heart failure; evaluate guideline-based management strategies for the treatment of chronic heart failure; develop an individualized pharmacotherapy and monitoring plan for the management of chronic heart failure, when given specific patient information.

Specific objectives: The student should know:	**Initial level of knowledge - abilities: The student should be able to:**
• Describe the chronic heart failure. • Describe the main mechanism of ethiopathogenesis. • Describe the main clinical features of chronic heart failure. • List and describe the group of drugs that are used in the treatment of chronic heart failure and give specific examples of each. • Make a treatment plan of patient with chronic heart failure	• analyze the complaints and anamnesis of patients. • recognize the clinical signs. • make a plan of examination of patients. • diagnose the main causative diseases and conditions. • interpret the data of instrumental and laboratory research techniques; • differential diagnosis of condition. • assess the possible complications as well as to evaluate the prognosis of these patients. • provide medical aid to the patient. • prescribe drugs, which are used in such patients • assess the patient's prognosis

List of practical skills that students must master:

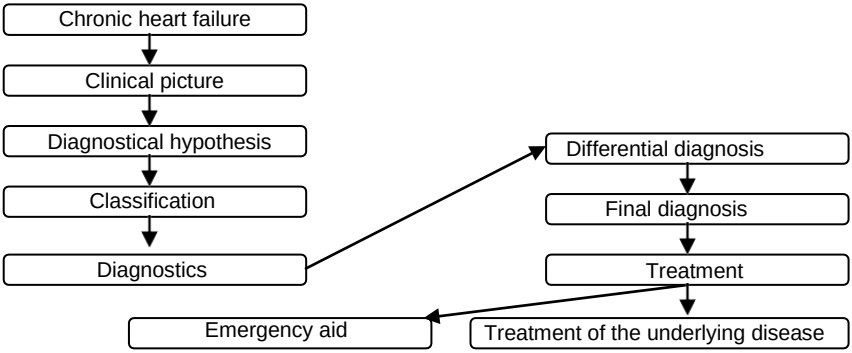
1. Evaluation of patients with chronic heart failure.
2. Interpretation of laboratory data that reflect pathology causing chronic heart failure.
3. Interpretation of tool data that reflect pathology leads to chronic heart failure.

4. Working out the scheme of diagnostic plan.
5. Prescribing basic treatment.

Materials for the self-study:

- Improving the interpretation of ultrasound examination data.
- Improving the interpretation of the results of laboratory methods.

Graphological structure of the topic.



Indicative map of the work of students:

a) diagnosis criteria for checking them at the bedside;

b) choice of the most knowledgeable tests, laboratory and instrumental studies (possibly performed by students), confirming the diagnosis;

c) the appointment of treatment; prescribing (knowledge of the mechanism of action of drugs)

d) the choice of method of physical therapy treatment;

d) determining the prognosis and the patient's ability to work;

g) definition of disability;

c) disease prevention.

Chronic heart failure is a clinical syndrome characterized by typical symptoms (e.g., shortness of breath, edema of the lower extremities, and fatigue) that may be accompanied by physical symptoms (e.g., increased jugular venous pressure, pulmonary crepitation, and peripheral edema) caused by structural and/or functional cardiac disorders, which leads to decreased cardiac output and/or increased intracardiac pressure at rest or during exercise.

Basic terms:

- clinical stage of CHF;
- variant of CHF;
- functional class (FC).

ICD codes – 10: I50; I50.0; I50.9.

The main terminology used to describe CHF is based on the value of LV EF. In patients with CHF, this figure varies widely: from normal values (they are usually stated if the LV EF is ≥ 50 %) to reduced (usually < 40 %) (*Table 1*). The division of patients with HF depending on the size of their LV EF is important given the differences in etiological factors, demographic characteristics, comorbidities and treatment effectiveness. In the current (2016) recommendations of the European Society of Cardiology distinguish the so-called gray area with a moderate decrease in LV EF (40–49 %). However, because evidence-based treatment standards have been developed only for patients with LV EF < 40 %, this "intermediate" category of patients has been grouped with patients with normal (≥ 50 %) EF for practical reasons. LV and is terminologically designated as CH with the saved LV EF (HFpEF).

Diagnosis of HFpEF (LV EF > 40 %) is more difficult than recognizing HFpEF. In general, patients with HFpEF do not have dilated LV, but they often experience thickening of the LV wall and/or an increase in the size of the left atrium as signs of increased filling pressure. Most patients have additional signs of LV filling or capacity filling disorders, which are also interpreted as diastolic dysfunction, which is usually considered the most likely cause of HF in such patients (hence the term "diastolic HF"). However, most people with CHF (formerly called "systolic heart failure") also have LV diastolic dysfunction. On the other hand, at HFpEF signs of insignificant disturbances of systolic function of LV are shown. Therefore, it is more expedient to state preservation or decrease not of systolic function, namely LV EF.

Table 1

Definition of heart failure with preserved (HFpEF), mid-range (HFmrEF) and reduced ejection fraction (HFrEF)

Type of HF		HFrEF	HFmrEF	HFpEF
CRITERIA	1	Symptoms ± Signs[a]	Symptoms ± Signs[a]	Symptoms ± Signs[a]
	2	LVEF <40%	LVEF 40–49%	LVEF ≥50%
	3	–	1. Elevated levels of natriuretic peptides[b]; 2. At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE), b. diastolic dysfunction (for details see Section 4.3.2).	1. Elevated levels of natriuretic peptides[b]; 2. At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE), b. diastolic dysfunction (for details see Section 4.3.2).

BNP = B-type natriuretic peptide; HF = heart failure; HFmrEF = heart failure with mid-range ejection fraction; HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction; LAE = left atrial enlargement; LVEF = left ventricular ejection fraction; LVH = left ventricular hypertrophy; NT-proBNP = N-terminal pro-B type natriuretic peptide.

[a]Signs may not be present in the early stages of HF (especially in HFpEF) and in patients treated with diuretics.

[b]BNP>35 pg/ml and/or NT-proBNP>125 pg/mL

The functional classification of HF according to the criteria of the New York Heart Association – NYHA (*Table 2*) is used to describe the severity of symptoms and intolerance. At the same time, the severity of symptoms correlates poorly with many indicators of LV function.

Table 2

NYHA functional classification based on the severity of subjective symptoms and limitation of physical activity

Functional Capacity	Objective Assessment
Class I. Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain.	**A.** No objective evidence of cardiovascular disease.
Class II. Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.	**B.** Objective evidence of minimal cardiovascular disease.
Class III. Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or anginal pain.	**C.** Objective evidence of moderately severe cardiovascular disease.
Class IV. Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.	**D.** Objective evidence of severe cardiovascular disease.

Clinical stages – I; II A; II B; III – meet the criteria of I, II A, II B and III stages of chronic circulatory failure according to the classification of MD Strazheska and VH Vasilenko (1935):

And – the initial insufficiency of blood circulation; manifested only during exercise (shortness of breath, tachycardia, fatigue); at rest hemodynamics and organ functions are not disturbed;

II – severe long-term circulatory failure; hemodynamic disorders (stagnation in the small and large circulatory system, etc.), disorders of organ function and metabolism are expressed at rest;

period A – the beginning of the stage, hemodynamic disorders are moderate; there is dysfunction of the heart or only one of its departments;

period B – deep hemodynamic disorders, the whole cardiovascular system suffers;

III – final, dystrophic circulatory failure; severe hemodynamic disorders, persistent changes in metabolism and organ functions, irreversible changes in the structure of tissues and organs.

Symptoms and clinical signs

The symptoms are often nonspecific and, therefore, do not help to distinguish between CHF and other conditions (*table 3*). Symptoms and signs of heart failure due to fluid retention can quickly disappear with the use of diuretics. Symptoms such as increased jugular venous pressure and apical pulse displacement may be more specific, but they are more difficult to detect and

difficult to reproduce. Symptoms and signs can be particularly difficult to detect and interpret in obese people, the elderly, and patients with chronic lung disease. In younger patients with HF, the etiology, clinical picture, and prognosis are often different from in older patients.

Table 3

Symptoms and signs typical of heart failure

Symptoms	Signs
Typical	**More specific**
Breathlessness Orthopnoea Paroxysmal nocturnal dyspnoea Reduced exercise tolerance Fatigue, tiredness, increased time to recover after exercise Ankle swelling	Elevated jugular venous pressure Hepatojugular reflux Third heart sound (gallop rhythm) Laterally displaced apical impulse
Less typical	**Less specific**
Nocturnal cough Wheezing Bloated feeling Loss of appetite Confusion (especially in the elderly) Depression Palpitations Dizziness Syncope Bendopnea[53]	Weight gain (>2 kg/week) Weight loss (in advanced HF) Tissue wasting (cachexia) Cardiac murmur Peripheral oedema (ankle, sacral, scrotal) Pulmonary crepitations Reduced air entry and dullness to percussion at lung bases (pleural effusion) Tachycardia Irregular pulse Tachypnoea Cheyne Stokes respiration Hepatomegaly Ascites Cold extremities Oliguria Narrow pulse pressure

You should always get a detailed history. HF is not characteristic of a person without a relevant medical history (eg, a potential cause of heart damage), whereas certain features, especially previous myocardial infarction, significantly increase the likelihood of HF in a patient with relevant symptoms and signs.

At each visit, it is necessary to assess the symptoms and signs of heart failure, especially data on congestion. Symptoms and signs are important for monitoring the patient's response to treatment and the stability of his condition. Persistence of symptoms, despite treatment, usually indicates the need for additional therapy, and worsening of symptoms is a serious development (exposing the patient to the risk of urgent hospitalization and death) and deserves emergency medical care (*Fig. 1*).

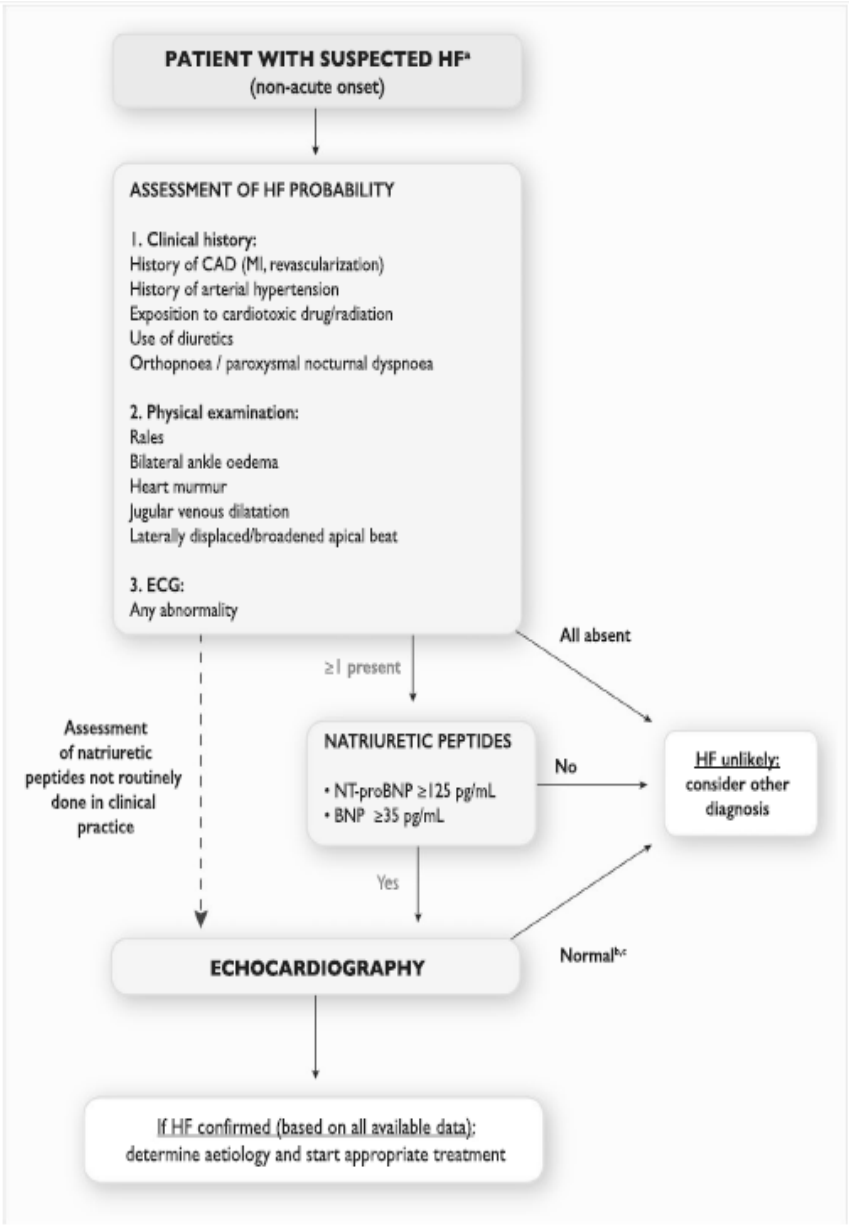


Figure 1. D iagnostic algorithm for a diagnosis of heart failure of non-acute onset

DIAGNOSIS

Basic initial studies: natriuretic peptides, electrocardiogram and echocardiography

Plasma natriuretic peptide (NUP) concentrations can be used as an initial diagnostic test, especially in non-acute conditions when echocardiography is not immediately available. Elevated NUPs help establish the initial working diagnosis by identifying those who need further heart examination; Echocardiography is not required for patients with values below the limit to exclude cardiac dysfunction. Patients with normal plasma concentrations of NSAIDs are unlikely to have HF.

Electrocardiography (ECG) is a non-specific method of diagnosing CHF, but if a patient with suspected CHF has an ECG schedule of 12 leads, the previous diagnosis of CHF is unlikely. The presence of signs of pathology on the ECG (scar cardiosclerosis, hypertrophy of the heart, blockade, sinus tachycardia, tachyarrhythmias) is not a diagnostic criterion for CHF, as such changes can also be observed in patients without significant impairment of pumping function of the heart. However, the detection of such changes in patients diagnosed with CHF may be useful in determining the etiology and aggravating factors of the clinical course of this syndrome, as well as treatment tactics (eg, assessment of indications for cardioresynchronizing therapy (CRT), heart rate or heart rate). (Heart rate), etc.). ECG recording plays an important role in monitoring patients with CHF, as it is a means of monitoring the effectiveness and safety of drug treatment with cardiac glycosides, beta-blockers, ivabradine, diuretics, amiodarone (assessment of heart rate / heart rate, changes in rhythm and conductivity, electrolyte disturbances, electrolyte disturbances). QT).

Echocardiography (EchoCG) is a term used to refer to all methods of cardiac imaging, including two-dimensional/three-dimensional echocardiography, pulsed and continuous Doppler, color Doppler, tissue Doppler, contrast echocardiography, and rapid echocardiography and rapid echocardiography.

Transthoracic echocardiography is the method of choice for assessing systolic and diastolic myocardial function of both left and right ventricles, and also provides information on the structural and anatomical state of the heart (valvular apparatus, size and geometry of heart chambers, myocardial mass, intracardiac shunts, aneurysm shunts , pericardial condition) and functional characteristics (systolic and diastolic ventricular function, regional LV contractility, valve function, pulmonary artery pressure). Echocardiography plays a leading role in the objectification of heart failure.

The most important parameter of intracardiac hemodynamics is LV EF – an integral indicator of systolic function of the heart, which shows what proportion of the end-diastolic volume of the LV is released into the aorta during its systole. Measurement of LV EF in CHF allows:

– to establish the presence of LV diabetes;

– assess the severity of the latter as an important indicator of the prognosis of survival of patients and one of the criteria for determining the

indications for the use of certain pharmacological, hardware and surgical methods of treatment (except for most acquired and congenital heart defects);

– to distinguish patients with CHF with LV diabetes and with preserved LV EF;

– to objectify the effectiveness of treatment measures.

The data obtained through clinical examination and the above tests allow to establish the initial diagnosis and develop a treatment plan for most patients. Other tests are usually needed when the diagnosis remains uncertain (for example, in the case of poor echocardiography or if there is a suspicion of an unusual cause of HF).

Chest X-rays are used to a limited extent to diagnose patients with suspected HF. This method is more useful for determining an alternative explanation for the patient's symptoms and signs, ie lung cancer and interstitial lung disease, although computed tomography (CT) of the chest is currently the standard of care. To diagnose asthma or chronic obstructive pulmonary disease, pulmonary function testing by spirometry is required. However, a chest x-ray may show pulmonary venous stasis or edema in a patient with HF, and it is more useful in acute conditions than in non-acute ones. It is important to note that significant LV dysfunction may be present without cardiomegaly on chest radiography.

Stress echocardiography (exercise or pharmacological) can be used to assess induced ischemia and/or myocardial viability, as well as in some clinical scenarios of patients with valve disease (eg, dynamic mitral regurgitation, low-flow, low-graded aortic stenosis). There are also suggestions that stress echocardiography may reveal exercise-related diastolic dysfunction in patients with exercise-induced shortness of breath, preserved LV EF, and inconclusive resting diastolic readings.

Transesophageal echocardiography (TEE) is not required for routine diagnostic assessment of HF; however, this method may be valuable in some clinical scenarios for patients with valvular disease, suspected aortic dissection, suspected endocarditis, or congenital heart disease, and to rule out intracavitary thrombi in patients with atrial fibrillation who require cardioversion. When the severity of mitral or aortic valve pathology according to echocardiography does not correspond to the patient's symptoms, TEE should be performed.

Magnetic resonance imaging of the heart (MRI) is a method recognized as the gold standard for measuring the volume, mass and PV of both the left and right ventricles. This is the best alternative method of heart imaging for patients with non-diagnostic echocardiographic examinations (especially for right heart imaging) and is the method of choice in patients with complex congenital heart defects. MRI is the best imaging technique for assessing myocardial fibrosis and may be useful in determining the etiology of CHF. For example, MRI allows to differentiate the ischemic and non-ischemic origin of HF and myocardial fibrosis/scarring can be visualized. In addition, MRI can characterize myocardial tissue in myocarditis, amyloidosis, sarcoidosis, Chagas disease, Fabry disease, cardiomyopathy and hemochromatosis.

Coronary angiography is recommended for patients with HF who suffer from angina insensitivity to drug therapy, provided that the patient can undergo coronary revascularization if necessary. Coronary angiography is also recommended for patients with a history of symptomatic ventricular arrhythmia or cardiac arrest. Coronary angiography should be considered in patients with HF and moderate to high probability of coronary heart disease before the test and the presence of ischemia in non-invasive stress tests to determine the ischemic etiology and severity of coronary heart disease.

The main use of *computed tomography* of the heart in patients with HF – as a non-invasive tool for visualization of coronary anatomy in patients with HF with a low intermediate probability of previous coronary heart disease test or those who have ambiguous non-invasive stress tests to exclude coronary heart disease, in the absence of relative contraindications. However, the test is necessary only when its results can affect the therapeutic decision.

Endomyocardial biopsy is indicated in case of heart failure of unknown etiology and if the disease is suspected, requires specific treatment – myocarditis (giant cell or eosinophilic), infiltrative diseases, or diseases of accumulation (amyloidosis, sarcoidosis, hemochromatic), hemochromatosis heart transplant rejection.

Standard (mandatory) laboratory tests for CHF include general blood tests (hemoglobin, erythrocytes, leukocytes, platelets, hematocrit, ESR); general analysis of urine; biochemical tests: K+, Na+, creatinine, plasma cholesterol, bilirubin, "liver" enzymes, glucose, uric acid. Among the *additional laboratory tests* most often there is a need to determine thyroid-stimulating hormone, uric acid in blood plasma, cardiospecific enzymes (especially troponin), the international normalized ratio.

TREATMENT

The goals of treating patients with CHF are to improve their clinical status, functionality and quality of life, prevent hospitalization and reduce mortality. A comprehensive approach to treatment solves the following tasks: treatment of the underlying disease, long-term treatment of CHF, prevention and treatment of exacerbations of CHF.

Treatment recommended for all patients with symptomatic heart failure with reduced ejection fraction:

Angiotensin-converting enzyme (ACE) inhibitors reduce mortality and morbidity in patients with CHF and are recommended, if there are no contra-indications or intolerances, in all patients with symptoms. ACE inhibitors should be titrated to the maximum tolerated dose (*table 4*) to achieve adequate inhibition of the renin-angiotensin-aldosterone system. There is evidence that in clinical practice, most patients receive suboptimal doses of ACE inhibitors. ACE inhibitors are also recommended in patients with asymptomatic left ventricular systolic dysfunction to reduce the risk of HF, hospitalization, and HF death.

Table 4

Evidence-based doses of disease-modifying drugs in key randomized trials in heart failure with reduced ejection fraction (or after myocardial infarction)

	Starting dose (mg)	Target dose (mg)
ACE-I		
Captopril[a]	6.25 *t.i.d.*	50 *t.i.d.*
Enalapril	2.5 *b.i.d.*	10–20 *b.i.d.*
Lisinopril[b]	2.5–5.0 *o.d.*	20–35 *o.d.*
Ramipril	2.5 o.d.	10 *o.d.*
Trandolapril[a]	0.5 *o.d.*	4 *o.d.*
Beta-blockers		
Bisoprolol	1.25 *o.d.*	10 *o.d.*
Carvedilol	3.125 *b.i.d.*	25 *b.i.d.*[d]
Metoprolol succinate (CR/XL)	12.5–25 *o.d.*	200 o.d.
Nebivolol[c]	1.25 *o.d.*	10 *o.d.*
ARBs		
Candesartan	4–8 *o.d.*	32 *o.d.*
Valsartan	40 *b.i.d.*	160 *b.i.d.*
Losartan[b,c]	50 *o.d.*	150 *o.d.*
MRAs		
Eplerenone	25 *o.d.*	50 *o.d.*
Spironolactone	25 *o.d.*	50 *o.d.*
ARNI		
Sacubitril/valsartan	49/51 *b.i.d.*	97/103 *b.i.d.*
If-channel blocker		
Ivabradine	5 *b.i.d.*	7.5 *b.i.d.*

Beta-blockers reduce mortality and morbidity in patients with symptoms of CHF, despite ACE inhibitor treatment and, in most cases, diuretics, but have not been tested in decompensated patients with signs of stagnation. There is a consensus that beta-blockers and ACE inhibitors are complementary and can be started together as soon as a diagnosis of CHF is diagnosed. There is no evidence in favor of initiating treatment with a beta-blocker prior to initiating ACE inhibitors. Beta-blockers should be used in clinically stable low-dose patients and gradually titrated to the maximum tolerated dose. In patients hospitalized with acute HF, beta-blockers should be carefully initiated in the hospital as soon as the patient stabilizes. Beta-blockers should be considered to monitor heart rate in patients with low blood pressure and atrial fibrillation, especially in patients with high heart rate. Beta-blockers are recommended in patients with a history of myocardial infarction and asymptomatic left ventricular systolic dysfunction to reduce the risk of death.

Mineralocorticoid/aldosterone receptor (AMP) antagonists, spironolactone and eplerenone, block aldosterone-binding receptors and, with varying degrees of affinity, other steroid hormone receptors (eg, corticosteroids, androgens). Spironolactone or eplerenone is recommended for all patients with symptoms (despite ACE inhibitors and beta-blockers) with CHF and LV EF $\leq$ 35 % to reduce MF mortality and hospitalization. Caution should be exercised when using AMP in patients with impaired renal function and in those with serum potassium levels of 0.5 mmol/L. Serum potassium and renal function should be monitored regularly according to clinical status.

Other drugs recommended for certain categories of patients with overt heart failure with reduced ejection fraction:

Diuretics are recommended to reduce the signs and symptoms of congestion in patients with CHF, but their effect on mortality and morbidity has not been studied. However, the Cochrane meta-analysis showed that in patients with chronic HF, loop and thiazide diuretics reduced the risk of death and worsening of HF compared with placebo, and compared with active control, diuretics improved physical activity. Loop diuretics cause more intense and shorter diuresis than thiazides, although they act synergistically, and this combination can be used to treat persistent edema. However, adverse effects are more likely, and these combinations should be used only with caution. The goal of diuretic therapy is to achieve and maintain euvolemia with the lowest achievable dose (*table 5*). The dose of the diuretic should be adjusted according to individual needs over time. In selected asymptomatic euvolemic/hypovolemic patients, the diuretic may be (temporarily) discontinued. Patients can be taught to adjust their diuretic dose on their own based on monitoring of symptoms/signs of congestion and daily weight measurement.

A new therapeutic class of drugs – *neprilysin angiotensin receptor inhibitor* (ARNI). The first in the class is LCZ696, which is a molecule that combines particles of valsartan and sacubitrile (neprilysin inhibitor) in one substance. By inhibiting neprilysin, the breakdown of NUP, bradykinin and other peptides is slowed down. Increases diuresis, natriuresis, myocardial relaxation and suppresses remodeling processes. Selective blockade of AT1 receptors reduces vasoconstriction, sodium and water retention, and myocardial hypertrophy.

The *IF channel inhibitor* Ivabradine slows the heart rate by suppressing the IF channel in the sinus node, so it should only be used in patients with sinus rhythm. Ivabradine reduced the combined endpoint of HF mortality or hospitalization in patients with symptomatic HF or LV EF $\leq$ 35 %, sinus rhythm, and heart rate $\geq$ 70 beats per minute (beats/min) who had been hospitalized for HF in the previous 12 months. taking the recommended evidence-based doses of beta-blockers, ACE inhibitors (or ARBs) and AMP.

Table 5

Doses of diuretics commonly used in patients with heart failure

Diuretics	Initial dose (mg)		Usual daily dose (mg)	
Loop diuretics[a]				
Furosemide	20–40		40–240	
Bumetanide	0.5–1.0		1–5	
Torasemide	5–10		10–20	
Thiazides[b]				
Bendroflumethiazide	2.5		2.5–10	
Hydrochlorothiazide	25		12.5–100	
Metolazone	2.5		2.5–10	
Indapamide[c]	2.5		2.5–5	
Potassium-sparing diuretics[d]				
	+ACE-I/ ARB	-ACE-I/ ARB	+ACE-I/ ARB	-ACE-I/ ARB
Spironolactone/ eplerenone	12.5–25	50	50	100–200
Amiloride	2.5	5	5–10	10–20
Triamterene	25	50	100	200

Angiotensin II receptor blockers (ARBs) are recommended only as an alternative to patients who do not tolerate ACE inhibitors. Candesartan has been shown to reduce cardiovascular mortality. Valsartan has been shown to affect HF hospitalization (but not hospitalization for all reasons) in patients with CHF who received ACE inhibitors as a baseline drug. The combination of ACE inhibitors/ARBs for CHF is assumed to have outweigh the risks only in a small group of patients with CHF in whom other treatments are ineffective. Therefore, ARBs are intended for the treatment of CHF only in patients who cannot tolerate ACE inhibitors due to serious side effects. The combination of ACE inhibitors/ARBs should be limited to symptomatic patients with CHDF who receive beta-blockers who do not tolerate AMP and should be used under strict supervision.

Other treatments with less obvious clinical effect in patients with overt heart failure with reduced ejection fraction:

Digoxin and other digitalis glycosides may be considered in patients with sinus rhythm with symptomatic CHF to reduce the risk of hospitalization (both hospitalization for all causes and CH), although its effect with beta-blockers has never been tested. In patients with symptomatic HF and AF, digoxin may be useful in slowing the high rate of ventricular contractions, but it is only recommended for the treatment of patients with HF and AF with a high rate of ventricular contractions when other therapeutic options are not possible.

Polyunsaturated fatty acids ω-3 (PUFA ω-3) showed a negligible effect of treatment in a large study. PUFA drugs ω-3 differ in composition and dose. Only preparations with eicosapentaenoic and decosahexaenoic acid as ethyl esters of at least 85 % (850 mg/g) showed an effect on the complex endpoint of cardiovascular death and hospitalization.

Not recommended drugs (unproven benefits) for the treatment of patients with symptomatic heart failure with reduced ejection fraction:

Inhibitors of 3-hydroxy-3-methylglutaryl coenzyme A reductase ("statins"), although they reduce mortality and morbidity in patients with atherosclerotic disease, these drugs are not effective in improving the prognosis in patients with CHF. Most statin studies have excluded patients with HF (because there was no certainty that they would benefit). Two large studies examining the effect of statin treatment in patients with chronic HF have shown no evidence of benefit. Therefore, the data do not support statin initiation in most patients with chronic HF. However, in patients already receiving statins due to major coronary heart disease and/or hyperlipidemia, consideration should be given to continuing this therapy.

Oral anticoagulants and antiplatelet therapy. With the exception of patients with AF (both CH-lower FV and CHzberFV), there is no evidence that oral anticoagulant reduces mortality/morbidity compared with placebo or aspirin. Patients with CHF who receive oral anticoagulant therapy due to concomitant AF or risk of venous thromboembolism should continue anticoagulant therapy. Similarly, there are no data on the benefits of antiplatelet drugs (including acetylsalicylic acid) in patients with HF without concomitant coronary heart disease, whereas there is a significant risk of gastrointestinal bleeding, especially in the elderly associated with this treatment.

Renin inhibitors – Aliskiren (a direct renin inhibitor) – have failed to improve the prognosis for patients hospitalized for HF after 6 months or 12 months in a single study, and are not currently recommended as an alternative to ACE inhibitors or ARBs.

Drugs not recommended (considered harmful) to patients with symptomatic heart failure with reduced ejection fraction:

Calcium channel blockers. Non-dihydropyridine calcium channel blockers (BCCs) are not indicated for the treatment of patients with CHF. Diltiazem and verapamil have been shown to be dangerous for patients with CHF. There are many dihydropyridine BCCs; it is known that some of them increase sympathetic tone, and they may have a negative safety profile in CHD. There are only data on the safety of amlodipine and felodipine in patients with CHF and can only be used if there are significant indications for patients with CHF.

Non-surgical hardware methods of treatment of heart failure with reduced ejection fraction:

An *implanted cardioverter-defibrillator* is effective in preventing bradycardia and correcting potentially lethal ventricular arrhythmias.

Cardioresynchronization therapy (CRT) improves heart function in properly selected patients, relieves symptoms, improves well-being and reduces the risk of hospitalization for exacerbation of heart failure and mortality.

Treatment of heart failure with preserved LV EF

The pathophysiological mechanisms of HFpEF can be various. HFpEF phenotypes are formed on the basis of various cardiovascular diseases and conditions (AF, arterial hypertension (AH), coronary heart disease, pulmonary hypertension) and non-cardiovascular pathologies (diabetes mellitus, chronic kidney disease, anemia, COPD, obesity). Compared with patients with CHD, among patients with CHF, hospitalizations and deaths are more often due to non-cardiovascular causes. Therefore, it is necessary to screen for cardiovascular and non-cardiovascular comorbidities and, if detected, to apply treatment strategies that improve symptoms, well-being or prognosis and do not worsen the course of HF. To date, the effectiveness of none of the treatments in reducing mortality in patients with HFpEF has been convincingly proven. However, these patients are mostly elderly, have severe symptoms and often a low quality of life. The main goals of therapy are to relieve symptoms and improve well-being.

The effect of treatment on the symptoms of heart failure with preserved LV EF.

Diuretics reduce congestion and thus alleviate the symptoms of heart failure. The positive effect of diuretics on symptoms has been proven regardless of the value of LV EF. There is a lack of evidence of a positive effect of beta-blockers and AMP on the symptoms in this category of patients. There is conflicting evidence of improved symptoms in patients taking ARBs or ACE inhibitors.

The effect of treatment on hospitalization for heart failure with preserved LV EF.

Evidence has been obtained that nebivolol, digoxin, spironolactone and candesartan are able to reduce the incidence of HF hospitalizations. Relevant evidence for other types of ARBs or ACE inhibitors is not convincing.

The effect of treatment on mortality in heart failure with preserved LV EF.

In none of the studies did ACE inhibitors, ARBs, beta-blockers, and AMP reduce overall mortality in patients with HF. In the combined group of patients (with HFpEF and HFrEF), bivolol did not reduce the incidence of combined endpoint - death or cardiovascular hospitalization.

Other aspects

Patients with AF and HFpEF should receive an anticoagulant to reduce the risk of thromboembolic events. Antiplatelet drugs are practically ineffective for this purpose. Renal dysfunction, which is quite common in this patient population, may be a contraindication or increase the risk of bleeding while taking new oral anticoagulants (NSAIDs). Optimal heart rate in patients with HFpEF and AF has not been established, and its aggressive control can be harmful. Verapamil or diltiazem should not be combined with a beta-blocker. We do not currently have sufficient

data to recommend ablation strategies (pulmonary veins or AV node) for HFpEF. Some evidence suggests the importance of treating hypertension in patients with HFpEF. ACE inhibitors and RA are considered acceptable for this purpose. Patients with hypertension and HFpEF should not be prescribed ARBs if they are receiving ACE inhibitors or beta-blockers. As a first-line hypoglycemic drug, patients with HFpEF should be prescribed metformin. Myocardial ischemia can further cause symptoms, morbidity and mortality, so it should be taken into account when examining patients. However, there are only isolated observations that revascularization improves symptoms or prognosis. Patients with angina should be treated according to the same principles as patients with CHF.

Mechanical support of blood circulation and heart transplantation.

Mechanical support of blood circulation

In patients with acute or chronic heart failure who cannot be stabilized by drug therapy, mechanical circulatory support (IPC) systems can be used to relieve ventricular failure and maintain adequate peripheral perfusion. Patients in cardiogenic shock usually need to be connected to extracorporeal life support systems, but they are used for a short period of time, and a further strategy should be planned at this time. Patients with refractory CHF may be implanted with permanent LV assistive devices (LVD).

Mechanical support of blood circulation at the final stage of CHF

Heart transplantation has always been a limited option for patients with end-stage CHF. The growing number of patients with refractory CHF and society's unwillingness to donate organs lead to a long stay on the waiting list for transplantation.

More than 60 % of transplants are performed in Europe on highly urgent patients, leaving little chance of waiting for patients with less urgent conditions. Three times more patients end up on the waiting list than actually perform transplants; the mortality rate among them in 2013 was 21.7 %. Recent data suggest that patients who are supported by PDLS have better survival rates pending transplantation.

As a result, IPC devices, especially PDLs, are increasingly being considered as an alternative to heart transplantation. Originally developed as a short-term bridge for transplantation, PDLs are now used for months or even years in patients who have to wait a long time (currently only 10 % of patients with IPC devices receive a donor organ as a bridge before transplantation within 1 year) or as lifelong therapy in patients who are not suitable for transplantation. High 2–3-year survival rates of carefully selected patients who are implanted with modern models of permanent blood flow devices, comparable to early survival after heart transplantation.

Heart transplantation

Indications and conditions:

– The final stage of heart failure with severe symptoms and poor prognosis, exhausted alternative treatment options.

– The patient is motivated, sufficiently informed and emotionally stable.

– The patient is able to adhere to the regime of intensive care after surgery.

Contraindications:

– Active infection.

– Severe peripheral artery disease or cerebrovascular disease.

– Pharmacologically uncontrolled pulmonary hypertension (consideration should be given to the implantation of PDLS with subsequent review of the transplant application).

– Cancer (with the participation of oncologists should determine the risk of recurrence of cancer in each patient).

– Uncontrolled renal dysfunction (creatinine clearance < 30 ml/min).

– Systemic disease with multiorgan damage. Other serious comorbidities with poor prognosis. BMI before transplantation > 35 kg/m^2 (it is recommended to lose weight to BMI < 35 kg/m^2).

– Alcohol or drug addiction. Insufficient social support of the patient to ensure proper care in an outpatient setting

Tasks for independent work:

1. What is the definition of chronic heart failure?
2. What are the main causes of chronic heart failure?
3. What are the main pathogenetic links of chronic heart failure?
4. What are the main types of chronic heart failure?
5. What are the clinical features of different chronic heart failure grade?
6. What laboratory tests are used in patients with chronic heart failure?
7. What imaging studies are used in patients with chronic heart failure?
8. What treatment methods are used to improve prognosis in patients with HFrEF?
9. What treatment methods are used to improve prognosis in patients with HFpEF?
10. What are indications and contraindications for heart transplantation in patients with chronic heart failure?

Tests

1. The symptoms of heart failure include all of the above, except:

A. Shortness of breath.
B. Edema.
C. Cardiomegaly.
D. Protodiastolic gallop rhythm.
E. Vinogradov-Durozier noise.

2. For the treatment of heart failure do not use:

A. Cardiac glycosides.
B. ACE inhibitors.
C. Diuretics.
D. Alpha-glucosidase inhibitors.
E. Peripheral vasodilators.

3. During the examination of a patient who has been suffering from arterial hypertension for 15 years, the general condition is satisfactory, blood pressure - 170/80 mm Hg. Art., heart rate – 70 beats/min, BH – 28 beats/min, revealed swelling of the legs, pastosity. What is the cause of heart failure?

A. Changes in the volume of circulating blood.
B. Increased peripheral vascular resistance.
C. Increased blood flow.
D. Disorders of general metabolism.
E. Disorders of neurohumoral regulation.

4. A 70-year-old patient during intensive detoxification therapy was administered intravenously 1.5 l of solutions (rheopolyglucin, NaCl 0.9 %) for 6 h, but the patient's condition worsened, pulmonary edema was diagnosed, after another 3 h – myocardial infarction. What is the cause of pulmonary edema?

A. General tissue hypoxia.
B. Reduction of oncotic blood pressure due to hemodilution.
C. Myocardial damage, reduction of stroke volume.
D. Overload of the right ventricle with volume.
E. Increase in osmotic pressure of blood.

5. A 25-year-old patient was diagnosed with rheumatic myocarditis. What is the main mechanism of heart failure?

A. Myocardial overload with increased resistance to blood flow.
B. Myocardial overload with increased blood volume.
C. Decreased circulating blood volume.
D. Increasing the volume of the vascular bed.
E. Myocardial damage.

6. The patient was diagnosed with aortic stenosis. What is the main mechanism of heart failure?

A. Myocardial overload with increased resistance to blood flow.
B. Increasing the volume of the vascular bed.
C. Myocardial damage.
D. Decreased circulating blood volume.
E. Myocardial overload with increased blood volume.

7. A 30-year-old patient complains of constant pain in the heart, shortness of breath when moving, general weakness. Objectively: pale and cold skin, acrocyanosis. Pulse 96 for 1 min, blood pressure – 105/70 mm Hg. Art. The border of the heart is shifted by 2 cm to the left. The first tone above the apex of the heart is weakened, systolic murmur above the apex. Diagnosed with mitral valve insufficiency. What is the main mechanism of heart failure?

A. Decrease in the volume of circulating blood.
B. Myocardial overload with increased blood volume.
C. Myocardial damage.
D. Increasing the volume of the vascular bed.
E. Myocardial overload with increased resistance to blood flow.

8. A 65-year-old patient complains of general weakness, palpitations and shortness of breath with moderate exercise, occasionally dizziness. In the evening there is swelling of the lower extremities. Heart rate – 80 per minute, blood pressure – 140/70 mm Hg. Art. Heart tones are muffled. On the ECG – signs of ischemia

and myocardial dystrophy. The ultrasound examination revealed a decrease in stroke volume. It was concluded that the woman had heart failure. As a result of which hemodynamic result did the described disorders occur?

A. Reduction of blood pressure.
B. Decreased blood flow velocity.
C. Increased venous pressure.
D. Decrease in minute volume of blood.
E. Increased blood pressure.

9. A 42-year-old man is worried about chest pain, palpitations. Shortness of breath during exercise has recently intensified, and asthma attacks have occurred at night. Intense systolic murmur with the epicenter on the left edge of the sternum is not conducted on the vessels, the second tone is preserved. According to echocardiography: pronounced hypertrophy of the upper third of the interventricular septum, left ventricle of normal size, the fraction of its emission – 65 %. What causes the progression of heart failure in a patient?

A. Diastolic dysfunction of the left ventricle.
B. Systolic dysfunction of the right ventricle.
C. Systolic dysfunction of the left ventricle.
D. Pulmonary arterial hypertension.
E. Left atrial insufficiency.

10. A 73-year-old patient complains of weakness, drowsiness, chills, memory loss, hair loss, constipation, edema. Objectively: normal nutrition. The skin is dry, yellowish. The face, extremities are swollen, at pressing the fossa does not remain. Heart tones are muffled, bradycardia. The size of the heart is expanded. The volume of the thyroid gland is reduced. Hb – 85 g/l, cholesterol – 8.5 mmol/l, TSH – 20.5 μmol/l. Make a preliminary diagnosis.

A. Chronic hepatitis.
B. Cardiosclerosis, heart failure.
C. Hypothyroidism.
D. Severe atherosclerosis of cerebral vessels.
E. Renal failure.

RECOMMENDED LITERATURE

Main references

1.Current Medical Diagnosis and Treatment 2016 /Michael W. Rabow, M. Papadakis, Stephen J. McPhee. – 2015. – 1920 p.

2.Harrisons Manual of Medicine, 20th Edition / Dennis L. Kasper, Anthony S. Fauci, Stephen L. Hauser, Dan L. Longo, J. Larry Jameson, Joseph Loscalzo. – 2020. – 1351 p.

3.2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure.

Additional references

1.Mayo Clinic Internal Medicine Board Review. 12th. / Edited by Christopher M. Wittich. – 2020. – 936 p.

2.Harrisons Principles of Internal Medicine Self-Assessment and Board Review 19th Edition/ Dennis Kasper, Joseph Loscalzo, J. Jameson, Anthony Fauci, Stephen Hauser, Dan Longo. – 2015. – 3000 p.

Навчальне видання

ВЕДЕННЯ ПАЦІЄНТІВ З ХРОНІЧНОЮ СЕРЦЕВОЮ НЕДОСТАТНІСТЮ

СУЧАСНА ПРАКТИКА ВНУТРІШНЬОЇ МЕДИЦИНИ З НЕВІДКЛАДНИМИ СТАНАМИ

Методичні вказівки для студентів та лікарів-інтернів

Упорядники Бабак Олег Якович,
Візір Марина Олександрівна,
Железнякова Наталія Мерабівна,
Шалімова Анна Сергіївна,
Лапшина Катерина Аркадіївна,
Панченко Галина Юріївна,
Молодан Володимир Ілліч,
Овчаренко Людмила Іванівна,
Кліменко Микола Іванович,
Просоленко Костянтин Олександрович,
Фролова Еліна Юріївна,
Рождественська Анастасія Олександрівна.

Відповідальний за випуск О. Я. Бабак

Комп'ютерна верстка О. Ю. Лавриненко

Формат А5. Ум. друк. арк.1,3. Зам. № 21-34087.

Редакційно-видавничий відділ
ХНМУ, пр. Науки, 4, м. Харків, 61022
izdatknmurio@gmail.com

Свідоцтво про внесення суб'єкта видавничої справи до Державного реєстру видавництв, виготівників і розповсюджувачів видавничої продукції серії ДК № 3242 від 18.07.2008 р.