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# ALGORITHM FOR THE TREATMENT OF PATIENTS WITH ACUTE HEART FAILURE

## Abstract

Acute heart failure (AHF) and acute decompensation of chronic heart failure (ADHF) are topic health issues. The main tasks of such patients managing are: to achieve optimal and stable resolution of edema and dyspnea; to improve tissue perfusion; to reduce the severity of clinical symptoms; to increase exercise tolerance; to prevent the progression of heart failure, target organs dysfunction, and complications development; to reduce decompensations and hospitalizations rate; to increase the survival rate, and to improve the quality of life. The diagnostic procedure, clinical patient patterns recognition, pharmacological (including diuretics, vasodilators, inotropes, vasopressors, anticoagulants, etc.) and non-pharmacological (including oxygen therapy, non-invasive and invasive ventilation, etc.) approaches to the management of AHF and ADHF are presented in accordance with the state-of-the-art guidelines.

***Key words:*** *acute heart failure, decompensation of chronic heart failure, acute decompensated heart failure, cardiogenic pulmonary edema, cardiogenic shock, oxygen therapy, invasive lung ventilation, inotropic support, vasopressors, diuretics, ultrafiltration, renal replacement therapy, natriuretic peptides*

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$FiO_2$ — fraction of inspired oxygen; $PaCO_2$ — partial pressure of carbon dioxide in the arterial blood; $PaO_2$ — oxygen partial pressure in the arterial blood; $SpO_2$ — blood oxygen saturation; IABP — intra-aortic balloon pump, PAWP — pulmonary artery wedge pressure; VT — ventricular tachycardia; IV — invasive ventilation; MI — myocardial infarction; CMP — cardiomyopathy; CS – cardiogenic shock; LV — left ventricle; MCS — mechanical circulatory support; NPs – natriuretic peptides; ADHF — acute decompensation of chronic heart failure; ACS — acute coronary syndrome; ICU — intensive care unit, AHF — acute heart failure; SBP — systolic blood pressure; CI — cardiac index; GFR — glomerular filtration rate; HF — heart failure; TSH — thyroid stimulating hormone; PE — pulmonary embolism; AF — atrial fibrillation; CHF — chronic heart failure; RR — respiration rate; ECG — electrocardiography; ECHO-CG — echocardiography

## Introduction

Despite healthcare progress, heart failure (HF) is still the leading cause of hospital admissions, decrease in the life quality, and mortality. Currently, heart failure affects 37.7 million people in the world and its prevalence continues to grow [7, 8]. In Europe, HF accounts for 5% of all hospital admissions [20]. HF is the most common cause of inpatient treatment among people over 65 years old [6, 8]. In most cases, an admission is due to acute HF (AHF) developed for the first time *(de novo)*, in 15–20%, or acute decompensation (worsening of the course) of previously diagnosed chronic heart failure (CHF), in 80–85% of patients [2]. In the latter case, it refers to acute decompensation of CHF, or acute decompensated HF (ADHF) [17].

After discharge from the hospital, about 50% of patients with HF are readmitted within 6 months, and 20–25% of patients are readmitted within

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30 days [19]. The in-hospital mortality for patients with HF is 2–20%, and 30-day mortality after the discharge is 11.3% [12]. The mortality in patients with HF remains high even despite treatment with angiotensin converting enzyme inhibitors / sartans, β-blockers, aldosterone receptor antagonists, and sacubitryl/valsartan, which showed a significant reduction in the relative mortality risk compared with placebo in numerous clinical trials [7, 8]. The main objectives of managing patients with AHF and ADHF are to achieve optimal and stable resolution of signs of congestion, to improve tissue perfusion, to decrease the severity of clinical symptoms, to increase exercise tolerance and quality of life, to prevent the worsening of HF progression, deterioration in the functional state of target organs, and complications, to decrease the frequency of subsequent decompensations and admissions, and to reduce in-hospital and post-hospital mortality [3]. Ways of achieving these objectives will be discussed in this lecture.

## Definitions and Terminology

*Acute heart failure* (AHF) is a condition characterized by the sudden appearance or rapid deterioration of symptoms and signs of heart failure (HF) up to the development of cardiac asthma, pulmonary edema or cardiogenic shock (CS) due to acute disruption of the structure and function of the heart, leading to progressive impairment of other organs and systems [3, 17].

The main symptoms (complaints) of HF are dyspnea on exertion, which worsens when lying in a horizontal position, orthopnea, choking at night, lower limb swelling, decreased exercise tolerance, weakness and fatigue. The main signs of HF (data of physical examination: inspection, palpation, percussion, auscultation) are swelling of the lower extremities, jugular vein distention, hepatomegaly, congestive rales, the third/fourth heart sound, pleural effusion, ascites, tachycardia and tachypnea [9, 17].

*Left ventricular failure* is a condition caused by a deterioration of the structure and function of the left ventricle (LV) of the heart and characterized by blood congestion in pulmonary circulation [3].

*Right ventricular failure* is a condition caused by a deterioration of the structure and function of the right ventricle characterized by congestion in systemic circulation [3].

*Cardiac asthma* is a variant of acute left ventricular HF associated with significant edema of the bronchial wall, manifested by attacks of dyspnea and suffocation [3].

*Cardiogenic pulmonary edema* is a variant of acute left ventricular HF due to leakage of blood plasma into the interstitial lung tissue and into the alveoli, manifested by severe suffocation, cyanosis and grunting respiration [1, 3].

*Cardiogenic shock* is the most severe variant of acute left ventricular HF associated with significant LV myocardial injury, manifested by severe hypotension: a decrease in systolic blood pressure (SBP) < 80 mm Hg (in patients with a history of hypertension, SBP may be above 80–90 mm Hg) lasting for more than 30 minutes, a significant decrease in the cardiac index (CI) usually < 1.8 L/min/m$^2$ and an increased pulmonary artery wedge pressure (PAWP) > 18 mm Hg, which leads to organ hypoperfusion. It is often combined with cardiogenic pulmonary edema [2].

*Acute decompensated heart failure (acute decompensated CHF, ADHF)* is the period of CHF course that is characterized by rapid (within a few hours, days) or gradual (within several weeks) aggravation of symptoms and signs of HF on the background of a long-term disruption of the structure and function of the heart. This is a kind of exacerbation of CHF, or AHF with the underlying CHF [15]. AHF, including ADHF, is a life-threatening condition requiring immediate medical intervention and admission to the hospital [2, 3, 17].

## Aggravating Factors and Causes of AHF and ADHF [9, 17]:

1. Acute coronary syndrome (ACS), myocardial infarction (MI), its mechanical complications, including rupture of the interventricular septum, LV free wall, mitral valve chords

and/or papillary muscles with the development of acute mitral regurgitation, etc.
2. Cardiac rhythm disturbances: tachyarrhythmias (atrial fibrillation — AF, ventricular tachycardia — VT), bradyarrhythmias and conduction disorders.
3. Pulmonary embolism.
4. Hypertensive crisis.
5. Aortic thrombosis and dissection.
6. Dysfunction of heart valves (aortic stenosis, mitral stenosis, mitral insufficiency, etc.) [1].
7. Infectious endocarditis, sepsis, pneumonia and other infections.
8. Myocarditis.
9. Pericarditis and cardiac tamponade.
10. Exacerbation of chronic obstructive pulmonary disease, asthma.
11. Alcohol and drug abuse.
12. Elevated sympathetic activity, stress-induced cardiomyopathy (CMP) — Takotsubo CMP.
13. Drug products: nonsteroidal anti-inflammatory drugs (NSAIDs), glucocorticoids (GCs), cardiotoxic chemotherapy drugs, drugs with negative inotropic effect and glitazones.
14. Metabolic and hormonal disorders (thyroid dysfunction, adrenal gland failure, diabetes mellitus decompensation, diabetic ketoacidosis, pregnancy and peripartum period).
15. Surgery and its complications.
16. Chest trauma.

In addition, non-compliance with directions concerning water-salt intake and discontinuation of the prescribed therapy can result in ADHF [3, 17].

## AHF Classification

There are many classifications of AHF based on various criteria. The clinical classification is the most practical for determining the tactics of managing patients and assessing the prognosis [17].

*AHF Clinical Classification*

1. With or without congestion ("wet"/"dry").
2. With or without peripheral hypoperfusion ("cold"/"warm").

Congestion signs in pulmonary circulation are orthopnea, paroxysmal nocturnal dyspnea, congestive rales in the lungs; congestion signs in systemic circulation are jugular vein distention, peripheral edema, hepatomegaly, hepatojugular reflux and ascites.

Clinical manifestations of hypoperfusion are impairment of consciousness, oliguria (urine output < 0.5 mL/kg/hour or < 20 mL/min) or anuria, cold sweat, mottled skin, pale skin, moist skin, cold and wet extremities, and a weak and thready pulse. Laboratory signs of hypoperfusion are metabolic acidosis (pH < 7.35), elevated serum lactate level (> 2 mmol/L), and elevated serum creatinine level. Hypoperfusion is not synonymous with hypotension (SBP < 90 mm Hg), and hypotension does not imply hypoperfusion, but hypoperfusion is often accompanied by hypotension and a decrease in pulse BP (< 20–25 mm Hg) [1, 3, 17].

4 clinical profiles of patients with AHF are defined depending on the presence/absence of congestion and hypoperfusion (Figure 1): "warm and wet" (good perfusion with congestion), which is the most common; "cold and wet" (hypoperfusion and congestion); "cold and dry" (hypoperfusion without congestion); "warm and dry" (compensated; good perfusion without congestion).

## Diagnosis of AHF

To diagnose AHF, the patient's medical history must be thoroughly taken; aggravating factors as well as causes of development, symptoms and signs of congestion and/or hypoperfusion must be identified; and electrocardiography (ECG), chest X-ray, echocardiography (ECHO-CG) and laboratory tests, including specific biomarkers, must be performed [17].

An ECG in 12 leads is useful for diagnosing the underlying heart disease (ACS, MI) and complications (AF) that have resulted in the development of AHF. If there are no abnormalities on the ECG, the clinical symptomatology most likely is not due to AHF [17].

In AHF, signs of venous congestion, interstitial or alveolar pulmonary edema, hydrothorax and cardiomegaly are discovered on chest X-ray. Up to 20% of patients with AHF have a normal chest X-ray. This study is also useful for identifying non-cardiac diseases, which AHF should be differentiated from (pneumonia, aortic dissection, etc.) [17].

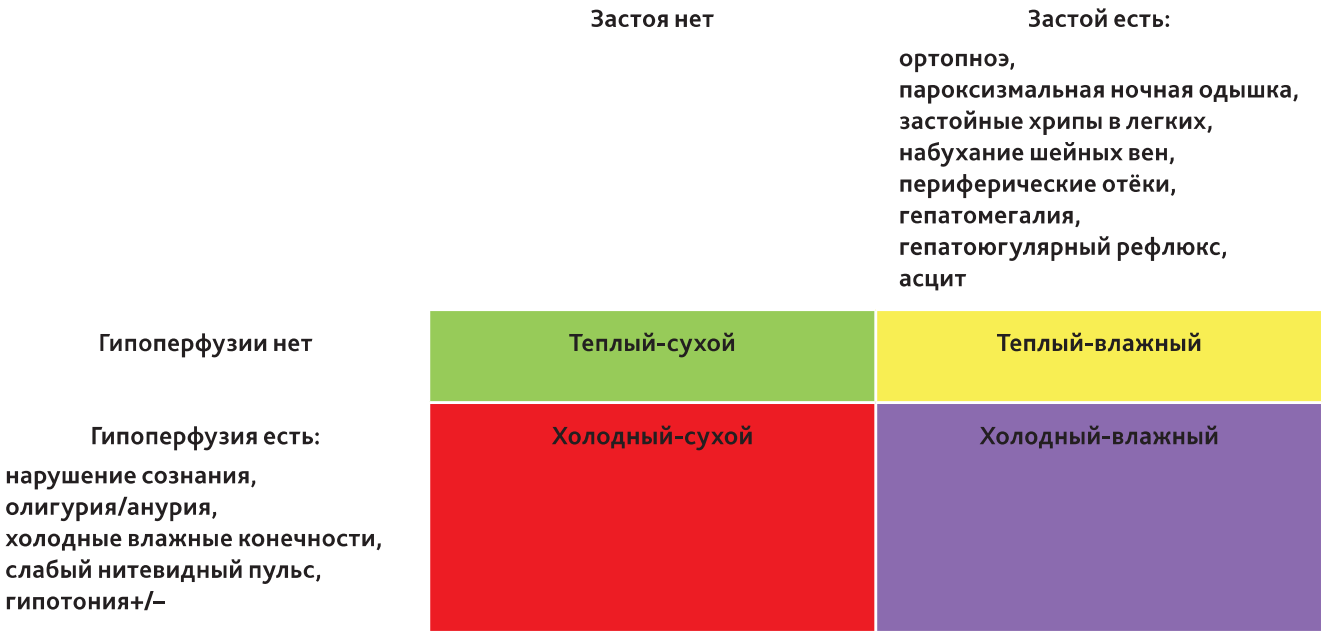


***Figure 1.*** *Clinical patterns of acute heart failure based on the presence/absence of congestion and/or hypoperfusion [17]*

An emergency ECHO-CG is indicated for all patients with hemodynamic instability (SBP < 90 mm Hg) as well as for patients with suspected life-threatening structural or functional cardiac disorders (mechanical complications, acute valvular failure and aortic dissection). The best time to perform ECHO-CG is the first 48 hours of the patient's stay in the hospital [17].

The level of natriuretic peptides — NPs — (NT-proBNP, BNP, MR-proANP) should be measured in all patients with suspected AHF on admission. Normal levels of NPs (BNP < 100 pg/mL, NT-proBNP < 300 pg/mL, MR-proANP < 120 pg/mL) make the AHF diagnosis unlikely [19]. When assessing the level of natriuretic peptides, it should be noted that this indicator is nonspecific and can be increased in a number of other conditions (Table 1).

In addition to screening laboratory tests (including complete blood count, biochemical assay of

***Table 1.*** *Causes of elevated concentrations of natriuretic peptides [17, 22]*

| Cardiac | Non-cardiac |
|---|---|
| Heart failure | Elderly age |
| Acute coronary syndrome | Ischemic stroke |
| Pulmonary embolism | Subarachnoid hemorrhage |
| Myocarditis | Renal dysfunction |
| Left ventricular hypertrophy | Liver dysfunction (mainly liver cirrhosis with ascites) |
| Hypertrophic or restrictive cardiomyopathy | Severe infections (including pneumonia and sepsis) |
| Acquired and congenital heart disease | Paraneoplastic syndrome |
| Atrial fibrillation and ventricular tachyarrhythmias | Chronic obstructive pulmonary disease |
| Cardioversion, implantable cardioverter-defibrillator shock | Sleep apnea |
| Cardiac contusion | Pulmonary hypertension |
| Cardiac surgery | Anemia |
| Pericarditis | Severe metabolic and endocrine disorders (e.g. thyrotoxicosis, diabetic ketoacidosis) |
| Chemotherapy-induced cardiotoxicity | Severe burns |

creatinine, sodium, potassium, glucose, and liver function tests), it is necessary to measure troponin levels to diagnose ACS, MI as a cause of AHF, and D-dimer levels to diagnose PE. It should be considered that an increased concentration of troponin is found in the vast majority of patients with AHF, often without obvious myocardial ischemia or acute coronary events, due to damage or necrosis of cardiomyocytes. Besides, elevated troponin levels may be present in patients with PE [17]. Since hypothyroidism and hyperthyroidism can exacerbate AHF, thyroid-stimulating hormone (TSH) should be evaluated in all patients with newly diagnosed AHF [17].

In addition, pulse oximetry is indicated in patients with AHF. Transcutaneous oxygen saturation values ($SpO_2$) < 90% are considered low. Normal $SpO_2$ does not exclude either hypoxemia (a decrease in the partial pressure of oxygen in the arterial blood ($PaO_2$) < 80 mm Hg) or tissue hypoxia. In cardiogenic shock (CS), an accurate measurement of $PaO_2$ and the partial pressure of carbon dioxide in the arterial blood ($PaCO_2$) are necessary. This requires an arterial blood gas test performing. In case the patient has a history of pulmonary edema or COPD, the determination of venous pH and $PaCO_2$ is enough. Hypoxemia is recorded at $PaO_2$ <80 mm Hg; hypoxemic respiratory failure is recorded at $PaO_2$ < 60 mm Hg; hypercapnia is recorded at $PaCO_2$ > 45 mm Hg; hypercapnic respiratory failure is recorded at $PaCO_2$ > 50 mm Hg.

## AHF Treatment

AHF is a life-threatening condition. Therefore, rapid transportation to the nearest hospital is necessary, preferably with an intensive care unit (ICU) [17]. Herewith, patients with pulmonary edema should be given a head-of-bed elevation position. Patients with CS should be placed on a bed with elevated foot end. Patients should only be transported on a stretcher [1, 2].

Indications for admission to a hospital/transfer of patients with AHF to the ICU:

1. Hemodynamic instability, SBP < 90 mm Hg.
2. Significant (progressive) dyspnea with involvement of additional respiratory muscles, respiration rate (RR) > 25 bpm.
3. The need for intubation, ventilation.
4. Symptoms of hypoperfusion (see above).
5. $SpO_2$ < 90% (in spite of oxygen therapy).
6. Brady- and tachyarrhythmias with heart rate < 40 or > 130 bpm, high degree AV block.
7. Life-threatening conditions: ACS, acute MI, its mechanical complications, acute heart valve failure, thoracic trauma, PE, aortic dissection, and other disorders [3, 17].

Non-invasive monitoring of vital cardiorespiratory functions, including pulse oximetry, measurement of BP, RR, and continuous ECG, is necessary for patients with AHF. Urine output should also be monitored. Routine bladder catheterization is not recommended. It should be considered at an urine output rate < 20 ml/min [2, 17].

In case of CS (see above), the patient should be immediately provided with hemodynamic support. In case of respiratory failure (RR > 25 bpm, $SpO_2$ < 90%, $PaO_2$ < 60 mm Hg, $PaCO_2$ > 50 mm Hg), the patient should be provided with respiratory support (see below). Within 60–120 minutes after admission to the hospital, it is necessary to diagnose and start treatment of life-threatening conditions that led to AHF (Figure 2), including ACS, acute MI, its complications, rhythm and conduction disorders, and PE [3]. In case of ACS with AHF, urgent revascularization within 2 hours after admission is recommended, regardless of ECG results or the detection of biomarkers [17]. In case of AHF with an underlying hypertensive crisis, an aggressive decrease of BP (by 25% during the first few hours, then with caution) is recommended using intravenous vasodilators and diuretics. In case of atrial or ventricular arrhythmias leading to hemodynamic instability, electrical cardioversion is recommended; in cases of bradyarrhythmias and conduction disorders, temporary cardiac pacing is recommended. In case of mechanical complications of MI (see above), chest trauma, acute valvular insufficiency, and aortic dissection, surgical intervention is usually required. In case of PE as a cause of shock or hypotension, immediate specific treatment with reperfusion is recommended using thrombolysis, catheterization or surgical embolectomy [17]. The tactics for managing these states are described in detail in the profile recommendations.

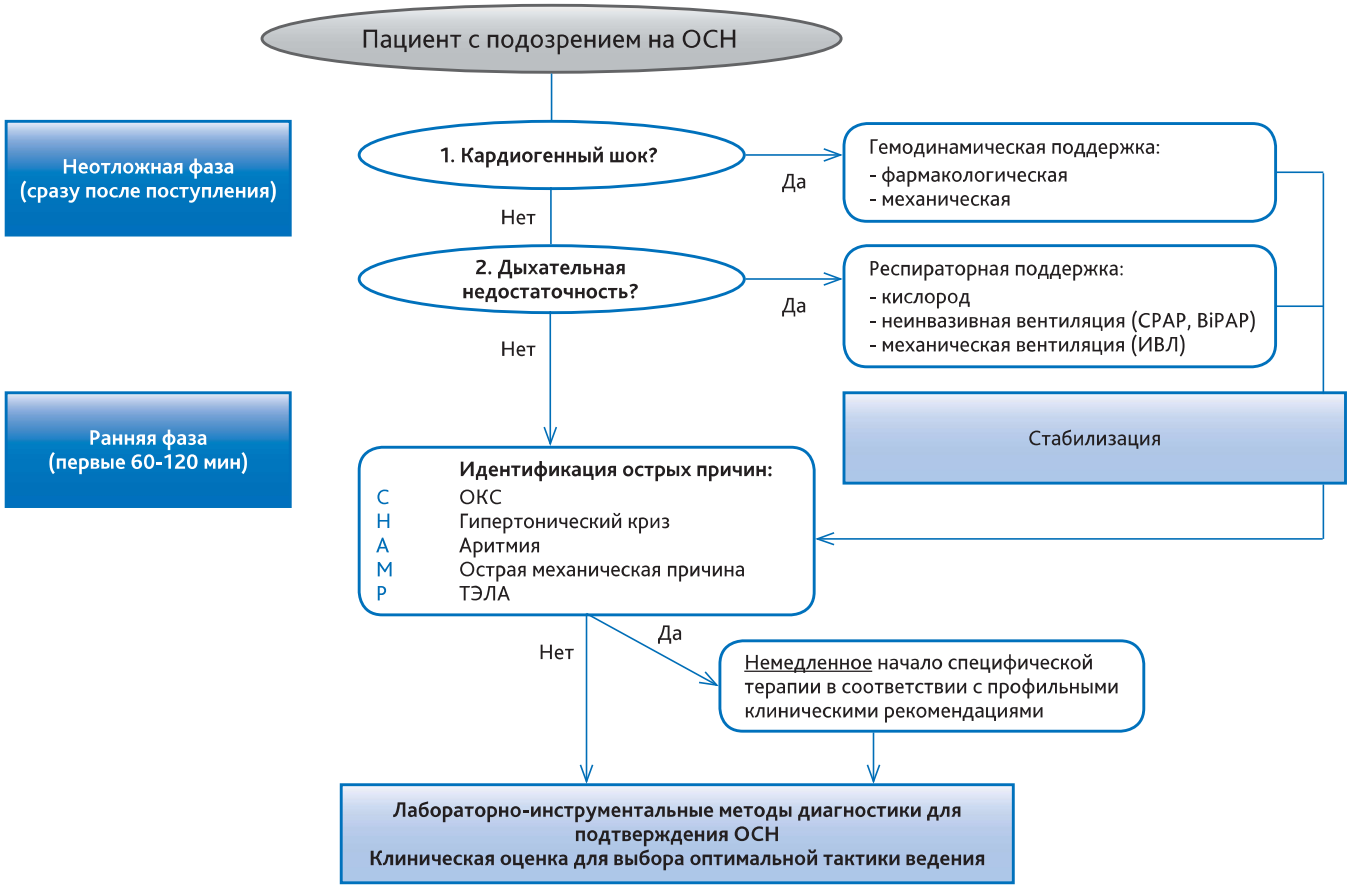


***Figure 2.*** *Management of a patient with acute heart failure according to CHAMP acronym [17]*

*Respiratory Support*

Oxygen therapy (inhalation of 40–60% oxygen at a rate of 4–8 L/min through a mask) is recommended in patients with AHF and $SpO_2$ < 90% and/or $PaO_2$ < 60 mm Hg until hypoxemia is eliminated (up to an increase of $SpO_2$ > 90%) [2, 4, 15, 17].

Oxygen therapy should not be given to patients with AHF without a decrease of saturation and hypoxemia, as it can lead to vasoconstriction and a decrease in cardiac output [17].

Noninvasive ventilation of the lungs (continuous positive airway pressure — CPAP, or biphasic positive airway pressure — BiPAP) is recommended for patients with respiratory distress (RR > 25 bpm and $SpO_2$ < 90%) and it should be started as early as possible to reduce symptoms of respiratory failure (Figure 3) [3]. Since noninvasive ventilation can help reduce BP, it should be used with caution in patients with hypotension [17]. The inspired oxygen fraction ($FiO_2$) should be increased, if necessary, to 100%, according to $SpO_2$, if there are no contraindications. However, hyperoxia should be avoided. Noninvasive ventilation can reduce the incidence of intubation and mortality, although there is insufficient evidence that it reduces mortality. Noninvasive ventilation should be continued in patients who have signs of respiratory failure upon admission to the hospital. PS-PEEP (Pressure Support Positive End-Expiratory Pressure) is preferable in case of acidosis and hypercapnia, especially if there is a history of COPD [15, 17].

Intubation and invasive ventilation (IV) are recommended for patients with respiratory failure if hypoxemia ($PaO_2$ < 60 mm Hg), hypercapnia ($PaCO_2$ > 50 mm Hg), and acidosis (pH < 7.35) cannot be corrected through noninvasive ventilation (Figure 3) [15, 17].

*Drug Therapy*

The algorithm for managing patients with AHF depends on the clinical profile (Figure 4).

*Diuretic Therapy*

If congestion signs are present (“wet” patients), intravenous loop diuretics are indicated. Diuretics should be avoided in “wet and cold” patients (with

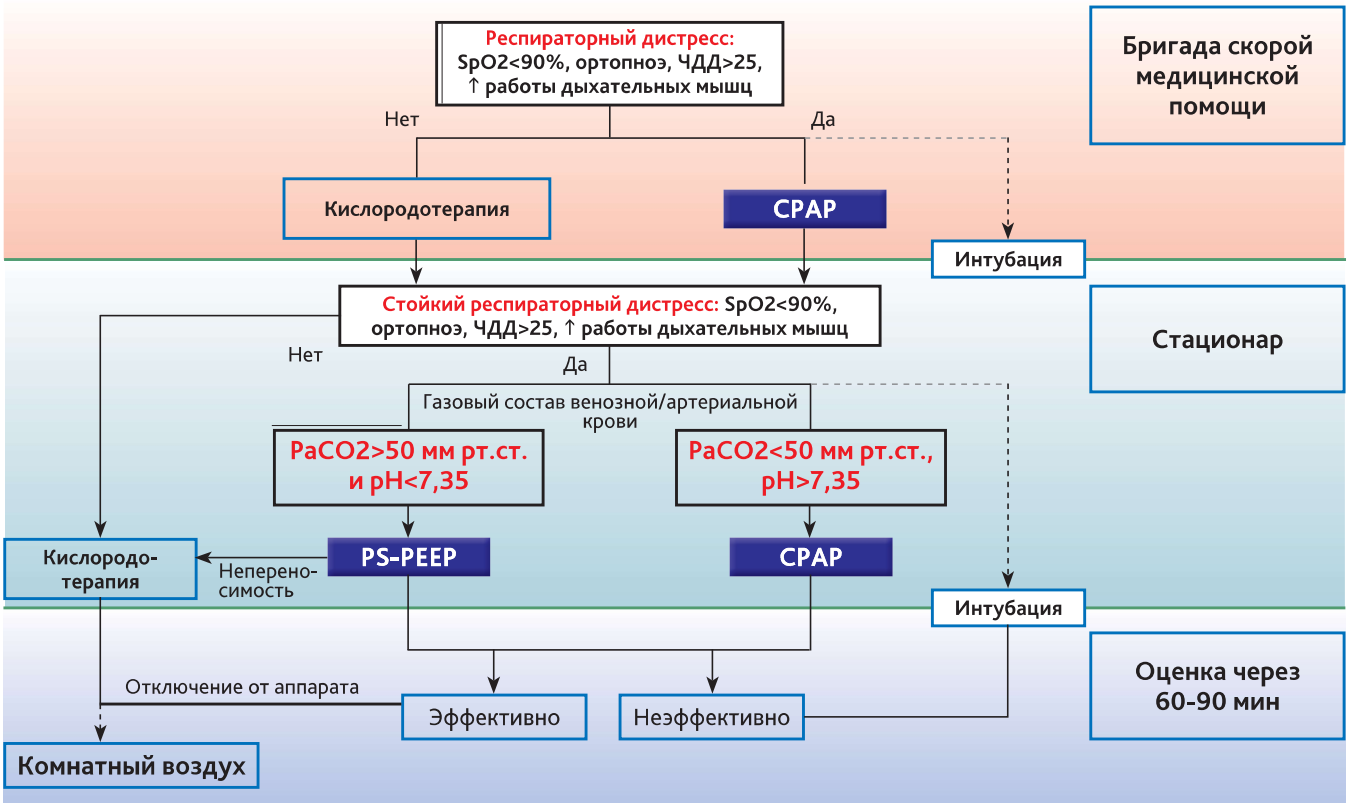


***Figure 3.*** *Respiratory support in acute heart failure [15]*

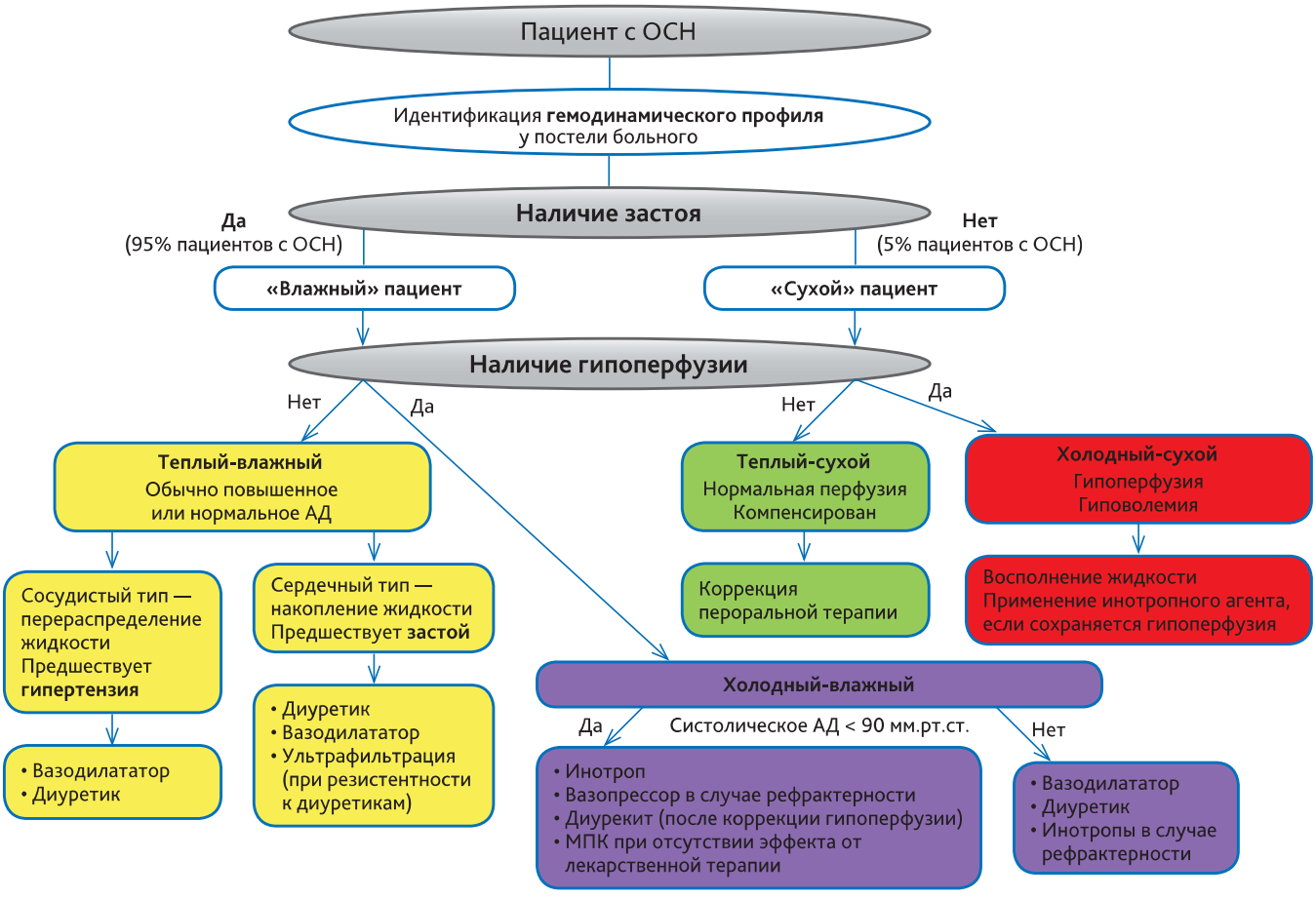


***Figure 4.*** *Management of patients with acute heart failure based on clinical pattern [17]*

signs of hypoperfusion) until an adequate level of perfusion is achieved. Patients with a newly diagnosed AHF or with ADHF who have not previously received oral diuretic therapy are recommended to use furosemide 20–40 mg (or 10–20 mg of torasemide) intravenously [17]. In patients with CHF who received pre-admission therapy with diuretics, the dose of intravenous diuretic should be equal to or greater than that of the oral diuretic used [17]. In accordance with national guidelines, in this case, the dose of furosemide should be 2.5 times higher than the last daily dose of the diuretic [2]. Diuretics must be given in the form of intermittent or continuous infusion. The dose and duration of diuretic therapy depend on the severity of clinical symptoms [17].

In case of resistance to the used doses of loop diuretics, it is possible to: 1) add small doses of thiazide diuretics in addition to loop diuretics; 2) use loop diuretics in combination with mineralocorticoid-receptor antagonists (MRA) in high doses (150–300 mg) if there is no hyperkalemia and renal dysfunction; 3) add carbonic anhydrase inhibitors (acetazolamide) to avoid the development of alkalosis, which weakens the effect of thiazide and loop diuretics [3].

### *Vasodilators*

Intravenous vasodilators (Table 2) are the second most frequent drugs used in the symptomatic therapy of AHF. They reduce pre- and post-load and increase the stroke volume. However, they have, unfortunately, no reliable evidence base.

In accordance with international guidelines, intravenous vasodilators are recommended for patients with SBP > 90 mm Hg in order to relieve the symptoms of AHF, especially for patients with AHF with the underlying hypertensive crisis. Vasodilators should be used with caution in patients with significant aortic and mitral stenosis [17].

According to national guidelines, the use of vasodilators can be considered only in patients with SBP ≥ 100 mm Hg [2, 3].

In the RELAX-AHF trial, it was discovered that patients with HF decompensation who are receiving treatment with serelaxin (human recombinant relaxin-2 peptide, which helps adapt the woman's body to pregnancy and is a potent renal vasodilator [11]) experience a significant decrease in the signs of dyspnea and congestion as well as an improvement in the glomerular filtration rate (GFR), and they also experience a decrease in the need for intravenous diuretics. The total 180-day mortality was also reduced in comparison with placebo [14, 21]. However, in the subsequent RELAX-AHF-EU trial, the drug effect on the combined endpoint (death + worsening of HF) was not confirmed, and further studies of this drug were suspended. The drug is not for sale on the market.

### *Inotropic Agents*

Inotropic agents include dobutamine, dopamine, levosimendan, and phosphodiesterase 3 (PDE 3) inhibitors: milrinone, enoximone (Table 3). Inotropic infusions should be considered for patients with hypotension (SBP < 90 mm Hg) and/or hypoperfusion ("cold" patients) to increase cardiac output and BP, to improve peripheral perfusion and to prevent/slow the development of dysfunction/failure of visceral organs. If hypoperfusion is due to the use of β-blockers, it is preferable to prescribe levosimendan rather than dobutamine. Since levosimendan has a vasodilating effect, it should be administered to patients with hypotension (SBP < 85 mm Hg) or CS only in combination with other inotropes or vasopressors [17].

***Table 2.*** *Intravenous vasodilators in acute heart failure treatment [17]*

| Vasodilator | Dosing | Side effects | Other |
|---|---|---|---|
| Nitroglycerine | Start with 10–20 μg/min, increase up to 200 μg/min | Hypotension, headache | Tolerance on continuous use |
| Isosorbide dinitrate | Start with 1 mg/h, increase up to 10 mg/h | Hypotension, headache | Tolerance on continuous use |
| Sodium nitroprusside | Start with 0.3 μg/kg/min and increase up to 5 μg/kg/min | Hypotension, isocyanate toxicity | Light sensitivity |
| Nesiritide | Bolus 2 μg/kg + infusion 0.01 μg/kg/min | Hypotension | |

***Table 3.*** *Inotropes and/or vasopressors in acute heart failure treatment [17]*

| Inotrope/ vasopressor | Mechanism of action | Bolus | Infusion rate |
|---|---|---|---|
| Dobutamine[a] | $\beta_1$-agonist, <$\beta_2$ and $\alpha_1$-agonist | No | >2-20 μg/kg/min: (beta+) |
| Dopamine | Stimulation of dopamine receptors, in large doses — β-agonist, in high — α, β-agonist | No | 3–5 μg/kg/min; inotropic (beta+)<br>>5 μg/kg/min: (beta+), vasopressor (alpha+) |
| Milrinone[a,b] | Phosphodiesterase 3 inhibitor | 25–75 μg/kg over 10–20 min | 0,375–0,75 μg/kg/min |
| Enoximone[a] | Phosphodiesterase 3 inhibitor | 0,5–1,0 mg/kg over 5–10 min | 5–20 μg/kg/min |
| Levosimendan[a,c] | Calcium sensitizer increases the sensitivity of contractile proteins to $Ca^{2+}$ by binding to troponin C of the myocardium | 12 μg/kg over 10 min (optional) | 0,1 μg/kg/min, which can be decreased to 0,05 or increased to 0,2 μg/kg/min |
| Norepinephrine | $\alpha_1$- and $\alpha_2$-agonist, <$\beta_1$-agonist | No | 0,2–1,0 μg/kg/min |
| Epinephrine | $\alpha_1$-, $\alpha_2$, $\beta_1$, $\beta_2$-agonist | Bolus: 1 mg can be administrated i.v. during resuscitation, repeated every 3–5 min | 0,05–0,5 μg/kg/min |

[a] — Also a vasodilator, [b] — Not recommended in ischemic heart failure, [c] — Bolus not recommended in hypotension

Inotropes, especially adrenergic agonists, can cause sinus tachycardia, myocardial ischemia and arrhythmia. Therefore, it is required to monitor the ECG when using them. There is a concern that they can increase mortality. In this regard, inotropic agents are not recommended in patients without hypotension and hypoperfusion for safety reasons [17].

### *Vasopressors*

Vasopressors (preferably norepinephrine) can be considered in patients with CS in order to increase blood pressure and perfusion of vital organs when other inotropic drugs prove to be ineffective. Since inotropic drugs and vasopressors can lead to the development of arrhythmia, myocardial ischemia, and also, in the case of levosimendan and PDE 3 inhibitors, to hypotension, ECG and BP monitoring is necessary if they are prescribed. In such cases, invasive blood pressure measurement can be considered [17].

When comparing dopamine with norepinephrine in the treatment of patients in a state of shock, it was shown that fewer side effects and lower mortality are recorded when norepinephrine treatment is used. Epinephrine should be administered only in patients with persistent hypotension regardless of the use of other vasoactive agents [17].

### *Anticoagulant Therapy*

Prevention of thromboembolism with heparin and low molecular weight heparins is recommended to reduce the risk of deep vein thrombosis and PE in patients who have not received oral anticoagulant therapy and who have no contraindications to it [17]. Patients who received oral anticoagulants should continue taking them if there are no contraindications to prescribing them.

### *Other Medications*

To control the heart rate, 0.25–0.5 mg of digoxin intravenously is indicated in patients with AF with ventricular response rate > 110 per min if they did not receive pre-admission therapy with digoxin. In moderate or severe renal dysfunction, doses of 0.0625–0.125 mg are sufficient. To this end it is also possible to use amiodarone, but its effectiveness has not been proven as well [17].

Intravenous opiates (morphine 4–8 mg, trimeperidine 10–20 mg) can be used with caution in case patients with severe dyspnea (mainly pulmonary edema) experience significant psycho-emotional

arousal, anxiety or fear [2]. Frequent use of opiates is not recommended [17]. It is necessary to remember the possible risk of respiratory depression, especially in elderly patients, on treatment with opiates. To minimize this risk, the administration should be titrated to 1–2 ml by first diluting the ampoule of opiate with 19 ml of physiological saline [2]. Side effects of opiates include nausea, vomiting, hypotension, and bradycardia. To prevent nausea and vomiting, 10 mg of metoclopramide intravenously can be added [2]. In addition, opiates can increase the need for invasive ventilation. Opinions are contradictory concerning the increased risk of mortality in patients receiving morphine [17].

Anxiolytics and sedatives may be necessary for patients with symptoms of agitation or delirium. The careful use of benzodiazepines (diazepam or lorazepam) is the safest [17].

Vasopressin antagonists (tolvaptan) block the action of antidiuretic hormone (ADH, vasopressin) on the renal tubules and promote the excretion of water. Vasopressin antagonists can be administered in patients with hypervolemia and persistent hyponatraemia [17].

*Instrumental Therapy*

Ultrafiltration includes the removal of plasma water through a semipermeable membrane. The advantage of ultrafiltration over loop diuretics in patients with AHF is not proven. Currently, routine use of ultrafiltration is not recommended and should only be used in patients who do not respond to diuretic therapy.

Criteria for starting dialysis are treatment-resistant oliguria, severe hyperkalemia ($K^+$ > 6.5 mmol/L), severe acidosis (pH < 7.2), and serum urea level > 36 mmol/L [5, 17].

In patients with AHF, whose condition cannot be stabilized by means of drug therapy, the systems of mechanical circulatory support (MCS) can be used to unload the ventricles and maintain a sufficient level of perfusion of target organs. Temporary MCS systems can be used, including percutaneous cardiac support devices, extracorporeal life support (ECLS) and extracorporeal membrane oxygenation (ECMO) systems to support patients with left ventricular or biventricular failure before restoring the function of the heart or other organs. Typically, the time of use of these devices is limited from several days to several weeks. The actual data concerning the benefits of temporal percutaneous MCS devices in patients not responding to standard therapy, including inotropes, are limited. In a meta-analysis of three randomized clinical trials (RCTs) comparing percutaneous MCS and intra-aortic balloon pump (IABP, balloon intra-aortic counterpulsation) the percutaneous MCS in a total of 100 patients with CS was shown to be safer and demonstrated better hemodynamics, but it did not improve the 30-day mortality and was associated with a large number of bleeding complications [10]. In RCT of the high-risk percutaneous coronary intervention (PCI) in patients with LV dysfunction (the PROTECT II trial), the 30-day frequency of major side effects was not different in patients with IABP or hemodynamic support devices [16]. Based on these results, temporary percutaneous MCS is not recommended as a proven or effective method of treating CS. MCS systems, in particular ECLS and ECMO, can be used as a "bridge to decision" in patients with rapidly deteriorating AHF or CS in order to stabilize hemodynamics, restore the functions of target organs, and perform a complete clinical evaluation of the possibility of heart transplantation or the insertion of a long-term MCS device [18].

Indications for IABP are the support of blood circulation before surgical correction of acute mechanical MI complications, during severe acute myocarditis, and in certain patients with acute myocardial ischemia or infarction before, during or after percutaneous or surgical revascularization [17].

*Other Interventions*

Thoracocentesis (pleural puncture with fluid evacuation) can be considered in patients with AHF and pleuritis to facilitate dyspnea. Paracentesis with fluid evacuation to relieve the symptoms can be discussed for patients with ascites. This procedure can partially increase the renal filtration pressure and GFR by decreasing intraabdominal pressure [17].

## CS Management Features

The main cause (80%) of CS is acute MI with a lesion of more than 40% of the myocardium. The other 20% are mechanical complications of MI.

A dramatic decrease in preload due to hypovolemia can also be a possible cause of CS [2].

It was believed in the 1980–1990's that the frequency of CS in MI reached 20%. However, based on data from recent years, the estimate has been adjusted to 5–8% [2]. Risk factors of CS are anterior MI localization, elderly age, diabetes mellitus, history of MI and CHF, and LV systolic dysfunction [2].

In CS, there is activation of the sympathetic nervous system; systemic inflammation; release of proinflammatory cytokines; vasodilation with impairment of systemic perfusion; increased myocardial oxygen demand; disturbance of diastolic LV relaxation, which promotes pulmonary edema and hypoxemia; an increase in total peripheral vascular resistance with postload increase; fluid retention due to reduced renal blood flow and increased preload; slowing of tissue blood flow; blood thickening; and a tendency to thrombosis. All of this occurs due to the formation of vicious circles, and it leads to progressive myocardial dysfunction and death of the patient[2].

ECG and ECHO-CG are recommended for all patients with suspected CS immediately followed by continuous monitoring of ECG and BP and invasive monitoring with an arterial line [3, 17].

It is extremely important to perform a rapid troponin test to exclude ischemic damage to the myocardium [2].

All patients with CS must be admitted/transferred to a hospital with a 24/7 cardiac surgical department, an interventional radiology surgical suite for possible coronary angioplasty, and a special ICU with IABP [2, 3, 17].

Immediate coronary angiography is recommended (within 2 hours of admission to hospital) with coronary revascularization for patients with CS that complicates ACS [3].

Oxygenotherapy, as mentioned above, is recommended at $SpO_2$ < 90% until $SpO_2$ > 90% [2].

A fast infusion of 200 ml of 0.9% sodium chloride in 10 minutes is recommended as a first-line therapy if there is no lung congestion and signs of hypovolemia. Repeated infusions of the solution are possible if needed until a total volume of 400 ml is reached [2, 3, 17].

Intravenous inotropic agents (dobutamine) can be used to raise blood pressure and increase cardiac output [17].

Vasopressors (norepinephrine is preferable to dopamine) can be considered if there is a need to maintain SBP in the presence of persistent hypoperfusion [17].

Epinephrine can be administered if there is no effect of dobutamine/dopamine/norepinephrine, and in case of progressive hypotension with SBP < 80 mm Hg [2].

A routine use of IABP is not recommended. Short-term IABP can be considered for the treatment of refractory CS before surgical correction of acute mechanical complications of MI, as well as before, during or after percutaneous or surgical revascularization [17].

In addition, the prescription of acetylsalicylic acid (250–325 mg chewable) and anticoagulants (heparin 70 IU/kg of body weight, not more than 4,000 IU, or enoxaparin 1 mg/kg body weight intravenously where the initial dose should not be more than 100 mg) should be considered [2].

Frequent errors in CS management:

1. Prescribing of cardiac glycosides (proarrhythmic effect under hypoxic conditions, delayed inotropic action, increased pulmonary congestion due to simultaneous stimulation of both ventricles).
2. Administration of vasopressors without a prior attempt to eliminate hypovolemia.
3. The use of glucocorticoids (since there is no evidence that they are clinically effective).
4. The use of mesatone (which causes vasoconstriction without increasing cardiac output) [2].

## Oral Therapy of CHF in ADHF

When ADHF occurs in patients with CHF, oral therapy of HF should be continued, except for cases of hemodynamic instability (symptomatic hypotension, hypoperfusion, bradycardia), hyperkalemia or severe renal failure (Table 4) [15]. In these cases, a temporary dose reduction or discontinuation of administered oral medications may be required until the condition stabilizes. In particular, the therapy with β-blockers should be continued for patients with ADHF if there is no CS. A recent meta-analysis showed that discontinuation of β-blockers in patients hospitalized with ADHF was associated with a significant increase

***Table 4.*** *Oral therapy of AHF in the first 48 hours [15]*

| | Normo-tension/ Hyper-tension | Hypotension, mmHg | | Low heart rate, bpm | | Potassium, mmol/l | | Renal function | |
|---|---|---|---|---|---|---|---|---|---|
| | | 85–100 | <85 | <60 ≥50 | <50 | ≤3.5 | >5.5 | Cr<2,5, eGFR>30 | Cr>2,5, eGFR<30 |
| ACE-I /ARB | Review/ Increase | Reduce/ Stop | Stop | No change | No change | Review/ Increase | Stop | Review | Stop |
| Beta-blocker | No change | Reduce/ Stop | Stop | Reduce | Stop | No change | No change | No change | No change |
| MRA | No change | No change | Stop | No change | No change | Review/ Increase | Stop | Reduce | Stop |
| Diuretics | Increase | Reduce | Stop | No change | No change | Review/ No change | Review/ Increase | No change | Review |
| Sacubitril/ valsartan | Review/ Increase | Stop | Stop | No change | No change | Review/ Increase | Stop | Review | Stop |
| Other vaso-dilators (Nitrates) | Increase | Reduce/ Stop | Stop | No change | No change | No change | No change | No change | No change |
| Other heart rate slowing drugs (amio-darone, CCB, Ivabradine) | Review | Reduce/ Stop | Stop | Reduce/ Stop | Stop | Review/ Stop (*) | No change | No change | No change |

**Note:** ACE-I –angiotensin converting enzyme inhibitor, ARB — antagonist receptor blocker, CCB — Calcium channel blockers (mg/dl), Cr — creatinine blood level (mg/dl), eGFR — estimated glomerular filtration rate ml/min/1,73 m2, MRA — mineralocorticoid receptor antagonist, (*) amiodarone

in in-hospital and post-hospital mortality as well as an increased frequency of repeated hospital admissions [17].

When AHF is newly diagnosed, an attempt should be made after the patient's condition has stabilized (adequate diuresis, decrease of dyspnea and signs of stagnation, normalization of blood pressure) to start the therapy that is recommended for patients with CHF, including angiotensin converting enzyme inhibitors (ACEI), or sartans, or sacubitryl/ valsartan; β-blockers, etc., with careful consideration of contraindications [2–4, 17].

Therefore, currently, a step-by-step procedure for managing patients with AHF has been developed based on evidence-based medical data, which must be known and applied in real clinical practice. Such a procedure will make it possible to improve the prognosis of patients with this life-threatening condition.

## Conflict of interests

The authors declare no conflict of interests.

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