

Review Article



KSHF Guidelines for the Management of Acute Heart Failure: Part II. Treatment of Acute Heart Failure

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ABSTRACT

The prevalence of heart failure (HF) is on the rise due to the aging of society. Furthermore, the continuous progress and widespread adoption of screening and diagnostic strategies have led to an increase in the detection rate of HF, effectively increasing the number of patients requiring monitoring and treatment. Because HF is associated with substantial rates of mortality and morbidity, as well as high socioeconomic burden, there is an increasing need for developing specific guidelines for HF management. The Korean guidelines for the diagnosis and management of chronic HF were introduced in March 2016. However, chronic and acute HF represent distinct disease entities. Here, we introduce the Korean guidelines for the management of acute HF with reduced or preserved ejection fraction. Part II of this guideline covers the treatment of acute HF.


Keywords: Heart failure; Guideline; Treatment

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Conflict of Interest

The authors have no financial conflicts of interest.

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INTRODUCTION

The number of patients with heart failure (HF) has been on the rise as a consequence of the aging of society and the improvement in screening and diagnostic techniques. Therefore, there is an increasing need for developing guidelines for the diagnosis and treatment of HF. Although guidelines for HF management have already been issued by American and European associations, many aspects of such guidelines do not reflect the domestic reality in Korea due to the social and anthropological characteristics of the Korean population. Thus, to help clinicians establish the best treatment plan for Korean patients with HF, it is necessary to develop specific guidelines that reflect the clinical situation in Korea. In 2012, the Korean Society of Heart Failure (KSHF) established the Guideline Writing Committee to develop the treatment guidelines for HF. The Korean guidelines for the diagnosis and management of chronic heart failure (CHF) were introduced in March 2016.¹⁾ However, CHF and acute heart failure (AHF) are distinct disease entities, warranting different approaches for diagnosis and treatment. Here, we introduce the Korean guidelines for the management of AHF with reduced or preserved ejection fraction (HFrEF and HFpEF, respectively). In Part II of this guideline, we discuss the treatment of AHF, including pharmacological and non-pharmacological therapies, monitoring, and discharge.

This guideline was developed based on previously issued international guidelines and amended to reflect the clinical situation in Korea. A committee of KSHF members decided on the format of the guideline, the selection of topics addressed, and the composition of the Writing Committee. To develop the guidelines, we considered all clinical studies and evidence included in the international guidelines, as well as domestic research conducted in Korean patients with HF. Members of the Writing Committee first drafted thematic manuscripts, which were then assembled and arranged according to the evidence-based scales. To ensure transparency and facilitate future revision of the guidelines, we documented the process followed for issuing a recommendation for each topic based on the gathered evidence. The guideline was drafted, reviewed by the advisory committee, and finalized after receiving endorsement from the Korean Society of Cardiology, Korean Society of Hypertension, Korean Society of Interventional Cardiology, Korean Society of Echocardiography, and Korean Society of Lipid and Atherosclerosis. While working on this guideline, the members of the Writing Committee were not affected by external influences and made every effort to exclude conflicts of interests.

The Writing Committee issued the level of recommendation upon a comprehensive analysis of evidence from studies describing real clinical experience, from surveys, from epidemiologic, observational, and randomized clinical studies, and from meta-analyses. The level of evidence and class of recommendation were defined so as to have a clear formulation, provide straightforward instructions, and be easily adopted in daily clinical practice (**Supplementary Tables 1 and 2**).

This guideline is intended to help improve clinical practice by providing recommendations based on clinical evidence. As such, the guideline does not serve as a basis for clinical judgement. The final decision in the treatment of each patient should be made by the treating physician according to their personal opinion and judgment, while using the guideline to support these decisions.

PHARMACOLOGICAL TREATMENT

General considerations

1. In HFrEF patients with acute exacerbation, the guideline-based medications should be continued if no hemodynamic instability or contraindications are evident (class of recommendation I, level of evidence B).
2. Low-dose beta-blockers should be started in stable patients who achieve an euvolemic state, after discontinuing the initial intravenous diuretics, vasodilators, and inotropic agents (class of recommendation I, level of evidence B).
3. If the clinical benefit of anticoagulant use is higher than the risk, anticoagulants should be used to prevent venous thrombosis (class of recommendation I, level of evidence B).

AHF represents an acute exacerbation of existing HF (acute decompensated HF) or de novo HF with acute manifestation. In patients hospitalized for acute exacerbations, the prescribed medications for HF should be checked closely and adjusted if necessary. Angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers and beta-blockers can be maintained in most patients with HFrEF, based on the findings of clinical studies that reported better clinical outcomes in patients who continue HF medication than those who do not.²⁻⁵⁾

The reduction or discontinuation of beta-blockers may be considered only if: 1) beta-blocker use has been initiated or increased recently; 2) there is an excessive increase in blood volume; or 3) the cardiac output has remained marginal or has decreased. In patients with significant deterioration of renal function, temporarily reducing or discontinuing ACE inhibitor, angiotensin receptor blocker, and mineralocorticoid receptor antagonist may be considered until the renal function improves. It is important to reevaluate and control the medication at the time of admission in patients admitted due to HF deterioration. Beta-blockers should be started in the stable euvolemic patients after the successful discontinuation of initial intravenous diuretics, vasodilators, and inotropic agents. Beta-blockers should be started at low doses and only for stabilized patients.²⁻⁴⁾ In addition, if a patient is not currently taking an ACE inhibitor, angiotensin receptor blocker, or mineralocorticoid receptor antagonist, these medications should be started as soon as possible after stabilization, with monitoring of renal function and blood pressure (see the Korean guideline for the management of CHF).¹⁾

On the other hand, no studies support the survival benefit of medical treatments in patients with HFpEF. Moreover, there is no evidence to support the maintenance of some medications that achieved symptomatic improvement in HFpEF patients during acute exacerbations.

HF is a risk factor for venous thrombosis due to decreased cardiac output, increased peripheral venous pressure, and increased blood coagulability. Although several studies have confirmed that various anticoagulants can prevent venous thrombosis, there are multiple limitations to such studies. First, various anticoagulants and definitions of treatment response were used in different studies. Second, such studies covered a variety of acute illnesses but included only small populations of patients with AHF exacerbation. Third, the rates of clinically significant pulmonary embolism and mortality associated with anticoagulant use remain unclear. Nevertheless, to prevent venous thrombosis in hospitalized patients with decompensated AHF, anticoagulant use should be considered if the associated clinical benefit is high compared to the risk.⁶⁻⁸⁾

Diuretics

1. In AHF patients with fluid retention, a parenteral diuretic should be used with careful monitoring of symptoms, urine output, electrolyte balance, and renal function (class of recommendation I, level of evidence B).
2. In patients without oral diuretic therapy, the initial recommended dose of loop diuretics is furosemide 20–40 mg, and at least the same dosage of loop diuretics should be used in patients with acute exacerbation of CHF (class of recommendation I, level of evidence B).
3. The intermittent or continuous injection of diuretics is recommended, and the dose and duration should be adjusted according to the patient's symptoms and clinical condition (class of recommendation I; level of evidence B).
4. If symptoms do not improve even with loop diuretic use, it is advisable to add other diuretics such as thiazide or spironolactone (class of recommendation IIa, level of evidence B).

Unlike for ACE inhibitors and beta-blockers, the efficacy of diuretics in reducing HF-associated mortality and morbidity has not been well studied. However, diuretics are recommended in patients with symptoms and signs of pulmonary congestion, to alleviate dyspnea and edema regardless of left ventricular ejection fraction, as administration of diuretics immediately upon admission to the emergency room is known to be associated with better outcomes.⁹⁾¹⁰⁾ The goal of diuretic use is to maintain the patient's dry weight by using a minimum dose of diuretics to adjust the fluid volume. Once dry weight is reached, cardiac output is reduced due to hypotension and renal dysfunction from dehydration, and the diuretic dosage must be adjusted to facilitate the use of drugs such as ACE inhibitors. However, if the patient is not responding well to diuretics, right heart catheterization can be performed to confirm diastolic pressure and cardiac output. Once fluid excess is detected, the dose of loop diuretics should be increased to ensure that the appropriate concentration reaches the kidney.¹¹⁾¹²⁾ Compared to thiazide diuretics, loop diuretics cause intensive diuresis for a shorter period of time. It is recommended that intravenous furosemide 20–40 mg be initially administered in patients with AHF who did not use oral diuretics, as well as in those with acute exacerbation of CHF. Thiazide is less effective in patients with reduced renal function. Although loop diuretics are preferred to thiazides in patients with HFrEF, synergistic effects can be seen with combination therapy (loop diuretics with thiazides) in patients with resistant edema. Therefore, diuretics based on different mechanisms may be added in patients with inadequate symptom relief.¹³⁻¹⁵⁾

In the initial treatment of AHF, it is necessary to measure daily body weight, blood pressure in the supine and erect positions, and fluid intake and output. In addition, since loop diuretics may reduce glomerular filtration rate, worsen neurohumoral activity, and cause electrolyte imbalance, it is recommended to measure electrolyte levels and renal function daily during diuretic treatment or during a period when the HF medication dose is adjusted. Patients are often instructed to adjust their diuretic dose by themselves, so symptoms/signs of congestion and body weight should be measured daily. Although diuretics can relieve congestive symptoms, their effects on mortality are not well studied.

A randomized controlled study of 20 patients reported that, compared to single-dose administration, continuous infusion of diuretics was more effective and less toxic.¹⁶⁾ However, the DOSE randomized study, which enrolled 308 patients, reported no significant difference between these administration modalities regarding symptom relief or renal toxicity.¹²⁾ On the other hand, intravenous administration of low-dose dopamine with loop

diuretics reportedly increases diuresis and preserves renal function.¹⁷⁾ Further clinical studies are needed to clarify the optimal administration modality for diuretic treatment.

Intravenous vasodilators

1. Intravenous vasodilators may improve AHF symptoms in patients with systolic blood pressure >90 mmHg, and it is advisable that symptoms and blood pressure be monitored frequently during intravenous injection (class of recommendation IIa, level of evidence B).
2. In patients with hypertensive AHF, intravenous vasodilators can be used to improve patient symptoms and reduce congestion (class of recommendation IIa, level of evidence B).

Intravenous vasodilators include nitrates, nitroprusside, and nesiritide (**Table 1**). Intravenous nitrates rapidly reduce pulmonary congestion by lowering preload through a vasodilatory effect.¹⁸⁾¹⁹⁾ Thus, the use of intravenous nitrates is helpful for relieving dyspnea in HF patients with hypertension, myocardial ischemia, or clinically significant mitral regurgitation. However, caution should be taken because drug resistance occurs in about 20% of patients, who no longer respond to high drug concentrations.²⁰⁻²²⁾

Nitroprusside is a commonly used balanced vasodilator with dual benefit that consists of decreasing venous tone (optimize preload) and arterial tone (decrease afterload). However, few studies have described the efficacy of this drug. Therefore, when administering nitroprusside, hemodynamic changes should be monitored frequently using invasive blood pressure monitoring methods. The long-term use of nitroprusside may result in isocyanate toxicity, which manifests as loss of appetite, general weakness, and altered mentality; therefore, caution should be taken in patients with impaired renal function. Because nitroprusside can cause serious hypotension, it is mainly used in intensive care settings and can be expected to be effective in patients with a combination of severe pulmonary congestion and hypertension or severe mitral regurgitation and cardiac dysfunction.²³⁾

Nesiritide has been shown to reduce left ventricular filling pressure, per the findings of a large randomized study of patients with decompensated AHF. While no favorable effects on mortality, re-admission rate, or renal protection were noted, there was a statistically significant benefit regarding dyspnea relief, though the risk of hypotension was increased.²⁴⁾²⁵⁾

Overall, no clinical studies reported that intravenous vasodilators improve clinical outcomes in hospitalized patients with HF. Among hospitalized patients with AHF, the use of intravenous vasodilators is limitedly recommended to relieve dyspnea in patients without hypotension. In particular, intravenous vasodilators can induce excessive lowering of blood pressure, which may be associated with increased mortality in AHF patients.²⁴⁾²⁵⁾

Table 1. Intravenous vasodilators for the treatment of AHF

Vasodilator	Recommended dose	Main side-effects	Other observations
Nitroglycerine	Start with 10–20 µg/min; increase to 200 µg/min	Hypotension, headache	Tolerance with continuous use
Nitroprusside	Start with 0.3 µg/kg/min; increase to 5 µg/kg/min	Hypotension, isocyanate toxicity	Light sensitivity
Isosorbide dinitrate	Start with 1 mg/hr, increase up to 10 mg/hr	Hypotension, headache	Tolerance with continuous use
Nesiritide	Bolus 2 µg/kg + infusion 0.01 µg/kg/min	Hypotension	-

AHF = acute heart failure.

Thus, all changes in symptoms and blood pressure should be closely monitored. Moreover, intravenous vasodilator injections should be given more cautiously in patients with HFpEF, who are more sensitive to volume changes. Special attention should be paid to the use of intravenous vasodilators in patients with mitral stenosis or aortic stenosis.

Intravenous inotropic agents and vasopressors

1. To increase cardiac output, elevate blood pressure, and improve peripheral perfusion, short-term intravenous infusion of inotropic agents may be considered in patients with hypotension, signs/symptoms of hypoperfusion, or shock despite adequate filling status (class of recommendation IIa, level of evidence C).
2. If the cause of hypoperfusion is related to the use of beta-blockers, the use of the phosphodiesterase antagonist, milrinone may be considered under continuous electrocardiographic and arterial blood pressure monitoring (class of recommendation IIb, level of evidence C).
3. In patients with persistent cardiogenic shock despite the use of intravenous inotropic agents, the use of vasoconstrictors such as dopamine or norepinephrine to increase blood pressure and blood flow to major organs may be considered under continuous electrocardiography and arterial blood pressure monitoring (class of recommendation IIb, level of evidence C).
4. In HF patients with pulmonary congestion, intravenous inotropic agents should not be used unless there is hypotension, signs of hypoperfusion to major organs, or shock, because it may cause serious arrhythmias or myocardial ischemia leading to death (class of recommendation III, level of evidence C).

Intravenous inotropic agents are drugs that increase cardiac output and have been used in AHF (**Table 2**). However, there is a lack of evidence regarding the clinical efficacy of drugs such as dobutamine and milrinone. In some small-scale clinical studies, dobutamine improved hemodynamic indices in patients with AHF; however, large-scale studies could not confirm such efficacy.^{26,27)} Because there is insufficient evidence for clinical effectiveness and side-effects such as arrhythmia or myocardial ischemia, intravenous inotropes should only be used when tissue perfusion is severely impaired, with low cardiac output.²⁸⁾

Inotropes such as dobutamine are medications that increase myocardial contractility and are widely used in patients with low blood pressure due to a severely decreased blood supply to the major organs. However, there is concern that these drugs can increase the risk of death associated with exacerbate myocardial ischemia and arrhythmia induced by the increased heart rate. Milrinone, a phosphodiesterase antagonist that does not act on beta-receptors, can theoretically be used even in patients who take beta-blockers and moreover has the advantage of lowering pulmonary vascular resistance. However, milrinone should be used cautiously because it can lower systemic blood pressure.²⁹⁻³²⁾

Vasoconstrictors such as norepinephrine, which acts on the peripheral arteries, are commonly used in patients with severe hypotension. These medicines increase blood pressure and reduce the blood supply above the lower limbs, thereby maintaining blood flow to the major organs. Norepinephrine and epinephrine are the most commonly used and have the effect of increasing myocardial contractility similar to intravenous inotropes. However, these medications can increase the afterload of the left ventricle and thus should be used only in patients with insufficient blood supply to the major organs despite adequate ventricular filling pressure.

Table 2. Positive inotropes and vasopressors used to treat AHF

Drug	Bolus	Infusion rate	Effects
Dobutamine	Not recommended	2–20 µg/kg/min	Increase cardiac contractility via interaction with beta-receptors
Dopamine	Not recommended	<3 µg/kg/min 3–5 µg/kg/min >5 µg/kg/min	Dilate renal blood vessels Increase cardiac contractility via interaction with beta-receptors Increase cardiac contractility via interaction with beta-receptors Vasoconstriction via interaction with alpha-receptors
Milrinone	25–75 µg/kg over 10–20 min	0.375–0.75 µg/kg/min	Increase cardiac output and heart rate Decrease systemic and pulmonary vascular resistance
Levosimendan	12 µg/kg over 10 min	0.1 µg/kg/min (0.05–0.2 µg/kg/min)	Increase cardiac contractility via increased Ca ²⁺ sensitivity Vasodilation via interaction with the ATP-dependent Ca ²⁺ channel
Norepinephrine	Not recommended	0.2–1.0 µg/kg/min	Vasoconstriction
Epinephrine	During resuscitation: 1 mg intravenously and every 3–5 min	0.05–0.5 µg/kg/min	Vasoconstriction

Dopamine increases myocardial contractility at relatively high doses (>5 µg/kg/min), contracts the blood vessels, and increases systemic blood pressure. However, at lower doses (3 µg/kg/min), dopamine can selectively dilate the renal blood vessels and increase urine volume. However, since dopamine may cause hypoxemia, oxygen saturation should be monitored, and supplementary oxygen administration may be required.³³⁾

Antiarrhythmic agents

1. Digoxin use is advised in patients with AHF and atrial fibrillation (class of recommendation IIa, level of evidence C).
2. The use of amiodarone can be considered in the presence of atrial fibrillation concomitant with AHF (class of recommendation IIb, level of evidence B).
3. Other antiarrhythmic agents except for amiodarone should not be used to treat atrial and ventricular tachyarrhythmia (class of recommendation III, level of evidence A).

Because of the increased morbidity and mortality associated with atrial and ventricular tachyarrhythmia in HF patients, several studies have investigated the use of antiarrhythmic agents. However, most antiarrhythmic agents did not increase the survival rate; these studies rather found that antiarrhythmic agents increased the mortality rate.^{34–36)} Most class I and class III antiarrhythmic agents have a beta-receptor blocking effect and thus are very likely to have an increased risk of HF deterioration when used in patients with AHF. Digoxin and amiodarone are the only medications that can be considered for treating atrial tachyarrhythmia in patients with AHF.

Digoxin is the first drug to consider when attempting to control heart rate in HF patients with atrial fibrillation. When heart rate is >110 bpm, intravenous digoxin 0.25–0.5 mg may be considered in digoxin-naïve patients. However, attention should be paid because digoxin increases the risk of arrhythmia in patients with renal dysfunction or electrolyte abnormalities. Because several clinical studies confirmed that amiodarone does not increase mortality, its use for controlling atrial tachyarrhythmia may be considered in patients with AHF.^{37–39)}

New drugs

1. In patients with AHF, vasopressin receptor antagonists may be considered when severe hyponatremia persists despite appropriate treatment including water restriction (class of recommendation IIb, level of evidence B).

Vasopressin receptor antagonists allow the elimination of free water via urination without electrolyte loss. Among such drugs, tolvaptan is a selective oral vasopressin V₂ receptor antagonist that inhibits free water reabsorption in the renal tubule and helps treat HF-related volume overload refractory to diuretic therapy.⁴⁰⁾ In HF patients with volume overload and hyponatremia, tolvaptan effectively improved hyponatremia.⁴⁰⁾ For treating hyponatremia, vasopressin receptor antagonists may be considered in AHF patients in whom hyponatremia persists despite adequate treatment including water restriction. However, further clinical studies are needed to clarify the long-term clinical efficacy and safety of such drugs.

Serelaxin reduces systemic vascular resistance and increases blood flow to the renal vessels, increasing cardiac output. Serelaxin is also known to participate in various cellular processes with antioxidative, anti-inflammatory, and antifibrotic actions.⁴¹⁾ A recent large-scale clinical trial found that the intravenous injection of serelaxin for 48 hours at the initial stage of AHF caused rapid hemodynamic improvement, which ameliorated symptoms associated with pulmonary congestion and improved some clinical outcomes including 180-day mortality.⁴²⁻⁴⁵⁾ However, the clinical use of serelaxin is not yet approved in the United States or Europe, warranting the need for data on long-term patient prognosis and stability.

DEVICE THERAPY AND SURGICAL TREATMENT

Ultrafiltration

1. Ultrafiltration may be used to remove excessive fluid and improve congestion symptoms in AHF patients with fluid retention (class of recommendation IIb, level of evidence B).
2. Ultrafiltration may be considered in patients with congestive HF unresponsive to conventional medical therapy (class of recommendation IIb, level of evidence C).

Diuretics are important in the treatment of congestion and fluid retention in AHF. However, if congestion is severe, ultrafiltration can be considered. Several early clinical trials have confirmed that ultrafiltration can effectively remove excessive fluid in the initial treatment of HF⁴⁶⁾⁴⁷⁾ and moreover provides the advantage of increased weight loss and reduced rehospitalization rate.⁴⁸⁾⁴⁹⁾ However, in a subsequent clinical study including patients with cardio-renal syndrome undergoing ultrafiltration versus medical treatment, ultrafiltration had negative effects in terms of renal dysfunction, persistent congestion symptoms, and renal function at 96 hours.⁵⁰⁾⁵¹⁾ A recent meta-analysis on the usefulness of ultrafiltration reported a beneficial effect on weight loss but no effect on creatinine reduction or mortality.⁵²⁾

Because ultrafiltration is invasive, its use should be considered according to the physician's experience, advice of nephrologist, and the additional cost. To remove excessive fluid, ultrafiltration may be considered in some AHF patients whose conditions are refractory to medical treatment including diuretic therapy.

Intra-aortic balloon pump

1. It is reasonable to use an intra-aortic balloon pump (IABP) in patients with AHF in a state of cardiogenic shock due to mechanical causes (e.g., ventricular septal rupture, acute mitral insufficiency) accompanied by acute myocardial infarction (AMI) (class of recommendation IIa, level of evidence C).
2. The routine use of IABP in patients with AHF and cardiogenic shock accompanied by AMI is not recommended (class of recommendation III, level of evidence B).

The use of an IABP increases cardiac output by the balloon situated inside the aorta deflates quickly at the start of ventricular systole results in decreasing cardiac afterload, and then expands during ventricular diastole to allow blood to move farther into the proximal aorta. IABP is used in AHF patients with cardiogenic shock, low cardiac output, and reduced ventricular contraction if hypoperfusion persists in multiple organs; however, the benefit of IABP use has only been clinically proven in a small number of cases. It is difficult to conduct clinical studies on patients with acute heart attack accompanied by cardiogenic shock. For this reason, evidence regarding the clinical outcomes of such patients is largely based on retrospective research or single-center case reports or studies, which could not exclude patient selection bias. A meta-analysis found that IABP use did not affect in-hospital mortality in patients with AMI but no cardiogenic shock; however, among patients with accompanying cardiogenic shock, IABP use was associated with a large and significant (28%) decrease in mortality rate.⁵³⁾ Another meta-analysis, which included patients with AMI and cardiogenic shock, IABP use did not affect in-hospital mortality among patients who received medical therapy without coronary revascularization, was associated with a significant decrease in mortality among patients treated with thrombolytics, and was associated with a significant increase in mortality among patients who underwent percutaneous coronary intervention; however, in the overall population of patients included in the analysis, there was no significant inter-group difference regarding in-hospital mortality rates.⁵⁴⁾ A similar influence of treatment method on the effectiveness of IABP use was also reported regarding 30-day mortality rates.⁵⁵⁾ In the IABP-SHOCK II study, which proved the efficacy of IABP in patients with AMI accompanied by cardiogenic shock, most patients first underwent percutaneous coronary intervention; the 30-day and 12-month mortality rates did not differ between the control group and the IABP group.⁵⁶⁾⁵⁷⁾ Therefore, if percutaneous coronary intervention is performed as primary treatment for AMI, routine IABP use is not recommended in patients with AMI, even in the presence of concomitant cardiogenic shock.⁵³⁾⁵⁵⁻⁵⁷⁾ To date, no randomized large-scale studies have reported data on the outcomes of patients with AMI and accompanying cardiogenic shock due to mechanical complications such as ventricular septal defect or papillary muscle rupture. However, based on reports from some single institutes and on retrospective observational study results, IABP use may be helpful as a bridge for hemodynamic stabilization before surgical correction.⁵⁸⁾⁵⁹⁾ No significant clinical research has evaluated the effectiveness of IABP use in patients with left ventricular systolic dysfunction due to causes other than acute coronary syndrome.⁶⁰⁻⁶²⁾

Mechanical circulatory support and cardiac transplantation

1. It is reasonable to use extracorporeal life support (ECLS) in patients with AHF and acute cardiac arrest refractory to existing drug therapies (class of recommendation IIa, level of evidence B).
2. It is reasonable to use ECLS when HF is unresponsive to drug treatment and progresses to cardiogenic shock (class of recommendation IIa, level of evidence B).
3. It is reasonable to use a percutaneous ventricular assist device before deciding the indication for cardiac transplantation or implantation of a left ventricular assist device (LVAD) in patients who are hemodynamically unstable and suspected to have organ damage (class of recommendation IIb, level of evidence B).

The use of a mechanical circulatory support device (MCSD) may be effective in hemodynamically unstable patients with decompensated AHF despite sufficient cardiac stimulation. MCSD use should be considered in cases in which a decision cannot be made about additional treatments such as heart transplantation or use of a surgical or implantable LVAD, as well as in cases in which recovery of heart function could be expected. However, MCSD use may be helpful only for the duration of several hours or days. If the patient is not a good candidate for LVAD implantation, the MCSD may have to be removed. Since MCSD use requires anticoagulant therapy, it carries the risk of complications such as thrombosis and hemorrhage; additionally, distal ischemia may occur during the process of catheter insertion and maintenance treatment. Therefore, careful consideration is necessary when deciding whether or not to use an MCSD.

The use of ECLS, typically in the form of extracorporeal membrane oxygenation, became more widespread starting in 2000, when Bartlett et al. reported a 44% increase in survival rate among patients with cardiogenic shock.⁶³⁾ The use of ECLS in AHF increased exponentially since Chen et al.⁶⁴⁾ reported a significant increase in survival rate associated with ECLS use during cardiopulmonary resuscitation for acute cardiac arrest due to a cardiac disorder. Eighty-four studies including a total of 1,494 patients analyzed the efficacy of ECLS in AHF or cardiac arrest and confirmed its usefulness.⁶⁵⁾

Recently developed percutaneous ventricular assist devices such as TandemHeart and Impella are widely used overseas. Small randomized studies found that the temporary use of an LVAD was associated with short-term hemodynamic improvement, but the effect on survival rate was unclear.⁶⁶⁻⁶⁸⁾ The extensive use of a temporary LVAD is difficult to implement in Korea due to economic constraints but may be considered depending on patient's state. Such MCSDs have their own merits, demerits and characteristics, which warrants restriction of their use, along with adequate indications.⁶⁹⁾ ECLS is superior to other strategies if both ventricles must be assisted simultaneously or if oxygenation capabilities are compromised.⁷⁰⁾ TandemHeart, a percutaneous ventricular assist device approved for domestic use in Korea, can be used as an implantable LVAD if the intravenous catheter is left in the left atrium. However, the use of TandemHeart is limited because it requires atrial septal puncture and as well as much expensive than ECLS. Therefore, in Korea, it is reasonable to prioritize the use of ECLS in AHF refractory to existing drug treatments.⁷¹⁾

Cardiac transplantation is the most fundamental treatment in patients with terminal HF refractory to drug treatment. Transplantation is commonly chosen in patients with CHF, but also in some patients with AHF, cardiogenic shock, and cardiac arrest who received a percutaneous circulatory support device that could not be successfully removed. However, in such cases, cardiac

transplant surgeries mostly proceed before sufficient pre-transplantation evaluation of the patient's state can be performed, and the long-term prognosis after transplantation is poor. Therefore, the choice of cardiac transplant surgery should be made carefully.

Surgical correction

Acute cardiac failure can be caused by mechanical complications secondary to various cardiovascular diseases. Patient prognosis can be improved by appropriate surgical therapy (Table 3).⁷²⁾⁷³⁾ Echocardiography is very important for differential diagnosis and in deciding the treatment methods.

Ventricular free wall rupture occurs in 0.8–6.2% of patients with myocardial infarction (MI).⁷⁴⁾ Making an early diagnosis is difficult because, if pericardial tamponade occurs, most patients die within a few minutes. However, it is possible to make the diagnosis in subacute cases involving thrombosis or adhesion at the rupture site. Rupture causes cardiogenic shock, rapid falls in blood pressure, and mental deterioration or loss of consciousness; in some patients, such symptoms are preceded by chest pain, nausea, ST-segment elevation, and T-wave changes.⁷⁵⁾ If ventricular free wall rupture is suspected, echocardiography must be conducted immediately. The diagnosis of ventricular free wall rupture can be established if there are signs of paroxysmal events and pericardial effusion >1 cm is noted.⁷⁶⁾ Pericardiocentesis, fluid infusion, and intravenous inotropics can be considered for stabilizing the patient's hemodynamics, but surgery must not be delayed.

Ventricular septal rupture was originally thought to occur within 1–5 days of MI in 1–2% of patients, but these rates have been decreasing due to the improvements in MI diagnosis rates.⁷⁷⁾⁷⁹⁾ AHF and cardiogenic shock are usually followed by MI, and ventricular septal rupture is suspected in patients with signs of pansystolic murmur in the left lower sternal border. Echocardiography can be used to confirm the diagnosis and assess the perforation location and size, as well as to determine whether mitral valve pathology is present. In order to avoid expansion of the rupture, surgery must be considered as soon as ventricular septal rupture is diagnosed, regardless of whether hemodynamic stability is maintained.

Table 3. Indication for surgical treatment in patients with AHF

Indication for surgical treatment
Cardiogenic shock in MI patients with multi-vessel coronary artery disease
Ventricular septal rupture
Ventricular free wall rupture
Acute exacerbation of valvular heart disease
Failure or thrombosis of a prosthetic valve
Rupture of an aortic aneurysm into the pericardium, or aortic dissection
Ischemic papillary muscle rupture or malfunction, chorda rupture, endocarditis, or acute mitral insufficiency due to external injury
Endocarditis, aortic dissection, or acute aortic insufficiency caused by closed chest trauma
Ruptured aneurysm of the sinus of Valsalva
Acute exacerbation of cardiac insufficiency in patients receiving mechanical circulatory support
Hemodynamically unstable pulmonary embolism for which thrombolytic treatment is not possible

Ponikowski P, et al.; 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) Developed with the special contribution of the Heart Failure Association (HFA) of the ESC, *European Heart Journal* 2016; 37 (27): 2129–2200, doi: 10.1093/eurheartj/ehw128. Reproduced by permission of Oxford University Press on behalf of the European Society of Cardiology. © European Society of Cardiology. AHF = acute heart failure; MI = myocardial infarction.

Acute mitral insufficiency within 2–7 days occurs in 10% of patients who experience cardiogenic shock after MI⁸⁰⁾ but can also be caused by total or partial papillary muscle rupture, papillary muscle dysfunction, trauma, and endocarditis, and can be accompanied by severe pulmonary congestion and cardiogenic shock. Since an apical systolic murmur might not be clearly heard due to a sharp rise in left atrial pressure, it is crucial to conduct an echocardiographic evaluation to check for mitral insufficiency and assess left ventricular systolic function. Transesophageal echocardiography might also be needed in some cases. If acute mitral insufficiency is diagnosed, surgery must be considered immediately.⁸¹⁾

Paroxysmal events of AHF can also be caused by prosthetic valve thrombosis, aortic disease, acute aortic insufficiency, or severe pulmonary embolism. Echocardiographic evaluation is needed to differentiate these diseases and plan appropriate treatment.

MONITORING ACUTE HEART FAILURE PATIENTS

1. In AHF patients, heart rate, rhythm, blood pressure, respiration rate, and oxygen saturation must be continuously monitored (class of recommendation I, level of evidence C).
2. The effectiveness of hypervolemia correction must be checked on a daily basis through the assessment of symptoms (class of recommendation I, level of evidence C).
3. When starting diuretics injections or renin-angiotensin-aldosterone antagonist treatment, renal function and serum electrolyte levels (sodium, potassium, etc.) must be checked daily (class of recommendation I, level of evidence C).
4. Using an arterial line to monitor blood pressure can be helpful in patients with low blood pressure or those with persistent symptoms despite treatment (class of recommendation IIa, level of evidence C).

Symptoms of AHF include dyspnea on exercise, orthopnea, paroxysmal nocturnal dyspnea, peripheral edema, abdominal discomfort, nausea, and vomiting. As most AHF patients show symptoms of dyspnea, the improvement in dyspnea represents a crucial aspect of treatment response and thus should be monitored. Orthopnea, one of the symptoms of AHF patients, has the strongest correlation with elevated pulmonary capillary wedge pressure, providing 90% sensitivity.⁸²⁾ However, there are many cases in which symptoms disappear after diuretic therapy even though left ventricular filling pressure remains elevated. Thus, improvement in symptoms such as dyspnea cannot be the sole criterion for judging treatment effectiveness.⁸³⁾⁸⁴⁾

Physical examinations used to assess congestion include evaluation of body weight, jugular venous pressure, and rales on auscultation, as well as the assessment of edema. Change in body weight can be caused by malnutrition or cardiac cachexia, but daily weight fluctuations are usually related to fluctuations in residual body fluid. Therefore, to assess congestion, it is important to obtain an accurate estimate of body weight. This can be achieved using a standardized scale with a precision of 50 g units and conducting measurements at pre-established times before urinating, eating, or taking drugs. It is commonly known that jugular venous pressure reflects right atrial pressure, which in turn reflects left ventricular filling pressure, which essentially corresponds to the pulmonary capillary wedge pressure.⁸³⁾ Jugular venous pressure represents an accessible indicator of congestion and is helpful for monitoring the effectiveness of HF treatment, having been shown to predict the rehospitalization rate.⁸⁵⁾ However, caution should be exercised when interpreting jugular venous pressure values in patients with primary pulmonary hypertension or tricuspid

insufficiency. Furthermore, it is challenging to measure and interpret jugular venous pressure in obese patients and in those with respiratory diseases.

The presence of rales on auscultation can indicate fluid overload, which can be caused by but is not specific to HF. Moreover, the absence of rales on auscultation does not mean that the lung is clear of pulmonary congestion, so interpretations must be done with caution.⁸³⁾ Similarly, chest radiography cannot accurately identify the presence of congestion in HF patients.⁸³⁾ Peripheral edema in HF patients is usually connected to elevated right atrial pressure due to left ventricular failure. Lower-extremity edema may resolve with diuretic therapy, but the excess fluid may be redistributed toward the sacrum because such patients spend most of their time in bed. The redistribution of excess fluid into the sacral area can be suspected if lower-extremity edema improves without weight loss.

Right cardiac catheterization represents the most standardized method of monitoring congestion and perfusion in HF patients. However, routine use of invasive monitoring is not advised; rather, it should only be performed if it is difficult to determine treatment direction by non-invasive methods (for details, please refer to section *Right heart catheterization* of Part I of this guideline, which discusses invasive diagnostic methods including right cardiac catheterization).

HOSPITAL DISCHARGE

Treatment objective

1. In HF patients, a clear and attainable treatment objective must be established, and appropriate education must be conducted prior to discharge (class of recommendation I; level of evidence A).

Since HF patients have high readmission and mortality rates after discharge, attainable treatment objectives must be established and suitable education should be provided before discharge.⁸⁶⁻⁹²⁾ The following aspects must be assessed before hospital discharge: state of acute aggravating factors; whether symptoms and signs of HF including congestion have improved; whether the maintenance dose of oral diuretics is stable. The following must be comprehensively assessed and confirmed: whether critical medication to improve HF prognosis is being injected at the right dosage; whether the patient is aware of medication usage precautions; how well appropriate treatments were implemented during hospitalization; whether appropriate assessment and treatment of associated diseases is maintained; whether the patient is well educated about smoking, eating, and exercise requirements; and whether the patient or their guardian has the capacity to manage the situation.⁹²⁻⁹⁵⁾

Improving quality of medical treatment using clinical quality indicators

Clinical quality can be understood as the degree of achieving the desired outcome and scientific relevance. Terms that refer to indicators measuring clinical quality are quality indicator, clinical indicator, and performance measure.⁹⁶⁾ Generally, the definition of a quality indicator includes the quantitative tool itself and is considered the same as a clinical quality indicator. Worldwide, there is a need to amass more data and conduct further evaluations in order to develop powerful quality indicators.

Domestically, medical institutions conduct quality evaluations based on clinical quality indicators aiming to improve clinical quality in MI patients. Moreover, the quality of medical

institutions or clinical systems can be compared using disease-specific quality indicators that include information obtained during diagnosis, treatment, post-discharge management, and outpatient follow-up. A recent trend is to use prognostic indicators to develop relevant performance measures. To do so for HF patients, further post-discharge outcome data should be collected from individual studies and, possibly, national health registries.⁹⁶⁻⁹⁸⁾

The American College of Cardiology recommends employing the following prognostic indicators: overall HF-related mortality, 30-day mortality, HF readmission rate, and 30-day readmission rate due to HF. Other performance measures include left ventricle ejection fraction during hospitalization, number of outpatient appointments, and use of ACE inhibitors/angiotensin receptor blockers and beta-blockers in hospitalized patients with HFrEF.⁹⁹⁾

Maeda conducted a systematic review with 2 prospective cohort studies and a randomized study, concluding that patients who received post-discharge ACE inhibitors/angiotensin receptor blockers and beta-blockers as well as pre-discharge education using printed materials had improved prognosis, but the benefit was not reflected in measuring left ventricular parameters or counselling for smoking cessation.¹⁰⁰⁾ Fonarow et al.¹⁰¹⁾ recently reported a multi-center prospective interventional clinical trials to determine the impact of various clinical performance indicators in terms of mortality rates. Treatment with ACE inhibitors/angiotensin receptor blockers, beta-blocker therapy, HF education, and use of an implantable cardioverter defibrillator reduced mortality rates by 49%, 55%, 31%, and 36%, respectively.¹⁰¹⁾

Domestic studies indicated that medication use during hospitalization affects the long-term prognosis of AHF patients and the use of ACE inhibitors/angiotensin receptor blockers and beta-blockers significantly decreases mortality rates. The representative clinical quality indicators can be selected based on these domestic and international evidence.¹⁰²⁾¹⁰³⁾ However, the lack of a platform for standardized patient education, low self-care ability, and limitations of the self-reporting system preclude the uniform application of international performance parameters in the domestic context. To improve clinical quality and prognosis of Korean patients with HF, the development and use of performance or clinical quality indicators must be promoted.

Management programs for heart failure patients

1. A multidisciplinary HF management program should encourage patients with a high risk of readmission to receive guideline-based treatments in order to decrease HF-related readmissions (class of recommendation I, level of evidence A).
2. It is reasonable to schedule hospital visits within 1–2 weeks from discharge or phone follow-up within 3 days from discharge (class of recommendation IIa, level of evidence B).

Among HF patients, self-care represents a challenging and multidimensional issue.¹⁰⁴⁾ Patients must understand how to monitor their symptoms and weight loss, restrict their salt intake, take medication as prescribed, and remain physically active. In fact, many HF patients need to participate in disease control educational programs, even after discharge (**Table 4**). Patients who received education within the hospital have more knowledge regarding HF both at discharge and at 1 year after discharge.¹⁰⁵⁾ One study reported that pre-discharge education decreased the hospitalization duration within 6 months after the initial discharge, thereby also decreasing costs and death rates.⁸⁹⁾

Table 4. Pre-discharge management and strategy for long-term management of AHF

Pre-discharge management and long-term management strategy

Plan follow-up strategy

Register for disease control programs, receive education, and plan appropriate lifestyle changes

Optimize medication dosage

Consider the usage of appropriate treatment aids

Prevent early readmission

Alleviate symptoms; improve quality of life and survival rates

AHF = acute heart failure.

Before hospital discharge, the acute phase of HF must be resolved. There must be no congestion, and oral diuretic prescriptions must have remained stable for at least 48 hours before the patient can be considered for discharge.⁸⁸⁾⁹⁰⁾¹⁰⁶⁾ Treatment regimens with agents such as beta-blockers, which can improve the long-term progression of HF, must be optimized, and appropriate education should be provided to patients, family members, and other caretakers. Care before and after discharge must follow the standardized consultation guide provided by the Korean Heart Failure Association, as such an approach has been shown to improve prognosis. Caution should be taken when administering beta-blockers to patients who received an inotropic drug during hospitalization, as well as when administering ACE inhibitors/angiotensin receptor blockers or aldosterone antagonists to patients who experienced severe azotemia or to patients at high risk for hyperkalemia. Body fluid levels must be maintained and blood pressure must be properly controlled. In patients with atrial fibrillation, heart rate must also be well controlled. Hospitalization can be an opportunity for educating patients and family members, while health management teams can plan appropriate treatments.

HF patients, especially those who are hospitalized repetitively, have poor prognosis and are vulnerable, especially during the transition from inpatient to outpatient status because of the naturally progressive nature of HF, complicated medication prescriptions, concomitant diseases, and involvement of many doctors. Patient education and printed materials should be provided during hospitalization and upon discharge. The printed material must include guidelines for appropriate activity levels, meals, discharge prescriptions, outpatient appointments, weight control, and actions to be performed when symptoms worsen (**Table 5**).⁸⁶⁾ Post-discharge medication treatment plans based on guidelines improve treatment results.⁸⁶⁾⁹²⁾⁹⁴⁾¹⁰⁷⁾ Many studies reported an association of improved treatment results with stronger discharge guidance on HF and unified follow-up.⁸⁷⁾¹⁰⁸⁾¹⁰⁹⁾ The addition of an hour of standardized HF guidance and education delivered by a nurse specialist at discharge enhanced clinical treatment results and self-care ability, leading to effective treatment maintenance, decreased medical costs, and reduced readmission and death rates.⁸⁹⁾

Table 5. Matters that must be addressed by HF management programs

Essentials in HF management program

Optimizing drug treatment and appliance therapy

Education on relevant topics including treatment compliance and self-care

Education on self-monitoring symptoms and controlling diuretics

Optimizing the follow-up strategy, including the timing of visits to the clinic, calling in and remote monitoring

Handling acute exacerbation

Appropriate adjustments according to changes in weight, nutritive condition, activity level, quality of life, and blood tests findings

Additional treatment plans in case of HF progression

Psychosocial support for the patients and their families

HF = heart failure.

Many aspects other than patient education are important for the success of follow-up management. All aspects of the patient's medical treatment, especially changes in prescription or additional diagnostic information, must be recorded clearly and in a timely manner to avoid misunderstandings between the many specialists that might handle follow-up management. One other important factor that must be addressed during transitional management is letting the patient and guardian know what will happen in the clinic, giving information about medication control and plans for follow-up management, and preparing them for detecting possible signs or symptoms of deterioration. Early follow-up after discharge can minimize the delay between a change in the patient's condition and the corresponding adjustment in the treatment plan, which will increase the understanding of the patient's condition and lower the risk of readmission.¹¹⁰⁾ Additional visits to the hospital within 7–14 days post-discharge or phone follow-up within 3 days is considered appropriate. Effective follow-up management of HF requires a good understanding of the socioeconomic and mental context of each patient, as well as providing the patient with adequate educational materials and inclusive plans, which are helpful for increasing self-care ability.^{111–113)}

Management plans for HF patients must incorporate guideline-based treatment methods. The HF patient and clinician must aim to establish a suitable time schedule for follow-up management, to clarify the requirements for meals and physical activity levels, and to plan cardiac rehabilitation and continuous education regarding complications, standardized management guidelines for cardiovascular diseases, and secondary prevention of such disease. Clinicians must also be aware of the psychosocial, ethological, and socioeconomic issues that HF patients and their caregivers might face.^{114–119)}

Palliative care

There are many cases in which HF progression becomes unpredictable, so it is difficult to decide when to start providing palliative care. However, palliative care is usually considered in patients who require repeated hospitalization for multiple acute episodes despite optimized drug treatment, who are not candidates for cardiac transplantation or MCS/D use, and who experience symptoms of New York Heart Association functional class IV accompanied by a chronic decrease in quality of life, cardiac cachexia, low serum albumin levels, or imminent death. In such patients, the focus of treatment shifts to improving quality of life, controlling symptoms, promptly detecting and treating acute exacerbations, and generally maintaining the patient's well-being from a physical, mental, social, and spiritual perspective. Moreover, in HF patients, palliative care should aim to completely resolve the symptoms of associated diseases by addressing the patient's physical, mental, and religious demands. Furthermore, the palliative treatment strategy should clarify the conditions under which cardiopulmonary resuscitation need not be conducted or the implantable cardioverter defibrillator should be stopped.

CONCLUSION

In this part of guideline, the treatment of AHF, including pharmacological and non-pharmacological therapies, monitoring, and discharge plan were covered. In AHF patients with fluid retention, a prompt diuretic use is encouraged with careful monitoring of symptoms, electrolyte imbalance and renal function. Intravenous vasodilators and short-term intravenous infusion of inotropic agents may improve symptoms in certain condition of AHF patients. As well as guideline-directed medical therapy, ultrafiltration, IABP, MCS/D,

cardiac transplantation, and surgical management can be considered according to the indications. A clear and attainable treatment objective must be established, and appropriate education must be conducted prior to discharge. A multidisciplinary HF management program should be applied to improve outcome especially in high-risk HF patients.

SUPPLEMENTARY MATERIALS

Supplementary Table 1

Criteria used to judge the level of evidence and establish the class of recommendation for AHF

[Click here to view](#)

Supplementary Table 2

Formulations typically used with each class of recommendation

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