CONTINUING MEDICAL EDUCATION

De Novo Acute Heart Failure and Acutely Decompensated Chronic Heart Failure

Astrid Hummel, Klaus Empen, Marcus Dörr, and Stephan B. Felix

SUMMARY

Background: Heart failure is one of the most common diseases of adults in Europe, with an overall prevalence of 1–2%. Among persons aged 60 and above, its prevalence is above 10% in men and 8% in women. Acute heart failure has a poor prognosis; it is associated with a high rate of rehospitalization and a 1-year mortality of 20–30%.

Methods: This review is based on pertinent literature, including guidelines, retrieved by a selective search in PubMed.

Results: There are different types of acute heart failure; the basic diagnostic assessment is performed at once and consists of ECG, echocardiography, and the measurement of N-terminal pro-brain natriuretic peptide (NTproBNP) and troponin levels. The most common causes of decompensation are arrhythmia, valvular dysfunction, and acute cardiac ischemia, each of which accounts for 30% of cases. The potential indication for immediate revascularization should be carefully considered in cases where acute heart failure is due to coronary heart disease. The basic treatment of acute heart failure is symptomatic, with the administration of oxygen, diuretics, and vasodilators. Ino-tropic agents, vasopressors, and temporary mechanical support for the circulatory system are only used to treat cardiogenic shock.

Conclusion: The treatment of acute heart failure is markedly less evidence-based than that of chronic heart failure. Newer treatment approaches that are intended to improve outcomes still need to be tested in multicenter trials.

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Heat failure (or congestive heart failure, as it is often called in the English-speaking countries) has an overall prevalence of 1–2% and is thus one of the most common diseases affecting adults in Europe today (1). In Germany, it is the most common main diagnosis leading to hospitalization (2). Its prevalence is under 0.5% in persons aged 20 to 40, but much higher in persons over age 60 (more than 10% in men, more than 8% in women) (2, 3). In recent years, the introduction of drug therapy with beneficial long-term effects (e1–e4), implantable defibrillators (e5), and cardiac resynchronization systems (e6) has lessened the 5-year mortality of chronic heart failure, which was previously more than 75% in men and about 60% in women (4). In contrast, there has been essentially no improvement in the prognosis of patients with acute heart failure. The in-hospital mortality of this condition was about 7% in the EuroHeart Failure Survey II, albeit with marked differences depending on the clinical type of acute heart failure (*Figure 1*) (5). The 1-year mortality was 20–30%; patients with de novo acute heart failure fared somewhat better than those with acutely decompensated chronic heart failure (ADCHF) (6).

Learning objectives

This article should enable readers to:

- know the epidemiology and pathogenesis of acute heart failure
- know, and apply knowledge of, the main symptoms and signs of acute heart failure, and the relevant diagnostic tests
- be familiar with the treatments of acute and acutely decompensated chronic heart failure.

University Medicine Greifswald, Department of Internal Medicine B:
Dr. med. Hummel, PD Dr. med. Empen, Prof. Dr. med. Dörr, Prof. Dr. med. Felix

Prevalence

Heart failure is one of the most common diseases of adults in Europe, with a prevalence of 1–2%.

Methods

This review is based on pertinent literature retrieved by a selective search in PubMed up to October 2014, including the guidelines of the European Society of Cardiology and the German Cardiac Society.

The definition of acute and chronic heart failure

Heart failure is defined pathophysiologically as the inability of the heart to supply the body's tissues with an adequate amount of blood under conditions of normal cardiac filling pressure (7).

Acute and chronic heart failure differ both in their temporal course and in their treatment.

Acute heart failure has two forms: newly arisen ("de novo") acute heart failure and acutely decompensated chronic heart failure (ADCHF). According to the EuroHeart Failure Survey II (5), two-thirds of all patients admitted to a hospital with acute heart failure already have a known history of heart failure.

The events precipitating acute decompensation mainly consisted of arrhythmias, valvular dysfunction, and acute cardiac ischemia, each of which accounted for about 30% of cases. Further precipitating factors are listed in *Box 1*.

Pathogenesis

The subtype of heart failure known as "heart failure with reduced ejection fraction" (HF-REF) is characterized by left-ventricular dilatation (ventricular remodeling) and a reduction of the left-ventricular ejection fraction (LVEF) below 40%. In contrast, "heart failure with preserved ejection fraction" (HF-PEF, diastolic heart failure) is characterized by normal left-ventricular volume and ejection fraction (LVEF >50%), although the thickness of the ventricular wall and the ratio of left-ventricular mass to end-diastolic volume is increased, as is the stiffness of the myocardium. Despite the structural and functional differences between HF-REF and HF-PEF, decompensated heart failure of either type displays the same pathophysiologic mechanisms, i.e., rising cardiac filling pressures and diminished intrinsic contractility of cardiac myocytes (3). Often, about two weeks before acute decompensation, backward failure of the left ventricle arises, resulting in pulmonary congestion (*Figure 2*) (8, 9). Sodium and fluid retention are major components of the clinical picture of heart failure, causing shortness of breath and peripheral edema. Cardiac and renal

FIGURE 1

In-hospital mortality as a function of the past history and clinical presentation of acute heart failure (from [5]). ADCHF, acutely decompensated chronic heart failure

function are linked; the treatment of heart failure with diuretics and the recommendation for salt restriction are based on this close relationship.

The neuroendocrine system plays a key role in the progression of heart failure. In order to keep the vital organs adequately perfused, the sympathetic nervous system is activated, leading to increased myocardial contractility. Prolonged activation of the adrenergic system and the renin-angiotensin-aldosterone (RAA) system impairs ventricular remodeling and leads to the destruction of myocardial tissue by apoptosis. Activation of the RAA system also leads to myocardial fibrosis, which increases the stiffness of the myocardium and impairs left-ventricular relaxation in diastole. Pharmacologic blockade of the adrenergic and RAA systems can improve the survival of patients with chronic heart failure; this clearly indicates the central importance of the neuroendocrine system in the treatment of heart failure (3). The clinical presentations of acute heart failure are delineated in *Figure 3*.

Clinical features and diagnostic assessment

According to data from the ADHERE registry (10), 89% of patients hospitalized for acute heart failure complain on admission of shortness of breath; 68% have pulmonary crackles and 66% have peripheral edema, indicating the retrograde effects of impaired left-ventricular pump function, with increased amounts of blood in the pulmonary vessels and in the peripheral

Mortality

Acute heart failure carries a high in-hospital mortality and a poor prognosis at 1 year with respect to recurrent hospitalization and mortality.

Pathophysiological definition

Heart failure is defined pathophysiologically as the inability of the heart to supply the body's tissues with an adequate amount of blood under conditions of normal cardiac filling pressure.

BOX 1

Causes of, and factors affecting, acute heart failure (AHF) and acutely decompensated chronic heart failure (ADCHF)*

Events with acute clinical deterioration (often, AHF)

- Coronary heart disease
 - Acute coronary syndrome
 - Mechanical complications of acute coronary syndrome, e.g., ventricular septal defect, acute mitral insufficiency, right-heart infarct
- Valvular diseases
- Myocarditis
 - Acute myocarditis
 - Peripartal cardiomyopathy
- Hypertension/arrhythmia
 - Hypertensive crisis
 - Tachycardia or severe bradycardia
- Circulatory failure
 - Acute pulmonary embolism
 - Pericardial tamponade
 - Aortic dissection
- Surgical interventions and perioperative complications

Events with delayed clinical deterioration (often, acutely decompensated chronic heart failure [ADCHF])

- Infections, e.g., endocarditis
- Acute exacerbation of chronic obstructive pulmonary disease/asthma
- Anemia
- Worsening of renal failure
- Inadequate fluid and salt intake, non-compliance with prescribed medication
- Drug side effects and interactions, e.g., non-steroidal anti-inflammatory drugs, corticosteroids
- Uncontrolled arterial hypertension
- Hypo- or hyperthyroidism
- Alcohol and drug abuse

* modified from (7, e7)

veins. Further typical findings include pleural effusions, a third heart sound, tachycardia, and congested neck veins (e8). The patient's past medical history should be carefully considered, including the chronology of the onset of symptoms, any already diag-

nosed cardiac illness, and precipitating factors (*Box 1*). The most important physical findings are peripheral edema and abnormalities of the heart and lungs. A heart murmur may indicate a significant valvular problem. Percussion and auscultation of the chest may arouse suspicion of a large pleural effusion, pulmonary congestion, or pulmonary edema.

The differential diagnostic evaluation of shortness of breath in suspected acute heart failure includes an ECG and a chest x-ray as basic tests, as well as two further investigations: echocardiography and measurement of the natriuretic peptides pro-brain natriuretic peptide (BNP) and/or NT-proBNP (*Figure 4*). The blood pressure, heart rate and rhythm, peripheral oxygenation, and urine excretion should be closely monitored and the measured values documented at frequent intervals. Immediate diagnostic evaluation enables the recognition of precipitating factors that may require treatment without delay (e.g., arrhythmias, a hypertensive crisis, or an acute coronary syndrome) and the early initiation of treatment to stabilize hemodynamic and respiratory function.

Echocardiography is the main imaging study and a standard test in all patients with suspected acute heart failure. It can detect severe valvular dysfunction or a pericardial effusion and can be used to assess the size of the cardiac ventricles and atria. In particular, it enables both global and local evaluation of left-ventricular function. A left-ventricular ejection fraction under 35% indicates heart failure with reduced left-ventricular systolic function (HF-REF).

The quotient of early-diastolic flow across the mitral valve to relaxation of the mitral ring (E/A ratio) can be determined by Doppler echocardiography and may indicate elevated left-ventricular end-diastolic pressure (e8).

Natriuretic peptide levels that are in the reference range (i.e., below the cutoff points of 100 pg/mL BNP or 300 pg/mL NT-proBNP), in a patient who has not yet received treatment, effectively rule out heart failure as the cause of symptoms (high negative predictive value) (7). Values above the reference range indicate probable heart failure, but other causes of shortness of breath must also be considered. A second determination of a BNP/NT-proBNP level on discharge can enable better prediction of the risk of rehospitalization and of 1-year mortality (e9): if the BNP/NT-proBNP level declines by less than 50%, the risk of rehospitalization or death within 12 months is elevated by 40% (e10).

Clinical manifestations

Acute heart failure is characterized by a rise in cardiac filling pressures, with dyspnea as the main symptom.

Diagnostic evaluation

Echocardiography is the main imaging study and a standard test in all patients with suspected acute heart failure.

FIGURE 2

The myocardium-specific troponin levels may be mildly elevated in acute, or severe chronic, heart failure. This is prognostically significant: patients in the ADHERE registry with acute heart failure who had elevated troponin levels had a markedly higher in-hospital mortality than those with normal troponin levels (8.0% vs. 2.7%, $p < 0.001$) (10). Myocardial troponin release is thought to be due to direct injury to cardiac myocytes as a result of cardiac decompensation (12). Depending on the patient's symptoms and signs and, in particular, on the time course of the myocardium-specific troponin levels, an acute coronary syndrome may have to be considered as a possible cause of acute heart failure, and then treated as necessary.

To identify other possible causes of the clinical manifestations, renal function parameters and the serum albumin, hemoglobin, electrolyte, and thyroid-stimulating hormone levels should be measured in all patients with suspected heart failure.

Treatment strategies

The goals of treating acute heart failure are

- to improve symptoms,
- to achieve hemodynamic stability,

- to prevent recurrent heart failure, and
- to reduce mortality.

The patients at highest risk of dying as a consequence of acute heart failure (elderly patients and those with a low systolic blood pressure, renal dysfunction, signs of peripheral hypoperfusion, and acute coronary syndrome [6]) should be monitored and treated on an intensive care unit (Figure 5).

The treatment of acute heart failure is markedly less evidence-based than that of chronic heart failure with reduced ejection fraction (HF-REF). In the following sections, treatment recommendations are accompanied by recommendation grades from the guideline of the European Society of Cardiology (7).

Acute coronary angiography and revascularization

Acute coronary syndrome accounts for 11% of cases of de novo acute heart failure (infarct with ST-segment elevation) and one-third of all cases of acutely decompensated chronic heart failure (5). Acute coronary syndrome with heart failure is an indication for immediate angiographic evaluation and revascularization (grade I recommendation, level A evidence) (13).

Biomarkers

In patients with acute heart failure, elevated biomarker levels signify a worse prognosis.

Laboratory tests for differential diagnosis

Renal function parameters and the serum albumin, hemoglobin, electrolyte, and thyroid-stimulating hormone levels should be measured in all patients with suspected acute heart failure.

The frequency of clinical subtypes of acute heart failure (from [5])

FIGURE 3

The Shock Trial led to the finding that rapid revascularization in cases of cardiogenic shock was associated with a 67% (relative) reduction in mortality that persisted over six years (14). It is currently being investigated whether the revascularization of all high-grade coronary artery stenoses in patients with cardiogenic shock confers an advantage with respect to survival compared to the revascularization only of the vessel responsible for the infarct (CULPRIT-SHOCK, NCT 01927549). Patients who undergo coronary angiography and (if indicated) revascularization during their first hospitalization for de novo acute heart failure have a significantly lower mortality and rehospitalization rate (15).

Oxygen administration and non-invasive vs. invasive ventilation

Patients with hypoxemia (oxygen saturation below 90% by pulse oximetry) should be given supplemental oxygen (grade I recommendation, level C evidence). The goal is to raise the arterial oxygen saturation to at least 95%. In patients who also suffer from chronic obstructive pulmonary disease, the risk of hypercapnia under oxygen therapy must be borne in mind.

Persistent hypoxemia and/or a respiratory rate above 20/min despite drug treatment and oxygen administration for pulmonary edema should be treated initially with non-invasive ventilation (grade IIa recommendation, level B evidence). Meta-analyses have shown that this lowers mortality by 37–45% compared to the

standard treatment of acute pulmonary edema (16, e11). Invasive ventilation is recommended for patients who show signs of respiratory exhaustion or are in cardiac shock, or whose consciousness is impaired.

Analgesia and sedation

Opioids are helpful for patients who are agitated because of anxiety and dyspnea; they should be given cautiously, with continuous monitoring of the peripheral oxygen saturation and the frequency and depth of breathing (grade IIa recommendation, level C evidence). Opioid administration for patients with pulmonary edema seems reasonable for pathophysiological reasons, as opioids are vasodilators that lessen preload.

Diuretics and ultrafiltration

Diuretics are commonly given to patients in heart failure and have a beneficial effect on symptoms (grade I recommendation, level B evidence); their clinically evident utility is pathophysiologically explicable by the reduction of pulmonary congestion, but a putative improvement in outcome through the use of diuretics has not yet been well documented in prospective trials (17). In particular, the optimal dose, mechanism of action, and mode of administration (oral, intravenous bolus, or continuous infusion) remain unclear. Intravenous loop diuretics should be given to treat acute decompensation because of their faster effect and the independence of their uptake from gastrointestinal resorption, which is

Acute coronary syndrome

Acute coronary syndrome accounts for 11% of cases of de novo acute heart failure and one-third of all cases of acutely decompensated chronic heart failure.

The goals of treatment

- To improve symptoms
- To achieve hemodynamic stability
- To prevent recurrent heart failure
- To reduce mortality

FIGURE 4

Diagnostic assessment of patients with suspected acute heart failure (based on the guidelines of the European Society of Cardiology [7])

unreliable in the setting of right-heart decompensation (18). The DOSE trial was the first to investigate the dosage of loop diuretics in acute heart failure; it did not reveal any significant difference between furosemide boli every twelve hours and a continuous infusion of the drug, or between a low and a high dose of furosemide, with respect to either symptomatic improvement or the worsening of renal failure if present (17). The higher diuretic dose was found to be superior with respect to secondary endpoints (improvement of dyspnea, negative fluid balance, weight loss) and had fewer serious side effects, although it more often led to a transient worsening of renal failure. For persistent (diuretic-resistant) edema, a combination of two diuretics with different mechanisms of action has been found useful (a loop diuretic combined with a Na^+/Cl^- -cotransport inhibitor for sequential nephron blockade) (19). This potent combination may, however, cause hypokalemia, renal failure, and excessive fluid loss. No prospective trials of this mode of treatment are yet available.

Aside from diuretic resistance, it is thought that long-term treatment with diuretics might increase morbidity and mortality, by way of neurohormonal ac-

tivation, electrolyte disturbances, or worsening of renal failure. The acute cardiorenal syndrome (type 1), defined as a worsening of renal function in patients with acutely decompensated heart failure, arises in 25–33% of patients with ADCHF (20). To determine the appropriate treatment, patients with this syndrome should be classified on pathophysiologic grounds as suffering from either prerenal renal failure with predominant left-heart failure (forward failure) or intrarenal renal failure due to renal venous congestion (backward failure) (20, 21).

In the UNLOAD trial, patients with more than two signs of volume overload were treated for 48 hours with either intravenous diuretics or ultrafiltration (22). Ultrafiltration led to a greater loss of volume and weight with a comparable improvement of dyspnea. There was no significant difference in the rise of creatinine concentration in the two groups. The patients in the ultrafiltration group needed fewer rehospitalizations for heart failure. The much-criticized CARRESS heart failure trial (23, e12) did not confirm these findings in patients with acutely decompensated chronic heart failure and worsening

Basic treatment of acute heart failure

The basic treatment of acute heart failure consists of the administration of oxygen, loop diuretics, and vasodilators, and of opioids when indicated.

Diuretics

Diuretics have a beneficial effect on symptoms; their utility is pathophysiologically explicable by the reduction of pulmonary congestion, but prospective trials have not yet shown that they improve the outcome of acute heart failure.

BOX 2

Indications for mechanical volume reduction and renal replacement therapy *

- Intractable symptomatic hypervolemia (ascites, pleural effusion, pulmonary edema)
- Recurrent hospitalization for cardiac decompensation (twice or more in 6 months) in the presence of KDIGO Stage IV renal failure (estimated glomerular filtration rate [eGFR] <30 mL/min)
- Isolated right-heart failure with recurrent cardiac decompensation (twice or more in 6 months)

*as recommended by the Heart and Kidney Working Group of the German Cardiac Society and the German Nephrological Society (21)

renal failure in the twelve weeks before, and the first ten days after, hospital admission for acutely decompensated chronic heart failure. Metra et al. showed that creatinine elevation is not, in itself, an unfavorable prognostic factor in acutely decompensated chronic heart failure (24). In the ESCAPE trial, for example, patients with higher creatinine values or hemoconcentration during the recompensation phase actually had a higher 180-day survival (25). Higher mortality, and a higher risk of rehospitalization, were associated only with worsening of renal failure with the simultaneous persistence of signs of congestion (24). The current indications for ultrafiltration and renal replacement techniques are listed in *Box 2*.

Vasodilators

Vasodilators lower the systolic blood pressure and should therefore only be used in normotensive patients (systolic blood pressure above 110 mm Hg). In particular, nitroglycerin and sodium nitroprusside can be used to treat pulmonary edema in the presence of hypertension (grade IIa, resp. IIb recommendation, level B evidence). Nitroglycerin lowers pulmonary capillary pressure by lessening cardiac preload. It is relatively contraindicated in patients with severe aortic or mitral stenosis. Sodium nitroprusside lowers cardiac preload and afterload; the dose should be

titrated slowly, and only in conjunction with invasive blood pressure monitoring.

Cotter et al, in a randomized trial on 110 patients with severe pulmonary edema in the setting of acutely decompensated chronic heart failure (26), found that a high nitrate dose combined with a low diuretic dose yielded better effects than the reverse, with respect to both oxygen saturation and the rate of mechanical ventilation and/or myocardial infarction (reduction of the latter endpoints from 46% to 25%).

The current recommendations of the European Society of Cardiology (ESC) regarding the use of nitrates in acute heart failure are based on this trial alone.

Inotropic drugs and vasopressors

Patients with refractory hypotension (cardiogenic shock) can be treated with inotropic agents such as dobutamine (grade IIa recommendation, level C evidence). The common side effects of inotropic agents are sinus tachycardia, arrhythmia, and myocardial ischemia. If inotropic agents are ineffective, vasopressors are recommended, above all norepinephrine (grade IIb recommendation, level C evidence). Increased left-ventricular afterload is a common side effect.

Milrinone, a phosphodiesterase-3 inhibitor, was studied as a putative treatment for chronic heart failure in the OPTIME-CHF trial; it was found that milrinone neither improved symptoms nor shortened the hospital stay, but was associated with higher rates of cardiac arrhythmias and hypotension (e13). Milrinone and dobutamine may also increase mortality (27); thus, they should be given as briefly as possible and in the lowest effective dose (grade IIb recommendation, level C evidence).

The calcium-sensitizer levosimendan has been approved for use in Germany and a number of other countries, but not in the USA. It increases myocardial contractility by sensitizing the contractile proteins to calcium, while simultaneously exerting a vasodilating effect by blocking the ATP-dependent calcium channels of vascular smooth muscle. In the REVIVE-I and REVIVE-II trials, patients with acute heart failure who were given a levosimendan infusion for 24 hours in addition to standard treatment experienced a rapid improvement of symptoms with persistent lowering of natriuretic peptide levels, but with a tendency toward symptomatic hypotension and cardiac arrhythmia (28).

Refractory edema (diuretic resistance)

In this situation, a combination of two diuretics with different mechanisms of action is useful (a loop diuretic combined with a Na⁺/Cl⁻-cotransport inhibitor for sequential nephron blockade).

Vasodilators

Because they lower the systolic blood pressure, vasodilators should only be used in normotensive patients (systolic blood pressure >110 mm Hg).

TABLE

Treatment approaches in acute heart failure

Substance	Mechanism of action	Effects	Major side effects	Reduction of mortality	References
Istaroxime	Calcium-ATPase activator	– Lowers PCWP – Improves ventricular filling in diastole		No data	(32)
Rolofylline	Adenosine-receptor antagonist	– Does not improve dyspnea – Does not alter rehospitalization rate – Does not improve renal failure	Seizures	No	(33)
Nesiritide	Natriuretic peptide	– Improves dyspnea	Hypotension	No	(34)
Tesozenan	Dual endothelin-receptor antagonist	– Does not improve dyspnea – Does not alter rehospitalization rate	Hypotension	No	(35)
Tolvaptan	Vasopressin antagonist	– Improves dyspnea – Increases diuresis – Improves hyponatremia		No	(36)
Omecamtiv mecarbil	Cardiac myosin activator	– Improves dyspnea only at highest dose		No data	Atomic AHF, ESC 2013 presentation*
Serelaxin	Recombinant human relaxin-2	– Improves dyspnea – Acts as a vasodilator – Improves renal failure	Hypotension	Yes, at 180 days (analysis of a pre-specified safety endpoint)	(37)
Cinaciguat	Guanylate cyclase activator	– Lowers PCWP	Severe hypotension	No data	(38)
Urodilatin	Natriuretic peptide	– Improves dyspnea – Lowers PCWP	Hypotension	No data	(39)

AHF, acute heart failure; PCWP, pulmonary capillary wedge pressure;

*Teerlink JR, McDonagh T: Atomic AHF. Acute treatment with Omecamtiv Mecarbil to increase contractility in acute heart failure. Congress Abstract 709 European Society of Cardiology 2013

The SURVIVE trial revealed no lowering of overall mortality at 180 days through the use of levosimendan (compared to dobutamine), despite a significant acute lowering of natriuretic peptide levels (29). The only evidence to date that levosimendan lowers the mortality of cardiac patients comes from meta-analyses (30).

The use of levosimendan is recommended when there is suspicion that chronic beta-blockade is worsening hypotension in cardiogenic shock and lessening the responsiveness to vasopressor drugs (grade IIb recommendation, level C evidence).

Multi-organ system failure is the most important predictor of death from cardiogenic shock (13). Accordingly, the prevention and treatment of multi-

organ system failure in the intensive care unit has a significant effect on survival (13, e14).

Cardiac glycosides have a positive inotropic effect. Their use in the treatment of acute heart failure is limited to the treatment of absolute tachycardia in atrial fibrillation; in this situation, the negative chronotropic effect of cardiac glycosides inhibits atrioventricular conduction (grade I recommendation, level C evidence). In atrial fibrillation with tachycardia and hemodynamic compromise, electrical cardioversion should be considered (grade I recommendation, level C evidence).

Dronedarone and class I antiarrhythmic drugs are contraindicated in acute heart failure (grade III recommendation, level A evidence). Only amiodarone can be

Inotropic agents

Patients with refractory hypotension (cardiogenic shock) can be treated with inotropic agents such as dobutamine.

Vasopressors

If inotropic agents are ineffective, vasopressors are recommended, above all norepinephrine. Increased left-ventricular afterload is a common side effect.

FIGURE 5

Treatment algorithm for acute heart failure [from 7] ESICM, European Society of Intensive Care Medicine; ICU, intensive care unit; SpO₂, blood oxygen saturation

used for the purpose of non-urgent pharmacological cardioversion (grade I recommendation, level C evidence).

Mechanical support of the circulation

If cardiogenic shock persists despite optimization of the patient's volume status and treatment with inotropic

drugs and vasopressors, and if it is considered to be potentially reversible, a reasonable treatment option is transient mechanical support of the circulatory system (hours to 30 days) with a microaxial pump in the left ventricle or a minimized heart-lung machine (extra-corporeal membrane oxygenation, ECMO). Such temporary measures serve as a "bridge to recovery"

Multi-organ system failure

Multi-organ system failure is the most important predictor of death from cardiogenic shock. Accordingly, the prevention and treatment of multi-organ system failure in the intensive care unit has a significant effect on survival.

Levosimendan

The REVIVE-I and REVIVE-II trials revealed a rapid improvement of symptoms with persistent lowering of natriuretic peptide levels, but with a tendency toward symptomatic hypotension and cardiac arrhythmia.

(grade IIa recommendation, level C evidence). The only application of mechanical circulatory support that has been tested in randomized trials is the use of an intra-aortic balloon pump (IABP) to treat cardiogenic shock due to myocardial infarction. Although this has been a standard treatment for many years, the IABP-Shock-II trial showed in 2012 that it did not reduce mortality (31).

New treatments

Various new treatment approaches have been proposed in recent years with the aim of improving the outcome of patients with acute heart failure, but a better outcome has not been documented in any of the clinical trials carried out to date (*Table*), nor did any of the treatments lessen the rehospitalization rate.

The only recent trial of a drug for acute heart failure that revealed a benefit of any kind was the RELAX trial, in which the administration of serelaxin (recombinant human relaxin-2, a peptide of pregnancy) was found to result in more rapid relief of symptoms, but did not lower the rate of rehospitalization (37). The hemodynamic effect of serelaxin is to lower both the pulmonary capillary and pulmonary arterial pressure and the pulmonary and systemic vascular resistance, without raising the cardiac index (40). Hypotension was found to be more common under treatment with serelaxin than with placebo (ca. 4–6 mm Hg). The RELAX trial was an acute trial involving a 48-hour infusion of serelaxin starting on admission to the hospital. Interestingly, the 180-day mortality of patients treated with serelaxin was 37% lower than that of those who were given a placebo (4% absolute risk reduction); although 180-day mortality was not a predefined secondary endpoint, this was found in a protocol-specified additional efficacy analysis. The finding is now being followed up in a trial on over 6000 patients, which ought to have sufficient power to document improved survival if this is, in fact, the case (RELAX-AHF-2, NCT01870778).

Prevention of thromboembolism

During the cardiac recompensation phase, and for as long as the patient is confined to bed, a prophylactic drug against thromboembolism should be given, e.g., a low-molecular-weight heparin (grade I recommendation, level A evidence). Atrial fibrillation is an indication for full anticoagulation (grade I recommendation, level A evidence).

Mechanical support of the circulation

If cardiogenic shock persists and is potentially reversible, a reasonable treatment option is transient mechanical support of the circulation (for up to 30 days) with a microaxial pump in the left ventricle or a minimized heart-lung machine.

The transition to chronic heart failure—further treatment

Once the patient with acute heart failure or acutely decompensated chronic heart failure has become stable, the question of further treatment of the cause of the condition should be addressed. Drug treatment for chronic heart failure should be prescribed on discharge in accordance with the guidelines, and follow-up appointments should be scheduled so that the effects of the medications can be monitored and their doses adjusted as needed.

Conflict of interest statement

Dr. Empen has served as a paid consultant for Novartis and has received honoraria from Novartis for preparing continuing medical education events.

Prof. Felix has served as a paid consultant for Novartis and Cardioventris. He has received reimbursement of congress participation fees and lecture honoraria relating to continuing medical education events from Novartis, Bayer, Berlin Chemie, Cardioventris, and Servier. He has received honoraria in a third-party account for carrying out clinical studies relating to the topic of this article, as well as financial support for a research project that he initiated, from Bayer, Novartis, and Medtronic.

Prof. Dörr and Dr. Hummel state that they have no conflict of interest.

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New treatments

New treatments have not yet been able to improve the prognosis of acute heart failure.

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Prevention of thromboembolism

During the cardiac recompensation phase, and for as long as the patient is confined to bed, a prophylactic drug against thromboembolism should be given, e.g., a low-molecular-weight heparin.

Further treatment

Once the patient with acute heart failure or acutely decompensated chronic heart failure has become stable, the question of further treatment of the cause of the condition should be addressed.

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Corresponding author

Prof. Dr. med. Stephan B. Felix
Universitätsmedizin Greifswald
Klinik und Poliklinik für Innere Medizin B
Ferdinand-Sauerbruch-Str.
D-17475 Greifswald, Germany
innereb@uni-greifswald.de

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Question 1

What clinical type of acute heart failure carries the highest mortality?

- a) Acute heart failure triggered by hypertension
- b) Right-heart decompensation
- c) Cardiogenic shock
- d) Acute decompensation of chronic heart failure
- e) Pulmonary edema

Question 2

How is the acute decompensation of chronic heart failure pathogenetically triggered?

- a) Rise of cardiac filling pressures
- b) Left-ventricular ejection fraction below 40%
- c) Increased myocardial stiffness
- d) Activation of the renin-angiotensin-aldosterone system
- e) Myocardial necrosis

Question 3

What is the main symptom of acute heart failure?

- a) Ankle edema
- b) Dyspnea
- c) Tachycardia
- d) Palpitations
- e) Cough

Question 4

What diagnostic test should be performed as soon as possible in acute heart failure, along with an ECG and a chest x-ray?

- a) Left-heart catheterization
- b) Right-heart catheterization
- c) Computed tomography of the heart
- d) Magnetic resonance imaging of the heart
- e) Echocardiography

Question 5

What laboratory test in the emergency room can rule out acute heart failure as the cause of dyspnea?

- a) Troponin
- b) Uric acid
- c) Norepinephrine
- d) BNP/NT-proBNP
- e) Albumin

Question 6

When does worsened renal failure in acute heart failure carry an elevated risk of rehospitalization and mortality?

- a) When the patient has persistent evidence of congestion
- b) When the creatinine level rises above 30 µmol/L
- c) When the hematocrit rises above 5%
- d) When sequential nephron blockade becomes necessary
- e) When the patient has hyperuricemia

Question 7

Which of the following measures has been shown to lower mortality (relatively) in cardiogenic shock?

- a) Levosimendan administration
- b) Non-invasive ventilation
- c) Coronary revascularization as soon as possible
- d) Ultrafiltration
- e) Serelaxin administration

Question 8

When is the use of inotropic agents and vasopressors indicated?

- a) When the patient is oliguric because of cardiorenal syndrome
- b) When there is refractory ankle edema
- c) When hypotension arises under treatment with sodium nitroprusside
- d) When cardiogenic shock arises
- e) When hypertensive pulmonary edema arises

Question 9

What is the indication for the administration of cardiac glycosides in acute heart failure?

- a) To treat hypotension
- b) To treat absolute tachyarrhythmia in atrial fibrillation
- c) To lower myocardial oxygen consumption
- d) To bring about pharmacological cardioversion
- e) To prevent ventricular arrhythmias

Question 10

When is ultrafiltration indicated in acute heart failure?

- a) When there is refractory, symptomatic hypervolemia
- b) In the setting of diuretic resistance
- c) If the creatinine level rises in negative fluid balance
- d) To prevent polyuria
- e) In the setting of hypertensive pulmonary edema

CONTINUING MEDICAL EDUCATION

De Novo Acute Heart Failure and Acutely Decompensated Chronic Heart Failure

Astrid Hummel, Klaus Empen, Marcus Dörr, and Stephan B. Felix

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