Complete Summary

GUIDELINE TITLE

Guidelines on the diagnosis and treatment of acute heart failure.

BIBLIOGRAPHIC SOURCE(S)

Task Force on Acute Heart Failure of the European Society of Cardiology. Guidelines on the diagnosis and treatment of acute heart failure. Sophia Antipolis (FR): European Society of Cardiology; 2005. 36 p. [241 references]

GUIDELINE STATUS

This is the current release of the guideline.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s)/intervention(s) for which important revised regulatory and/or warning information has been released.

- February 28, 2008, Heparin Sodium Injection: The U.S. Food and Drug Administration (FDA) informed the public that Baxter Healthcare Corporation has voluntarily recalled all of their multi-dose and single-use vials of heparin sodium for injection and their heparin lock flush solutions. Alternate heparin manufacturers are expected to be able to increase heparin production sufficiently to supply the U.S. market. There have been reports of serious adverse events including allergic or hypersensitivity-type reactions, with symptoms of oral swelling, nausea, vomiting, sweating, shortness of breath, and cases of severe hypotension.
- June 8, 2007, Troponin-I Immunoassay: Class I Recall of all lots of the Architect Stat Troponin-I Immunoassay. The assay may report falsely elevated or falsely decreased results at and near a low level, which may impact patient treatment.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Acute heart failure (AHF)

GUIDELINE CATEGORY

Diagnosis
Evaluation
Treatment

CLINICAL SPECIALTY

Cardiology
Critical Care
Emergency Medicine

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To describe the rationale behind the diagnosis and treatment of acute heart failure (AHF) in the adult population

TARGET POPULATION

Adults with acute heart failure (AHF)

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis/Monitoring/Evaluation

1. Clinical evaluation
    - Chest auscultation
    - Heart palpation and auscultation
2. Chest x-ray
3. Chest computed tomography (CT) with or without contrast angiography or scintigraphy
4. Electrocardiography (ECG)
5. Magnetic resonance imaging (MRI)
6. Transoesophageal echocardiography

7. Cardiac index (CI)
8. Laboratory tests
    - Arterial blood gas
    - Blood count
    - Platelet count
    - International Normalized Ratio (INR)
    - C-reactive protein
    - D-dimer
    - Urea and electrolytes
    - Blood glucose
    - Creatine kinase muscle band (CKMB), cardiac troponin I (TnI)/troponin T (TnT)
    - Transaminases
    - Urinalysis
    - Plasma B-type natriuretic protein (BNP) or N-terminal prohormone brain natriuretic peptide (NTproBNP)
9. End-tidal CO_2
10. Echocardiography with or without Doppler imaging
11. Angiography
12. Coronary arteriography
13. Insertion of pulmonary artery catheter (PAC)
14. Non-invasive monitoring
    - Temperature
    - Respiratory rate
    - Heart rate
    - Blood pressure
    - Laboratory tests
    - Pulse oximetry (SaO_2)
    - Doppler techniques (cardiac output)
15. Invasive monitoring
    - Arterial line (blood pressure)
    - Central venous pressure line for monitoring venous oxygen saturation (SvO_2)
    - Pulmonary artery catheter

Management/Treatment

1. Oxygen support
    - Ventilatory support (non-invasive)
        - Continuous positive airway pressure (CPAP)
        - Non-invasive positive pressure ventilation (NIPPV)
    - Endotracheal intubation
2. Morphine
3. Anticoagulation
    - Low-molecular-weight heparin
    - Unfractionated heparin
4. Vasodilators
    - Nitrates (glyceryl trinitrate, 5-mononitrate; isosorbide dinitrate)
    - Sodium nitroprusside (SNP)
    - Nesiritide
    - Calcium antagonists (Considered, but not recommended)
    - Brain natriuretic peptides (BNP)

5. Angiotensin-converting enzyme (ACE) inhibitors
6. Diuretics
    - Loop diuretics
        - Furosemide
        - Bumetanide
        - Torasemide
    - Thiazide diuretics (e.g., hydrochlorothiazide)
    - Metolazone
    - Spironolactone
7. Beta-blockers
    - Metoprolol
    - Bisoprolol
    - Carvedilol
8. Inotropic agents
    - Dopamine
    - Dobutamine
    - Phosphodiesterase inhibitors (PDEIs)
        - Milrinone
        - Enoximone
    - Levosimendan
    - Vasopressor therapy
    - Epinephrine
    - Norepinephrine
    - Cardiac glycosides (digitalis)
9. Surgical treatment
10. Mechanical assist devices
11. Heart transplantation
12. Assessment and treatment of underlying diseases and comorbidities in acute heart failure, including coronary artery disease, valvular disease, prosthetic valve thrombosis, aortic dissection, hypertension, renal failure, pulmonary diseases and bronchoconstriction, arrhythmias, and perioperative acute heart failure

MAJOR OUTCOMES CONSIDERED

- Mortality
- In-hospital mortality
- Re-hospitalization
- Incidence of ventricular tachycardia
- Need for endotracheal intubation
- Survival

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

Level of evidence A: Data derived from multiple randomized clinical trials or meta-analyses

Level of evidence B: Data derived from a single randomized clinical trial or large non-randomized studies

Level of evidence C: Consensus of opinion of the experts and/or small studies, retrospective studies and registries

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Classes of Recommendations

Class I: Evidence and/or general agreement that a given diagnostic procedure/treatment is beneficial, useful, and effective

Class II: Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the treatment

- Class IIa: Weight of evidence/opinion is in favour of usefulness/efficacy
- Class IIb: Usefulness/efficacy is less well established by evidence/opinion

Class III*: Evidence or general agreement that the treatment is not useful/effective and in some cases may be harmful

*Use of Class III is discouraged by the European Society of Cardiology (ESC)

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The Task Force recommendations were circulated among a review board and approved by the Committee for Practice Guidelines (CPG), and by the European Society of Intensive Care Medicine (ESICM).

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The class of recommendations (I-III) and levels of evidence (A-C) are defined at the end of the "Major Recommendations" field.

Definitions, Diagnostic Steps, Instrumentation, and Monitoring of the Patients with Acute Heart Failure (AHF)

Definition and Clinical Classification of AHF

Definition

Acute heart failure is defined as the rapid onset of symptoms and signs secondary to abnormal cardiac function. It may occur with or without previous cardiac disease. The cardiac dysfunction can be related to systolic or diastolic dysfunction, to abnormalities in cardiac rhythm, or to preload and afterload mismatch. It is often life threatening and requires urgent treatment.

AHF can present itself as acute *de novo* (new onset of acute heart failure in a patient without previously known cardiac dysfunction) or acute decompensation of chronic heart failure (CHF).

The patient with AHF may present with one of several distinct clinical conditions (see Table 2 in the original guideline document):

- Acute decompensated heart failure (*de novo* or as decompensation of CHF) with signs and symptoms of AHF, which are mild and do not fulfill criteria for cardiogenic shock, pulmonary oedema, or hypertensive crisis.
- Hypertensive AHF: Signs and symptoms of heart failure are accompanied by high blood pressure and relatively preserved left ventricular function with a chest radiograph compatible with acute pulmonary oedema.
- Pulmonary oedema (verified by chest x-ray) accompanied by severe respiratory distress, with crackles over the lung and orthopnoea, with O_2 saturation usually <90% on room air prior to treatment.
- Cardiogenic shock: Cardiogenic shock is defined as evidence of tissue hypoperfusion induced by heart failure after correction of preload. There is no clear definition for haemodynamic parameters, which explains the differences in prevalence and outcome reported in studies (see Table 2 in the original guideline document), but cardiogenic shock is usually characterized by reduced blood pressure (BP) (systolic BP <90 mmHg or a drop of mean arterial pressure >30 mmHg) and/or low urine output (<0.5 ml/kg/h), with a pulse rate >60 bpm with or without evidence of organ congestion. There is a continuum from low cardiac output syndrome to cardiogenic shock.
- High output failure is characterized by high cardiac output, usually with high heart rate (caused by arrhythmias, thyrotoxicosis, anaemia, Paget's disease, iatrogenic or by other mechanisms), with warm peripheries, pulmonary congestion, and sometimes with low BP as in septic shock.
- Right heart failure is characterized by low output syndrome with increased jugular venous pressure, increased liver size and hypotension.

Various other classifications of the AHF syndrome are utilized in coronary care and intensive care units. The Killip classification is based on clinical signs and chest x-ray findings, and the Forrester classification is based on clinical signs and haemodynamic characteristics. These classifications have been validated in AHF after AMI and thus are best applied to *de novo* AHF. The third "clinical severity" classification has been validated in a cardiomyopathy service and is based on clinical findings. It is most applicable to chronic decompensated heart failure.

The Clinical Syndrome of AHF

AHF is a clinical syndrome, with reduced cardiac output, tissue hypoperfusion, increase in the pulmonary capillary wedge pressure, and tissue congestion. The underlying mechanism may be cardiac or extra-cardiac, and may be transient and reversible with resolution of the acute syndrome or may induce permanent damage leading to chronic heart failure. The cardiac dysfunction can be related to systolic or diastolic myocardial dysfunction (mainly induced by ischaemia or infection), acute valvular dysfunction, pericardial tamponade, abnormalities of cardiac rhythm, or preload/afterload mismatch. Multiple extra-cardiac pathologies may result in AHF by changing the cardiac loading conditions for example (i) increased afterload due to systemic or pulmonary hypertension or massive pulmonary emboli, (ii) increased preload due to increased volume intake or reduced excretion due to renal failure or endocrinopathy, or (iii) high output state due to infection, thyrotoxicosis, anaemia, and Paget's disease. Heart failure can be complicated by co-existing end-organ disease. Severe heart failure can also induce multi-organ failure, which may be lethal.

Appropriate long-term medical therapy and, if possible, anatomical correction of the underlying pathology may prevent further AHF syndrome "attacks" and improve the poor long-term prognosis associated with this syndrome. The clinical AHF syndrome may be classified as predominantly left or right forward failure, left or right backward failure, or a combination of these. (See the original guideline document for further discussion of these.)

Pathophysiology of AHF

The Vicious Cycle in the Acute Failing Heart

The final common denominator in the syndrome of AHF is a critical inability of the myocardium to maintain a cardiac output sufficient to meet the demands of the peripheral circulation. Irrespective of the underlying cause of AHF, a vicious cycle is activated that, if not appropriately treated, leads to chronic heart failure and death. This is shown in Figure 2 in the original guideline document, and is described elsewhere in the literature.

In order for patients with AHF to respond to treatment the myocardial dysfunction must be reversible. This is particularly important in AHF due to ischaemia, stunning or hibernation, where a dysfunctional myocardium can return to normal when appropriately treated.

Myocardial Stunning

Myocardial stunning is the myocardial dysfunction that occurs following prolonged ischaemia, which may persist in the short-term even when normal blood flow is restored. This phenomenon has been described experimentally as well as clinically. Mechanisms of dysfunction are excessive oxidative stress, changes in Ca^{++} homeostasis, and Ca^{++} desensitization of contractile proteins, as well as myocardial depressant factors. The intensity and duration of stunning is dependent on the severity and duration of the preceding ischaemic insult.

Hibernation

Hibernation is defined as an impairment of myocardial function due to severely reduced coronary blood flow although myocardial cells are still intact. By improving blood flow and oxygenation, hibernating myocardium can restore its normal function. Hibernation can be regarded as an adaptive mechanism to reduce oxygen consumption to prevent ischaemia and necrosis following reduced blood flow to the myocardium.

Hibernating myocardium and stunning can co-exist. Hibernation improves in time with reinstitution of blood flow and oxygenation, whilst stunned myocardium retains inotropic reserve and can respond to inotropic stimulation. Since these mechanisms depend on the duration of myocardial damage, a rapid restoration of oxygenation and blood flow is mandatory to reverse these pathophysiological alterations.

Diagnosis of AHF

The diagnosis of AHF is based on the symptoms and clinical findings, supported by appropriate investigations such as electrocardiography (ECG), chest x-ray, biomarkers, and Doppler-echocardiography (see figure 3 of the original guideline document). The patient should be classified according to previously described criteria for systolic and/or diastolic dysfunction (see figure 4 of the original guideline document), and by the characteristics of forward or backward left or right heart failure.

Clinical Evaluation

Systematic clinical assessment of the peripheral circulation, venous filling, and peripheral temperature are important.

Right ventricular filling in decompensated heart failure may usually be evaluated from the central jugular venous pressure. When the internal jugular veins are impractical for evaluation (e.g., due to venous valves) the external jugular veins can be used. Caution is necessary in the interpretation of high measured central venous pressure (CVP) in AHF, as this may be a reflection of decreased venous compliance together with decreased right ventricular compliance even in the presence of inadequate right ventricular filling.

Left sided filling pressure is assessed by chest auscultation, with the presence of wet rales in the lung fields usually indicating raised pressure. The confirmation, classification of severity, and clinical follow up of pulmonary congestion and pleural effusions should be done using the chest x-ray.

Class I recommendation, level of evidence C

Again, in acute conditions the clinical evaluation of left sided filling pressure may be misleading due to the rapidly evolving clinical situation. Cardiac palpation and auscultation for ventricular and atrial gallop rhythms (S3, S4) should be performed. The quality of the heart sounds, and presence of atrial and ventricular gallops and valvular murmurs are important for diagnosis and clinical assessment. Assessment of the extent of arteriosclerosis by detecting missing pulses and the presence of carotid and abdominal bruits is often important, particularly in elderly subjects.

ECG

A normal ECG is uncommon in AHF. The ECG is able to identify the rhythm and may help determine the aetiology of AHF and assess the loading conditions of the heart. It is essential in the assessment of acute coronary syndromes. The ECG may also indicate acute right or left ventricular or atrial strain, perimyocarditis, and pre-existing conditions such as left and right ventricular hypertrophy or dilated cardiomyopathy. Cardiac arrhythmia should be assessed in the 12-lead ECG as well as in continuous ECG monitoring.

Chest X-ray and Imaging Techniques

Chest x-ray and other imaging should be performed early for all patients with AHF to evaluate pre-existing chest or cardiac conditions (cardiac size and shape) and

to assess pulmonary congestion. It is used both for confirmation of the diagnosis, and for follow-up of improvement or unsatisfactory response to therapy. Chest x-ray allows the differential diagnosis of left heart failure from inflammatory or infectious lung diseases. Chest computed tomography (CT) scan with or without contrast angiography and scintigraphy may be used to clarify the pulmonary pathology and diagnose major pulmonary embolism. Computed tomography scan, transesophageal echocardiography, or magnetic resonance imaging (MRI) should be used in cases of suspicion of aortic dissection.

Laboratory Tests

A number of laboratory tests should be performed in AHF patients (see table below). Arterial blood gas analysis (Astrup) enables assessment of oxygenation (pO_2), respiratory adequacy (pCO_2), acid-base balance (pH), and base deficit, and should be assessed in all patients with severe heart failure. Non-invasive measurement with pulse oximetry and end-tidal CO_2 can often replace Astrup (**Level of evidence C**) but not in very low output, vasoconstricted shock states. Measurement of venous O_2 saturation (i.e., in the jugular vein) may be useful for an estimation of the total body oxygen supply-demand balance.

Laboratory Tests in Patients Hospitalized with AHF	
Blood Count	Always
Platelet Count	Always
International Normalized Ratio (INR) of thromboplastin time	If patient anticoagulated or in severe heart failure
C-Reactive Protein (CRP)	To be considered
D-dimer	To be considered (may be falsely positive if C-reactive protein elevated or patient has been hospitalized for prolonged period)
Urea and Electrolytes (Na^+, K^+, urea, creatinine)	Always
Blood Glucose	Always
Creatine kinase muscle band (CKMB), cardiac troponin I (TnI)/troponin T (TnT)	Always
Arterial blood gases	In severe heart failure or in diabetic patients
Transaminases	To be considered
Urinalysis	To be considered
Plasma B-type natriuretic peptide (BNP) or N-terminal prohormone brain natriuretic peptide (NTproBNP)	To be considered
Other specific laboratory tests should be taken for differential diagnostic purposes or in order to identify end-organ dysfunction.	

Plasma B-type natriuretic peptide (BNP) is released from the cardiac ventricles in response to increased wall stretch and volume overload and has been used to exclude and/or identify congestive heart failure in patients admitted for dyspnoea to the emergency department. Decision cut points of 300 pg/mL for NT-proBNP and 100 pg/mL for BNP have been proposed, but the older population has been poorly studied. During "flash" pulmonary oedema, BNP levels may remain normal

at the time of admission. Otherwise, BNP has a good negative predictive value to exclude heart failure. The data are not consistent on reference values and on the effect of treatment. Various clinical conditions may affect the BNP concentration, including renal failure and septicaemia. If elevated concentrations are present, further diagnostic tests are required. If AHF is confirmed, increased levels of plasma BNP and NT-pro BNP carry important prognostic information. The exact role of BNP remains to be fully clarified.

Echocardiography

Echocardiography is an essential tool for the evaluation of the functional and structural changes underlying or associated with AHF as well as in the assessment of acute coronary syndromes.

Class I recommendation, level of evidence C

Echocardiography with Doppler imaging should be used to evaluate and monitor regional and global left and right ventricular function, valvular structure and function, possible pericardial pathology, mechanical complications of acute myocardial infarction, and, on rare occasions, space occupying lesions. Cardiac output can be estimated by appropriate Doppler aortic or pulmonary time velocity contour measurements. An appropriate echo-Doppler study can also estimate pulmonary artery pressures (from the tricuspid regurgitation jet) and has been also used for the monitoring of left ventricular preload. Echocardiography has not been validated with right heart catheterisation in patients with AHF.

Other Investigations

In cases of coronary artery related complications such as unstable angina or myocardial infarction, angiography is important and angiography-based revascularization therapy has been shown to improve prognosis.

Class I recommendation, level of evidence B

Coronary arteriography is also often indicated in prolonged AHF, unexplained by other investigations, as recommended in the guidelines for diagnosis of CHF. Insertion of a pulmonary artery catheter (PAC) may assist the diagnosis of and follow up AHF. See the section below on pulmonary artery catheter for further details.

Goals of the Treatment of AHF

The immediate goals are to improve symptoms and to stabilize the haemodynamic condition (see Table 4, Figure 5 in the original guideline document).

An improvement in the haemodynamic parameters (primarily an increase in cardiac output and stroke volume and a reduction in the pulmonary capillary wedge pressure and right atrial pressure) have traditionally been regarded as beneficial effects of the treatment of AHF. An improvement in haemodynamic parameters only may be misleading, and a concomitant improvement in symptoms (dyspnoea and/or fatigue) is generally required. These short-term

benefits must also be accompanied by favourable effects on longer term outcomes. This is likely to be achieved by avoidance, or limitation, of myocardial damage.

Dyspnoea is the dominant symptom in AHF but is subjective. Objective assessment can be made by standardized tools, such as the Borg Rating of perceived exertion, indexes of dyspnoea, and various visual analogue scales. Changes from the initial assessment may be used as measures of improvement or deterioration. Another objective of treatment is the reduction in the clinical signs of heart failure, although these may often be difficult to quantify. A reduction in body weight and/or an increase in diuresis are beneficial effects of therapy in congestive and oliguric patients with AHF. Similarly, an improvement in oxygen saturation and in laboratory tests such as renal and/or hepatic function and/or serum electrolytes are meaningful goals of treatment. Plasma BNP concentration can reflect haemodynamic improvement and decreased levels are beneficial. However, short-term haemodynamic benefits may be dissociated from a favourable effect on prognosis. Thus, a beneficial (or at least a neutral) effect on patient outcome is required in addition to an improvement in symptoms and/or clinical signs.

Beneficial effects of therapy on outcome include a reduction in the duration of intravenous vasoactive therapy, the length of stay (both in the intensive care unit and in the hospital), and a reduction in the readmission rate with an increase in the time to readmission. A reduction in both in-hospital and long-term mortality is the major goal of treatment although the effect of short-term treatment may be dissociated from the long-term effects.

Lastly, a favourable safety and tolerability profile is also necessary for any treatment used in patients with AHF. Any agent used in this condition should be associated with a low withdrawal rate with a relatively low incidence of untoward side effects.

Organization of the Treatment of AHF

Best results are achieved if patients with AHF are treated promptly by expert staff in areas reserved for heart failure patients, be it an emergency area, acute coronary care, or surgical or medical intensive care. An experienced cardiologist and/or other suitably trained staff should treat AHF patients. The diagnostic services should provide early access to diagnostic procedures such as echocardiography and coronary angiography, as needed.

Treatment of patients with AHF requires a treatment plan in the hospital system.

Class I recommendation, level of evidence B

Comparative studies have shown shorter hospitalization time in patients treated by staff trained in heart failure management. The treatment of AHF should be followed by a subsequent HF clinic programme when applicable and as recommended by European Society of Cardiology (ESC) guidelines.

The care and information needs of the acutely ill patient and his/her family will usually be addressed by expert nurses. Heart failure staff nurses and cardiologist/heart failure/intensive care specialists should be given the opportunity for continuing professional education.

Instrumentation and Monitoring of Patients in AHF

Monitoring of the patient with AHF should be initiated as soon as possible after his/her arrival at the emergency unit, concurrently with ongoing diagnostic measures addressed at determining the primary aetiology. The types and level of monitoring required for any individual patient vary widely depending on the severity of the cardiac decompensation and the response to initial therapy. Local logistic issues may also be relevant. There are no prospective randomized controlled outcome-based studies on the use of different monitoring modalities in AHF. The guidelines discussed here are therefore based on expert opinion.

Non-Invasive Monitoring

In all critically ill patients, monitoring the routine basic observations of temperature, respiratory rate, heart rate, the ECG, and blood pressure are mandatory. Some laboratory tests should be done repeatedly (i.e., electrolytes, creatinine and glucose or markers for infection or other metabolic disorders). Hypo- or hyperkalaemia must be controlled. These can all be monitored easily and accurately with modern automated equipment. If the patient becomes more unwell, the frequency of these observations will need to be increased.

ECG monitoring (arrhythmias and ST segment) is necessary during the acute decompensation phase, particularly if ischaemia or arrhythmia is responsible for the acute event.

Class I recommendation, level of evidence C

Blood pressure monitoring is critical during the institution of therapy and should be checked regularly (e.g., every 5 min), until the dosage of vasodilators, diuretics, or inotropes has been stabilized. The reliability of non-invasive, automatic plethysmographic measurement of blood pressure is good in the absence of intense vasoconstriction and very high heart rate.

Class I recommendation, level of evidence C

The pulse oximeter is a simple non-invasive device that estimates the arterial saturation of haemoglobin with oxygen (SaO_2). The estimate of the SaO_2 is usually within 2% of a measured value from a co-oximeter, unless the patient is in cardiogenic shock. The pulse oximeter should be used continuously on any unstable patient who is being treated with a fraction of inspired oxygen (FiO_2) that is greater than air. It should also be used at regular intervals (every hour) in any patient receiving oxygen therapy for an acute decompensation.

Class I recommendation, level of evidence C

Cardiac output and preload can be monitored non-invasively with the use of Doppler techniques (see section above titled "Echocardiography"). There is little to no evidence to help choose which of these monitors to use and it makes no difference as long as the limitations of an individual device are understood and the data are used appropriately.

Class IIb recommendation, level of evidence C

Invasive Monitoring

Arterial Line

The indications for the insertion of an indwelling arterial catheter are the need for either continuous beat-to-beat analysis of arterial blood pressure due to hemodynamic instability especially with intra-aortic balloon counter-pulsation (IABC) or the requirement for multiple arterial blood analyses. The complication rate for the insertion of a 20-gauge 2-inch radial artery catheter is low.

Class IIb recommendation, level of evidence C

CVP Lines

CVP lines provide access to the central venous circulation and are therefore useful for the delivery of fluids and drugs and can also be used to monitor the CVP and venous oxygen saturation (SvO_2) in the superior vena cava (SVC) or right atrium, which provides an estimate of oxygen transport.

Class IIa recommendation, level of evidence C

Caution has to be advised, however, to avoid the over-interpretation of right atrial pressure measurements, as these rarely correlate with left atrial pressures (and therefore left ventricular [LV] filling pressures) in patients with AHF. CVP measurements are also affected by the presence of significant tricuspid regurgitation and positive end-expiratory pressure (PEEP) ventilation.

Class I recommendation, level of evidence C

Pulmonary Artery Catheter (PAC)

The PAC is a balloon flotation catheter that measures pressures in the superior vena cava (SVC), right atrium, right ventricle, and pulmonary artery as well as cardiac output. Modern catheters can measure the cardiac output semi-continuously as well as the mixed venous oxygen saturation and right ventricular end-diastolic volume and ejection fraction. The acquisition of these data can allow for a comprehensive evaluation of the cardiovascular haemodynamics.

Although the insertion of a PAC for the diagnosis of AHF is usually unnecessary, PAC can be used to distinguish between a cardiogenic and a non-cardiogenic mechanism in complex patients with concurrent cardiac and pulmonary disease. PAC is also frequently used to estimate pulmonary capillary wedge pressure (PCWP), cardiac output (CO), and other haemodynamic variables and therefore

guide therapy in the presence of severe diffuse pulmonary pathology or ongoing haemodynamic compromise not resolved by initial therapy. However, it should be remembered that PCWP is not an accurate reflection of left ventricular end-diastolic pressure (LVEDP) in patients with mitral stenosis (MS) or aortic regurgitation (AR), pulmonary and occlusion disease, ventricular interdependence, high airway pressure, and stiff LV (due to, e.g., left ventricular hypertrophy [LVH], diabetes, fibrosis, inotropes, obesity, ischaemia). Severe tricuspid regurgitation, frequently found in patients with AHF, can overestimate or underestimate cardiac output measured by thermodilution.

Several retrospective studies assessing the use of the PAC in AMI demonstrated increased mortality with the PAC. These observations were partially explained by case-mix differences between the groups of the study. Similar observational findings have subsequently been reported in other groups of patients. A recent prospective randomized study enrolled a mixed group of critically ill patients to either a PAC group or to treatment without the use of data from a PAC. This study did not follow a protocol therapy in either group and failed to demonstrate a difference in outcome. Management with PAC led to increased fluid resuscitation within the first 24 h. The PAC did not cause harm to patients; rather it was the use of the information derived from the catheter (sometimes in an inappropriate fashion) that was detrimental.

The use of a PAC is recommended in haemodynamically unstable patients who are not responding in a predictable fashion to traditional treatments, and in patients with a combination of congestion and hypoperfusion. In these cases, it is inserted in order to ensure optimal fluid loading of the ventricles and to guide vasoactive therapies and inotropic agents (see table below titled "General therapeutic approach in AHF by findings on invasive haemodynamic monitoring"). Because the complications are increasing with the duration of its utilization, it is critical to insert the catheter when specific data are needed (usually regarding the fluid status of the patient) and to remove it as soon as it is not of further help (i.e., when diuretic and vasodilating therapy have been optimized).

Class IIb recommendation, level of evidence C

In cardiogenic shock and prolonged severe low-output syndrome, it is recommended to measure the mixed venous oxygen saturation from the pulmonary artery as an estimation of oxygen extraction (SpO_2-SvO_2). The aim should be to maintain SvO_2 >65% in patients with AHF. Yet, severe mitral regurgitation (MR) may be misleading by increasing O_2 saturation measured from PAC.

Table: General Therapeutic Approach in AHF by Findings on Invasive Haemodynamic Monitoring

Haemodynamic Characteristic	**Suggested Therapeutic Approach**				
Cardiac index (CI)	Decreased	Decreased	Decreased	Decreased	Maintained
PCWP	Low	High or Normal	High	High	High

Haemodynamic Characteristic	Suggested Therapeutic Approach				
Systolic blood pressure (SBP) (mmHg)		>85	<85	>85	
Outline of therapy	Fluid loading	Vasodilator (nitroprusside, nitroglycerin [NTG]) Fluid loading may become necessary	Consider inotropic agents (dobutamine, dopamine) and intravenous (i.v.) diuretics	Vasodilators (nitroprusside, nitroglycerin) and i.v. diuretics and consider inotrope (dobutamine, levosimendan, phosphodiesterase inhibitor	i.v. diuretics If systolic blood pressure is low, vasoconstrictive inotropes

Note: In AHF patients: decreased cardiac index, <2.2 L/min/m^2; PCWP: low if <14 mmHg, high if >18-20 mmHg.

Treatment of AHF

General Medical Issues in the Treatment of AHF

Infections: Patients with advanced AHF are prone to infectious complications, commonly respiratory or urinary tract infections, septicaemia, or nosocomial infection with Gram positive bacteria. In elderly patients with heart failure, infection such as pneumonia may be a cause for worsening heart failure and dyspnoea. An increase in C-reactive protein (CRP) and a decrease in general condition may be the only signs of infection--fever may be absent. Meticulous infection control and measures to maintain skin integrity are mandatory. Routine cultures are recommended. Prompt antibiotic therapy should be given when indicated.

Diabetes: AHF is associated with impaired metabolic control. Hyperglycemia occurs commonly. Routine hypoglycemic drugs should be stopped and glycaemic control should be obtained by using short acting insulin titrated according to repeated blood glucose measurements. Normoglycemia improves survival in diabetic patients who are critically ill.

Catabolic state: Negative caloric and nitrogen balance is a problem in ongoing AHF. This is related to reduced caloric intake due to reduced intestinal absorption. Care should be undertaken to maintain calorie and nitrogen balance. Serum albumin concentration, as well as nitrogen balance, may help to monitor metabolic status.

Renal failure: A close interrelationship exists between AHF and renal failure. Both may cause, aggravate, and influence, the outcome of the other. Close monitoring of renal function is mandatory. Preservation of renal function is a major consideration in the selection of the appropriate therapeutic strategy for these patients.

Oxygen and Ventilatory Assistance

Rationale for Using Oxygen in AHF

The main priority in treating patients with AHF is the achievement of adequate levels of oxygenation at the cellular level in order to prevent end-organ dysfunction and the onset of multiple organ failure. The maintenance of an SaO_2 within the normal range (95-98%) is thus important in order to maximize oxygen delivery to the tissues and tissue oxygenation.

Class I recommendation, level of evidence C

This is best achieved first by ensuring that there is a patent airway and then by administration of an increased FiO_2. Maintenance of a patent airway is imperative. This can be achieved by using simple manoeuvres or equipment. Endotracheal intubation is indicated if these measures fail to improve tissue oxygenation.

Class IIa recommendation, level of evidence C

Despite this intuitive approach to giving oxygen, there is little to no evidence available that giving increasing doses of oxygen results in an improved outcome. The evidence available is controversial. Studies have demonstrated that hyperoxia can be associated with reduced coronary blood flow, reduced cardiac output, increased blood pressure, and increased systemic vascular resistance. A study that randomized 200 patients with AMI to receive either oxygen via a variable-performance facemask or to breathe room air reported a trend to higher mortality and an increased incidence of ventricular tachycardia.

The administration of increased concentrations of oxygen to hypoxaemic patients with acute cardiac failure is unquestionably warranted.

Class IIa recommendation, level of evidence C

The use of increased concentrations of oxygen to patients without evidence of hypoxaemia is more controversial and may cause harm.

Ventilatory Support without Endotracheal Intubation (Non-Invasive Ventilation)

Two techniques are used for ventilatory support: continuous positive airway pressure (CPAP) or non-invasive positive pressure ventilation (NIPPV). Non-invasive positive pressure ventilation is a method of providing mechanical ventilation to patients without the need for endotracheal intubation. There is a strong consensus that one of these two techniques should be used before endotracheal intubation and mechanical ventilation. Utilization of non-invasive techniques dramatically reduces the need for endotracheal intubation and mechanical ventilation.

See the original guideline document for discussion of the rationale and evidence for the use of CPAP and NIPPV in LV failure.

Conclusions: The randomized controlled trials suggest that the use of continuous positive airway pressure and non-invasive positive pressure ventilation in acute

cardiogenic pulmonary oedema is associated with a significant reduction in the need for tracheal intubation and mechanical ventilation.

Class IIa recommendation, level of evidence A

Mechanical Ventilation with Endotracheal Intubation in AHF

Invasive mechanical ventilation (with endotracheal intubation) should not be used to reverse hypoxemia that could be better restored by oxygen therapy, CPAP, or NIPPV, but rather to reverse AHF-induced respiratory muscle fatigue. The latter is the most frequent reason for endotracheal intubation and mechanical ventilation. AHF-induced respiratory muscle weakness is only rarely related to the worsening of already diseased respiratory muscles. More usually, worsening respiratory muscle contraction is due to the decrease in oxygen delivery related to hypoxaemia (pulmonary oedema) and low cardiac output. Respiratory muscle fatigue may be diagnosed by a decrease in respiratory rate, which is associated with hypercapnia and confusion. Intubation and mechanical ventilation are needed: (i) to relieve respiratory distress (decrease in work of breathing); (ii) to protect airways from gastric regurgitation; (iii) to improve pulmonary gas exchange, mostly to reverse hypercapnia and hypoxaemia and if the patient is unconscious due to prolonged resuscitation and anaesthetic medication; and (iv) to ensure bronchial lavage and prevent bronchial plugging and atelectasis.

Invasive mechanical ventilation should only be used if acute respiratory failure does not respond to vasodilators, oxygen therapy, and/or CPAP or NIPPV. Another consideration should be the need for immediate intervention in a patient with pulmonary oedema secondary to acute coronary syndrome.

Medical Treatment

Morphine and Its Analogues in AHF

Morphine is indicated in the early stage of the treatment of patient admitted with severe AHF especially if they present with restlessness and dyspnoea.

Class IIb recommendation, level of evidence B

Morphine induces venodilatation and mild arterial dilatation and has the ability to reduce heart rate. In most studies, intravenous boluses of morphine 3 mg were administered as soon as the intravenous line was inserted in AHF patients. It acts to relieve breathlessness and other symptoms in patients with CHF and AHF. This dosing can be repeated if required.

Anticoagulation

Anticoagulation is well established in acute coronary syndrome with or without heart failure. The same is true in atrial fibrillation. There is less evidence for the initiation of unfractionated heparin or low molecular heparin (LMWH) in AHF. A large placebo controlled trial of enoxaparine 40 mg subcutaneously in acutely ill and hospitalised patients including a major group of heart failure patients showed no clinical improvement but less venous thrombosis. There are no large

comparative studies comparing LMWH with unfractionated heparin (given as 5000 IU twice or three times daily). Careful monitoring of the coagulation system is mandatory in AHF as there is often concomitant liver dysfunction. LMWH is contraindicated if the creatinine clearance is <30 mL/min or should be used with extreme care with monitoring of the anti-Factor Xa level.

Vasodilators in the Treatment of AHF

Vasodilators are indicated in most patients with AHF as first line therapy, if hypoperfusion is associated with an adequate blood pressure and signs of congestion with low diuresis, to open the peripheral circulation and to lower preload (see table 6 of the original guideline document).

Nitrates

Nitrates relieve pulmonary congestion without compromising stroke volume or increasing myocardial oxygen demand in acute left heart failure, particularly in patients with acute coronary syndrome. At low doses they only induce venodilation, but as the dose is gradually increased they cause the arteries, including the coronary arteries, to dilate. With appropriate doses, nitrates exert balanced vasodilation of the venous and arterial side of the circulation, thereby reducing left ventricular preload and afterload, without impairing tissue perfusion. Their effect on cardiac output depends on pre-treatment preload and afterload and the ability of the heart to respond to baroreceptor-induced increases in sympathetic tone.

Initially nitrates may be given orally but i.v. nitrates are also well tolerated in acute myocardial infarction (AMI). Two randomized trials in AHF have established the efficacy of i.v. nitrates in combination with furosemide and have demonstrated that dose titration to the highest haemodynamically tolerable dose of nitrates with low dose furosemide is superior to high dose diuretic treatment alone.

Class I recommendation, level of evidence B

In one of these randomized studies, furosemide and isosorbide dinitrate as bolus injections was tested and reported that intravenous high dose nitrate was more effective than furosemide treatment in controlling severe pulmonary oedema.

In practical use, nitrates have a U-shaped curve effect. If given in sub-optimal doses vasodilators may have a limited effect in preventing acute heart failure recurrences. However, administration of high doses may also reduce their effectiveness. One disadvantage of nitrates is the rapid development of tolerance especially when given intravenously in high doses, limiting their effectiveness to 16-24 h only. Nitrates should be given at doses aimed at achieving optimal vasodilation, leading to an increase in cardiac index (CI) and decrease in pulmonary wedge pressure. Inappropriate vasodilation may induce a steep reduction in blood pressure, which may result in haemodynamic instability.

Nitroglycerin can be administered orally or by inhalation [glycerylnitrate (GTN) spray 400 micrograms (2 puffs) every 5-10 min)] or buccally (isosorbide dinitrate 1 or 3 mg), while monitoring blood pressure. The intravenous administration and

dosing of nitrates (GTN 20 micrograms/min increasing dose up to 200 micrograms/min, or isosorbide dinitrate 1-10 mg/h) should be done with extreme caution, under careful blood pressure monitoring, titrating the dose administered against blood pressure decrease. One should be particularly cautious when administering nitrates to a patient with aortic stenosis, although this therapy may help in these complex situations. The dose of nitrates should be reduced if systolic blood pressure decreases below 90-100 mmHg and discontinued permanently if blood pressure drops further. From a practical point of view a reduction of 10 mmHg in mean arterial pressure should be achieved.

Sodium Nitroprusside (SNP)

Sodium nitroprusside (0.3 micrograms/kg/min uptitrating carefully to 1 micrograms/kg/min up to 5 micrograms/kg/min) is recommended in patients with severe heart failure, and in patients with predominantly increased afterload such as hypertensive heart failure or mitral regurgitation.

Class I recommendation, level of evidence C

SNP should be titrated cautiously and usually requires invasive arterial monitoring and close supervision. Prolonged administration may be associated with toxicity from its metabolites, thiocyanide and cyanide, and should be avoided especially in patients with severe renal or hepatic failure. Controlled trials with SNP in AHF are lacking and its administration in AMI has yielded equivocal results. SNP should be tapered down to avoid rebound effects. In AHF caused by acute coronary syndromes, nitrates are favoured over SNP as SNP may cause 'coronary steal syndrome'.

Nesiritide

Recently, nesiritide, a new class of vasodilator, has been developed for the treatment of AHF. Nesiritide is a recombinant human brain peptide or BNP which is identical to the endogenous hormone produced by the ventricle in response to increased wall stress, hypertrophy, and volume overload. Nesiritide has venous, arterial, and coronary vasodilatory properties that reduce preload and afterload, and increase cardiac output without direct inotropic effects.

Systemic infusion of nesiritide in patients with congestive heart failure has beneficial haemodynamic actions, results in an enhanced sodium excretion and suppression of the renin-angiotensin-aldosterone and sympathetic nervous system. The drug has been shown to be efficacious in improving subjective dyspnoea score as well as inducing significant vasodilation. Nesiritide was compared with intravenous nitroglycerin and resulted in improvement in haemodynamics more effectively and with fewer adverse effects. Clinical experience with nesiritide is still limited. Nesiritide may cause hypotension and some patients are non-responders. Use of nesiritide has not translated into improvement in clinical outcome.

Calcium Antagonists

Calcium antagonists are not recommended in the treatment of AHF. Diltiazem, and verapamil, and dihydropyridines should be considered contraindicated.

Angiotensin-Converting Enzyme (ACE) Inhibitors in AHF

Indications

ACE-inhibitors are not indicated in the early stabilisation of patients with AHF.

Class IIb recommendation, level of evidence C

However, as these patients are at high risk, ACE inhibitors have a role in early management of AHF patients and AMI. There is still debate on the selection of patients and the timing of initiation of ACE-inhibitor therapy.

Refer to the original guideline document for discussion of the effects and mechanisms of action of ACE Inhibitors in AHF.

Practical Use

Intravenous ACE-inhibition should be avoided. The initial dose of the ACE-inhibitor should be low and increased progressively after early stabilization within 48 hours with monitoring of blood pressure and renal function. The duration of therapy, when initiated, should be at least 6 weeks.

Class I recommendation, level of evidence A

ACE inhibitors should be used with caution in patients with marginal cardiac output as they may significantly reduce glomerular filtration. The risk of intolerance to the ACE-inhibitors is increased by the concomitant administration of non-steroid anti-inflammatory agents and in the presence of bilateral renal artery stenosis.

Diuretics

Indications

Administration of diuretics is indicated in patients with AHF decompensated heart failure in the presence of symptoms secondary to fluid retention.

Class I recommendation, level of evidence B

The symptomatic benefits and their universal clinical acceptance has precluded a formal evaluation in large scale randomized clinical trials to clearly establish their safety and efficacy profile in patients with congestive heart failure, including their possible impact on outcomes. For the same reasons, the data on the relative efficacy and tolerability of the various types of diuretics are scarce and further clinical research is encouraged.

Refer to the original guideline document for a discussion on the effects and mechanisms of action of diuretics.

Practical Use

Intravenous administration of loop diuretics (furosemide, bumetanide, torasemide) with a strong and brisk diuretic effect is the preferred choice in patients with AHF. Therapy can safely be initiated before hospital admission and the dose should be titrated according to the diuretic response and relief of congestive symptoms. Administration of a loading dose followed by continued infusion of furosemide or torasemide has been shown to be more effective than bolus alone. Thiazides and spironolactone can be used in association with loop diuretics, the combination in low doses being more effective and with less secondary effects than the use of higher doses of a single drug. Combination of loop diuretics with dobutamine, dopamine or nitrates is also a therapeutic approach that is more effective and produces fewer secondary effects than increasing the dose of the diuretic.

Class IIb recommendation, level of evidence C

The table below lists the recommendations for the practical use of diuretics. Table 8 of the original guideline document gives the recommended doses of commonly used diuretics in heart failure.

Practical Use of Diuretics in AHF
• Start with individualized dose depending on clinical condition (See table 8 of the original guideline document). • Titrate according to clinical response. • Reduce dose when fluid retention is controlled. • Monitor serum K^+, Na^+, and renal function at frequent intervals (every 1-2 days), according to diuretic response. • Replace K^+ and Mg^+ loss. • In case of diuretic resistance, follow suggestions in table 10 of the original guideline document titled "Managing resistance to diuretics."

Diuretic Resistance

Diuretic resistance is defined as the clinical state in which diuretic response is diminished or lost before the therapeutic goal of oedema relief has been achieved. Such resistance is associated with a poor prognosis. It is more frequent in patients with chronic, severe heart failure on longterm diuretic therapy, although it has also been reported with acute volume depletion after intravenous administration of loop diuretics. Diuretic resistance can be attributed to a number of factors (see Table 9 in the original guideline document). A number of therapeutic approaches to overcome diuretic resistance have been explored (see Table 10 in the original guideline document), and in clinical practice different strategies may be of value in a particular patient. Continuous infusion of furosemide is more effective than individual boluses.

Secondary Effects, Drug Interactions

Although diuretics can be used safely in the majority of patients, secondary effects are frequent and may be life-threatening. These include neurohormonal activation, especially of the angiotensin-aldosterone system and the sympathetic nervous system; hypokalemia, hypomagnesemia and hypochloraemic alkalosis which may lead to severe arrhythmias; nephrotoxicity and aggravation of renal failure. Excessive diuresis may reduce venous pressure, pulmonary wedge pressure, and diastolic filling excessively, leading to a reduction in stroke volume and cardiac output, particularly in patients with severe heart failure and predominant diastolic failure or ischaemic right ventricular dysfunction. Intravenous administration of acetazolamide (one or two doses) may be helpful for the correction of alkalosis.

New Diuretic Agents

Some new compounds with diuretic and other effects are under investigation, including vasopressin V2 receptor antagonists, brain natriuretic peptides, and adenosine receptor antagonists. Vasopressin V2 receptor antagonists inhibit the action of vasopressin on the collecting duct, thereby increasing free water clearance. The diuretic effect is independent of the levels of sodium and these agents could be helpful in the presence of hyponatraemia. Adenosine receptor antagonists exert a diuretic effect reducing proximal tubular Na^+ and water reabsorption without inducing kaliuresis.

Beta-blocking Agents

Refer to the original guideline document for a discussion on the indications and rationale for use of beta-blocking agents.

Practical Use

In patients with overt AHF and more than basal pulmonary rales, beta-blockers should be used cautiously. Among such patients where ongoing ischaemia and tachycardia are present, intravenous metoprolol can be considered.

Class IIb recommendation, level of evidence C

However, in patients with an acute myocardial infarction (AMI), who stabilize after developing AHF, beta-blockers should be initiated early.

Class IIa recommendation, level of evidence B

In patients with chronic heart failure (CHF), beta-blockers should be initiated when the patient has stabilized after the acute episode (usually after 4 days).

Class I recommendation, level of evidence A

The initial oral dose of bisoprolol, carvedilol, or metoprolol should be small and increased slowly and progressively to the target dose used in the large clinical trials. Up-titration should be adapted to individual response. Beta-blockers may reduce blood pressure and heart rate excessively. As a general rule, patients on beta-blockers admitted to hospital due to worsening heart failure should be

continued on this therapy unless inotropic support is needed but the dose could be reduced if signs of excessive dosages are suspected (i.e., bradycardia and hypotension).

Inotropic Agents

Clinical Indications

Inotropic agents are indicated in the presence of peripheral hypoperfusion (hypotension, decreased renal function) with or without congestion or pulmonary oedema refractory to volume replacement diuretics and vasodilators at optimal doses (see figure 6 of the original guideline document).

Class IIa recommendation, level of evidence C

Their use is potentially harmful, as they increase oxygen demand and calcium loading, and they should be used with caution.

In patients with decompensated CHF the symptoms, clinical course, and prognosis of the disease may become critically dependent on the haemodynamics. Thus, improvements in the haemodynamic parameters may become a goal of treatment and inotropic agents may be useful and life saving in this setting. The beneficial effects of an improvement in the haemodynamic parameters is, however, partially counteracted by the risks of arrhythmias and, in some cases, myocardial ischaemia and by the possible long-term progression of myocardial dysfunction caused by an excessive increase in energy expenditure. The risk-benefit ratio may not, however, be the same for all the inotropic agents. Those acting through the stimulation of the $beta_1$-adrenergic receptors which increase cytoplasmic myocardial cell Ca^{++} concentration may be associated with the greatest risk. Lastly, only a few controlled trials with inotropic agents in patients with AHF have been performed, and very few have assessed their effects on the symptoms and signs of heart failure and their long-term effects on prognosis.

Dopamine

Dopamine is an endogenous catecholamine, and a precursor of norepinpephrine. Its effects are dose-dependent and they involve three different receptor populations: dopaminergic, beta-adrenergic, and alpha-adrenergic receptors.

At low doses (<2 micrograms/kg/min i.v.) it acts only on peripheral dopaminergic receptors and lowers peripheral resistance both directly and indirectly. Vasodilation occurs predominantly in the renal, splanchnic, coronary, and cerebral vascular beds. At this dosage, its action may cause an improvement in the renal blood flow, glomerular filtration rate, diuresis and sodium excretion rate, with an increased response to the diuretic agents, in patients with renal hypoperfusion and failure.

At higher doses (>2 micrograms/kg/min i.v.) dopamine stimulates the beta-adrenergic receptors both directly and indirectly with a consequent increase in myocardial contractility and cardiac output. At doses>5 micrograms/kg/min dopamine acts on alpha-adrenergic receptors with an increase in the peripheral

vascular resistance which, though potentially useful in the hypotensive patients, may be deleterious in the patients with heart failure as it may augment the left ventricular afterload, pulmonary artery pressure, and resistance.

The effects of dopamine in patients with AHF have been studied only in small study groups and no controlled trials regarding its long-term effects on renal function and survival have been performed. In addition, concerns regarding its potential untoward effects on pituitary function, T-cell responsiveness, gastrointestinal perfusion, chemoreceptor sensitivity, and ventilation have been raised.

Dobutamine

Dobutamine is a positive inotropic agent acting mainly through stimulation of $beta_1$-receptors and $beta_2$-receptors in a 3:1 ratio. Its clinical action is the result of direct dose-dependent positive inotropic and chronotropic effects and secondary adaptation to increased cardiac output, such as a decrease in sympathetic tone in heart failure patients, leading to a decrease in vascular resistance. The resultant benefit may therefore differ from patient to patient. At low doses, dobutamine induces mild arterial vasodilatation, which augments stroke volume by reductions in afterload. At higher doses dobutamine causes vasoconstriction.

Heart rate is generally increased in a dose-dependent manner to a lesser extent than with other catecholamines. However, in patients with atrial fibrillation, heart rate may be increased to undesirable rates, due to facilitation of atrio-ventricular conduction. Systemic arterial pressure usually increases slightly, but may remain stable, or decrease. Similarly pulmonary arterial pressure and capillary wedge pressure usually decrease, but may remain stable or even increase in some patients with heart failure.

The improved diuresis observed during dobutamine infusion in patients with CHF is the result of improved haemodynamics with an increased renal blood flow in response to improved cardiac output.

Practical Use

Dopamine may be used as an inotrope (>2 micrograms/kg/min i.v.) in AHF with hypotension. Infusion of low doses of dopamine ($\leq$2-3 micrograms/kg/min i.v.) may be used to improve renal blood flow and diuresis in decompensated heart failure with hypotension and low urine output. However if no response is seen, the therapy should be terminated (see table 11 of the original guideline document).

Class of recommendation IIb, level of evidence C

Dobutamine is used to increase the cardiac output. It is usually initiated with a 2-3 micrograms/kg/min infusion rate without a loading dose. The infusion rate may then be progressively modified according to symptoms, diuretic response or haemodynamic monitoring. Its haemodynamic actions are proportional to its dosage, which can be increased to 20 micrograms/kg/min. The elimination of the drug is rapid after cessation of infusion, making it a very convenient inotropic agent.

In patients receiving beta-blocker therapy with metoprolol, dobutamine doses have to be increased as high as 15-20 micrograms/kg/min to restore its inotropic effect. The effect of dobutamine differs in patients receiving carvedilol: It can lead to an increase in pulmonary vascular resistance during the infusion of increasing doses of dobutamine (5-20 micrograms/kg/min).

On the basis of haemodynamic data alone, the inotropic effect of dobutamine is additive to that of phosphodieasterase inhibitors (PDEI), the combination of PDEI and dobutamine produces a positive inotropic effect greater than each drug alone.

Prolonged infusion of dobutamine (>24-48 h) is associated with tolerance and partial loss of haemodynamic effects. Weaning from dobutamine may be difficult because of recurrence of hypotension, congestion, or renal insufficiency. This can sometimes be solved by very progressive tapering of dobutamine (i.e., decrease in dosage by steps of 2 micrograms/kg/min every other day) and optimization of oral vasodilator therapy such as with hydralazine and/or an ACE-inhibitor. It is sometimes necessary to tolerate some renal insufficiency or hypotension during this phase.

Infusion of dobutamine is accompanied by an increased incidence of arrhythmia originating from both ventricles and atria. This effect is dose-related and may be more prominent than with PDEI and should prompt strict potassium compensation during intravenous diuretic use. Tachycardia may also be a limiting parameter, and dobutamine infusion may trigger chest pain in patients with coronary artery disease. In patients with hibernating myocardium, dobutamine appears to increase contractility in the short term at the expense of myocyte necorosis and loss in myocardial recovery. There are no controlled trials on dobutamine in AHF patients and some trials show unfavourable effects with increased untoward cardiovascular events.

Dobutamine is currently indicated when there is evidence of peripheral hypoperfusion (hypotension, decreased renal function) with or without congestion or pulmonary oedema refractory to volume replacement diuretics and vasodilators at optimal doses (see table 11 of the original guideline document).

Class IIa recommendation, level of evidence C

Phosphodiesterase Inhibitors (PDEIs)

The Type III PDEIs block the breakdown of cyclic-AMP (cAMP) into AMP. Milrinone and enoximone are the two PDEIs used in clinical practice. When administered to patients with advanced heart failure, these agents are associated with a significant inotropic, lusitropic, and peripheral vasodilating effects, with an increase in cardiac output and stroke volume and a concomitant decline in pulmonary artery pressure, pulmonary wedge pressure, and systemic and pulmonary vascular resistance. Their haemodynamic profile is intermediate between that of a pure vasodilator, like nitroprusside, and that of a predominant inotropic agent, like dobutamine. As their site of action is distal to the beta-adrenergic receptors, PDE-Is maintain their effects even during concomitant beta-blocker therapy.

Type III PDEI are indicated when there is evidence of peripheral hypoperfusion with or without congestion refractory to diuretics and vasodilators at optimal doses, and preserved systemic blood pressure.

Class of recommendation IIb, level of evidence C

These agents may be preferred to dobutamine in patients on concomitant beta-blocker therapy and/or with an inadequate response to dobutamine.

Class of recommendation IIa, level of evidence C

In practical use milrinone is administered as a 25 microgram/kg bolus over 10-20 min followed by a continuous infusion at 0.375-0.75 microgram/kg/min. Similarly, enoximone is administered as a bolus of 0.25-0.75 microgram/kg followed by a continuous infusion at 1.25-7.5 microgram/kg/min (see table 11 in the original guideline document). Hypotension caused by excessive peripheral venodilation is an untoward effect observed mainly in the patients with low filling pressures. It may be avoided by starting the infusion without any bolus. Distinctly from amrinone, the incidence of thrombocytopenia is relatively rare with milrinone (0.4%) and enoximone.

Milrinone or enoximone are used for the treatment of AHF on the basis of their favourable haemodynamic effects. No information is available regarding their effects on heart failure symptoms and signs. The data regarding the effects of PDEI administration on the outcome of the patients with AHF are insufficient, but raise concerns about safety, particularly in patients with ischaemic heart failure.

Levosimendan

Levosimendan has two main mechanisms of action: Ca^{++} sensitization of the contractile proteins responsible for a positive inotropic action, and smooth muscle K^{+} channel opening responsible for peripheral vasodilation. Some data suggest levosimendan may also have PDEI effect. Levosimendan has a potent acetylated metabolite that is also a Ca^{++}-concentration dependent Ca^{++} sensitizer. Its half-life is approximately 80 h, which probably explains the prolonged haemodynamic effects of a 24 h levosimendan infusion.

Levosimendan is indicated in patients with symptomatic low cardiac output heart failure secondary to cardiac systolic dysfunction without severe hypotension (see table 11 of the original guideline document).

Class of recommendation IIa, level of evidence B

Levosimendan is generally administered as a continuous intravenous infusion at a dose of 0.05-0.1 microgram/kg/ min preceded by a loading dose of 12-24 microgram/kg, administered over 10 min. Its haemodynamic effects are dose-dependent and the infusion rate may be uptitrated to a maximal rate of 0.2 microgram/kg/min. Most of the clinical data have been obtained with intravenous infusions lasting from 6 h to 24 h, but the haemodynamic effects persist for >48 h after the end of the infusion.

Levosimendan infusion in patients with acutely decompensated HF caused by LV systolic dysfunction has been associated with a dose-dependent increase in the cardiac output and stroke volume; a decline in the pulmonary wedge pressure, systemic vascular resistance, and pulmonary vascular resistance; and a slight increase in the heart rate and decrease in the blood pressure. An improvement in symptoms of dyspnoea and fatigue and a favourable outcome has been shown in randomized trials comparing levosimendan with dobutamine. Differently from dobutamine, the haemodynamic response to levosimendan is maintained, or even of greater magnitude, in patients on concomitant beta-blocker therapy.

Tachycardia and hypotension are described with high dose levosimendan infusion and it is not currently recommended in patients with systolic blood pressure <85 mmHg. Levosimendan has not been associated with an increased frequency of malignant arrhythmias in comparative trials with either placebo or dobutamine. A reduction in the haematocrit, haemoglobin, and plasma potassium, likely secondary to vasodilation and secondary neurohumoral activation, have been described and seem to be dose dependent.

Vasopressor Therapy in Cardiogenic Shock

When the combination of inotropic agent and fluid challenge fails to restore adequate arterial and organ perfusion despite an improvement in cardiac output, therapy with vasopressors may be required. Vasopressors may also be used, in emergencies, to sustain life and maintain perfusion in the face of life-threatening hypotension. Since cardiogenic shock is associated with high vascular resistances, any vasopressor should be used with caution and only transiently, because it may increase the afterload of a failing heart and further decrease end-organ blood flow.

Epinephrine

Epinephrine is a catecholamine with high affinity for beta1-, beta2-, and alpha-receptors. Epinephrine is used generally as an infusion at doses of 0.05-0.5 micrograms/kg/min when dobutamine refractoriness is present and the blood pressure remains low. The use of epinephrine requires direct arterial pressure monitoring, and monitoring of haemodynamic response by PAC is recommended (see Table 11 of the original guideline document).

Norepinephrine

Norepinephrine is a catecholamine with high affinity for alpha-receptors and is generally used to increase systemic vascular resistance. Norepinephrine-induced increases in heart rate are less than with epinephrine. The dosing is similar to epinephrine. The choice between epinephrines depends on clinical situation. Norepinephrine (0.2-1 micrograms/kg/min) is favoured in situations with low blood pressure related to reduced systemic vascular resistances such as septic shock. Norepinephrine is often combined with dobutamine to improve haemodynamics. Norepinehrine may reduce end-organ perfusion. Other new modes of treatments in septic shock are out of the scope of this report.

Cardiac Glycosides

Cardiac glycosides inhibit myocardial Na^+/K^+ ATPase, thereby increasing Ca^{++}/Na^+ exchange mechanisms, producing a positive inotropic effect. In heart failure, the positive inotropic effect following beta-adrenergic stimulation is attenuated and the positive force-frequency relationship is impaired. In contrast to beta-adrenoceptor agonists, the positive inotropic effect of cardiac glycosides is unchanged in failing hearts and the force-frequency relationship is partially restored. In CHF, cardiac glycosides reduce symptoms and improve clinical status, thereby decreasing the risk of hospitalization for heart failure without effects on survival (The Digitalis Investigation Group). In the AHF syndrome, cardiac glycosides produce a small increase in cardiac output and a reduction of filling pressures. In patients with severe heart failure following episodes of acute decompensation, cardiac glycosides have shown to be efficacious in reducing the re-occurrence of acute decompensation. Predictors for these beneficial effects are a third heart sound, extensive LV dilatation, and distended jugular veins during the AHF episode.

However, in patients following myocardial infarction with heart failure, a substudy of the AIRE Investigation has shown adverse effects on the outcome after AMI accompanied by heart failure. Furthermore, following AMI, an increase of creatine kinase was more pronounced in patients receiving cardiac glycosides. In addition, for patients with myocardial infarction and AHF, digitalis was a predictor for life-threatening pro-arrhythmic events. Therefore, inotropic support with cardiac glycosides cannot be recommended in AHF, in particular following myocardial infarction.

Indication for cardiac glycosides in AHF may be tachycardia-induced heart failure (e.g., in atrial fibrillation with insufficient rate control by other agents such as beta-blockers). Rigorous control of heart rate in tachyarrhythmia during the course of AHF can control heart failure symptoms. Contraindications to the use of cardiac glycosides include bradycardia, second and third degree atrioventricular (AV)-block, sick sinus syndrome, carotid sinus syndrome, Wolff-Parkinson-White syndrome, hypertrophic obstructive cardiomyopathy, hypokalaemia, and hypercalcaemia.

Underlying Diseases and Co-Morbidities

There are several acute morbidities which can cause *de novo* AHF or trigger decompensation in CHF. Coronary heart disease and acute coronary syndromes are the most frequent causes for AHF. Non-cardiac comorbidities may also significantly complicate the therapy of AHF.

Coronary Artery Disease

AHF induced or complicated by coronary artery disease may present with forward failure (including cardiogenic shock), left-heart failure (including pulmonary oedema), or right-heart failure. The diagnosis is indicated by appropriate history (with background risk factors and suggestive chest pain), and a typical ECG with evidence of AMI or dynamic ST/T changes suggestive of myocardial ischaemia.

In acute coronary syndromes (unstable angina or myocardial infarction) complicated by AHF, coronary angiography is indicated (see figure 7 of the original guideline document). In AMI, reperfusion may significantly improve or

prevent AHF. Emergency balloon angioplasty (PCI), or on occasion surgery, should be considered at an early stage and performed as indicated. Such procedures can be life saving. If neither PCI nor surgery is readily available or can only be provided after a long delay, early fibrinolytic therapy is recommended.

For further diagnostic purposes, an echocardiogram is helpful for the assessment of regional and global ventricular function, associated valve dysfunction (mainly mitral regurgitation) and ruling out other disease states (e.g., perimyocarditis, cardiomyopathy, and pulmonary embolism). All patients with AMI and signs and symptoms of heart failure should undergo an echocardiographic study.

Class I recommendation, level of evidence C

Special tests to provide evidence of reversible myocardial ischaemia are sometimes necessary.

In cardiogenic shock caused by acute coronary syndromes, coronary angiography and revascularization should be performed as soon as possible.

Class I recommendation, level of evidence A

Temporary stabilization of the patient can be achieved by adequate fluid replacement, intra-aortic balloon counter-pulsation, pharmacological inotropic support, nitrates, and artificial ventilation. Repeated blood samples for monitoring of electrolytes, glucose, renal function, and arterial blood gases should be taken, particularly in diabetic patients.

Metabolic support with high-dose glucose, insulin, and potassium cannot be recommended (except in diabetic patients) until the results from larger scale studies in AMI become available.

Class II recommendation, level of evidence A

When the haemodynamic state continues to be unstable for several hours, the introduction of an indwelling PAC may be considered. Repeated measurements of mixed venous blood oxygen saturation from the PAC can be helpful.

Class II recommendation, level of evidence B

When all these measures fail to achieve stabilization of the haemodynamic status, mechanical support with a left ventricular assist device should be considered, particularly if heart transplantation is contemplated.

In left-heart failure/pulmonary oedema, the acute management is similar to other causes of pulmonary oedema. Inotropic agents may be deleterious. Intra-aortic balloon counter-pulsation should be considered.

The long-term management strategy should include adequate coronary revascularization and where there is evidence of reduced LV function long-term treatment with RAAS-inhibition and beta-blockade should follow.

Acute right-heart failure is usually related to acute right ventricular ischaemia in acute coronary syndromes, particularly right ventricular infarction with a characteristic ECG and echocardiogram. Early revascularization of the right coronary artery and its ventricular branches is recommended. Supportive treatment should focus on fluid-loading and inotropic support.

Valvular Disease

AHF can be caused by valvular conditions unrelated to acute coronary syndromes such as acute mitral or aortic valve incompetence (i.e., from endocarditis or trauma), aortic or mitral stenosis, thrombosis of a prosthetic valve, or aortic dissection.

In patients with endocarditis, treatment is initially conservative with antibiotics and other medical means of treatment of AHF. Cardiac dysfunction may be aggravated by myocarditis. However, acute valve incompetence is the most common cause of AHF in patients with infective endocarditis. Heart failure should be promptly treated. Rapid diagnosis and therapeutic decisions require expert consultation. Surgical consultations are warranted. Surgical intervention should be performed early in severe acute aortic or mitral regurgitation.

If there is a prolonged period of acute mitral regurgitation and the cardiac index has decreased to <1.5 L/min/m^2 and the ejection fraction is <35%, urgent surgical intervention usually will not improve the prognosis. Stabilization of the patient with intra-aortic balloon counterpulsation can be of great value.

Urgent surgery is indicated in patients with endocarditis and severe acute aortic regurgitation.

Management of AHF Due to Prosthetic Valve Thrombosis

AHF from prosthetic valve thrombosis (PVT) is associated with a high mortality. All patients with heart failure symptoms and suspected prosthetic valve thrombosis should undergo chest fluoroscopy and an echocardiographic study (transthoracic and/or transesophageal if visualization of the prosthetic valve area is inadequate).

Class I recommendation, level of evidence B

The management remains controversial. Thrombolysis is used for right-sided prosthetic valves, and for high-risk surgical candidates. Surgery is preferred for left sided prosthetic valve thrombosis.

Class IIa recommendation, level of evidence B

Surgical mortality is high for emergency operations in critically ill patients with haemodynamic instability (NYHA Class III/IV, pulmonary oedema, hypotension). However, thrombolysis takes several hours to be effective and this delay may lead to further deterioration of the patient, dramatically increasing the risk of re-operation if thrombolytic treatment fails.

For patients who are in NYHA I/II or with non-obstructive thrombus, surgical mortality is lower. Recent data from non-randomized studies suggest that long term antithrombotic and/or thrombolytic therapy may be equally effective in these patients.

Thrombolytic therapy is not effective when fibrous tissue ingrowth (pannus) is implicated in the obstruction with minor secondary thrombosis.

In patients with very large and/or mobile thrombi, thrombolytic therapy is associated with a much higher risk for major embolism and stroke. In all these patients surgical intervention should be considered as an alternative. Before deciding therapy, pannus formation or structural defects of the prosthetic valve should be ruled out by transesophageal echocardiography.

Echocardiography should be performed in all patients after thrombolytic therapy. Surgical intervention should be considered in all cases if thrombolysis fails to resolve the obstruction although repeated infusions of thrombolytic therapy is an alternative.

The thrombolytics used are: rtPA 10 mg intravenous bolus followed by 90 mg infused over 90 min; streptokinase 250-500 000 IU over 20 min followed by 1-1.5 million IU infused over 10 h. After thrombolysis, unfractionated heparin should be administered by intravenous infusion in all patients (activated partial thromboplastin time 1.5-2.0 times control). Urokinase is also an alternative in a dose of 4400 IU/kg/h for 12 h without heparin or 2000 IU/kg/h with heparin for 24 h.

Aortic Dissection

Acute aortic dissection (particularly Type 1) may present with symptoms of heart failure with or without pain. Following a period of pain, heart failure may become the main symptom. The AHF is usually related to a hypertensive crisis, acute aortic valve incompetence, or myocardial ischaemia. Immediate diagnosis and surgical consultation are warranted. Transoesophageal echocardiography is the best technique to assess the morphology and function of the valve. Speed in surgical intervention is usually vital.

AHF and Hypertension

AHF is one of the well-known complications of hypertensive emergencies. The latter are defined as situations that require immediate blood pressure reduction (not necessarily to the normal values) to prevent or limit organ damage including encephalopathy, aortic dissection, or acute pulmonary oedema. The pathophysiology of hypertensive crisis is multifactorial and well described elsewhere. The epidemiology of hypertension-induced pulmonary oedema shows that it usually appears in older patients (particularly in women >65 years of age) with a long-lasting history of hypertension, LV hypertrophy (present in more than half of patients), and inadequate treatment of their hypertension. The clinical signs of AHF associated with a hypertensive crisis are almost exclusively the signs of pulmonary congestion. The latter can be mild or very severe with an acute pulmonary oedema throughout both lungs. It is called "flash pulmonary oedema" because of its rapid onset. Rapid treatment with specific interventions is required.

Systolic function is often preserved in patients hospitalized with pulmonary oedema and hypertension (more than half of patients have an LVEF >45%). In contrast, diastolic abnormalities with decreased LV compliance are often present.

The goals of the treatment of acute pulmonary oedema with hypertension are reduction in LV preload and afterload, reduction of cardiac ischaemia, and maintenance of adequate ventilation with clearing of the oedema. Treatment should be started immediately and in the following order: O_2 therapy, CPAP or non-invasive ventilation, and if necessary, invasive mechanical ventilation, for usually a very short period, and administration of intravenous antihypertensive agent(s).

Antihypertensive therapy should aim for an initial rapid (within a couple of minutes) reduction of SBP or DBP of 30 mmHg, followed by a more progressive decrease of BP to the values measured before the hypertensive crisis: this may take several hours. No attempt should be made to restore normal values of BP as this may cause a deterioration in organ perfusion. The initial rapid reduction of BP may be achieved by the following medications given alone or combined if hypertension persists: (i) intravenous loop diuretics, particularly if the patient is clearly fluid overloaded with a long history of CHF; (ii) intravenous nitroglycerin or nitroprusside to decrease venous preload and arterial afterload and increase coronary blood flow; (iii) a calcium-channel blocker (such as nicardipine) may be considered as these patients usually have diastolic dysfunction with an increased afterload. Nicardipine has a similar spectrum of use as nitrates, but may cause adrenergic activation (tachycardia), an increase in intrapulmonary shunt (hypoxaemia), and central nervous system complications.

Among the medications usually given to treat hypertensive crisis, beta-blockers should not be advised in cases of concomitant pulmonary oedema. However, in some cases, and particularly in hypertensive crisis related to phaeochromocytoma, intravenous labetalol given as slow boluses of 10 mg while monitoring heart rate and blood pressure and followed by an infusion of 50-200 mg/h can be effective. Acute pulmonary oedema associated with hypertension, and in the absence of other complications, is often very easily treated and does not necessarily need admission to an intensive care unit

Renal Failure

Heart failure and renal failure frequently co-exist, and either one of them may cause the other. Heart failure causes renal hypoperfusion both directly and through the activation of neurohumoral mechanisms. Concomitant therapies (e.g., diuretics and ACE-inhibitors through efferent glomerular artery dilatation, and nonsteroid anti-inflammatory agents through inhibition of afferent glomerular artery dilatation) may also contribute to the development of renal failure. Initially, the autoregulation of renal blood flow and the constriction of the efferent glomerular artery may compensate for renal hypoperfusion but, at later stages renal function becomes critically dependent on afferent glomerular flow so that renal failure and oliguria are a common finding in patients with severe acute heart failure.

Urinalysis may vary depending on the cause of renal failure. When renal failure is secondary to hypoperfusion, the urinary sodium/potassium ratio is

characteristically less than 1. Acute tubular necrosis may be diagnosed on the basis of an increase in urinary sodium, reduction in urine nitrogen concentration and typical urinary sedimentation findings.

A mild-to-moderate impairment in renal function is generally asymptomatic and well tolerated. However, even a mild-to-moderate increase in serum creatinine and/or decrease in glomerular filtration rate (GFR) are independently associated with a worse prognosis.

Concomitant acute renal failure requires the recognition and treatment of its associated disorders. The prevalence of anaemia, electrolyte abnormalities, and metabolic acidosis is greater in patients with concomitant renal failure. Electrolyte abnormalities (hypo- and hyperkalaemia, and hypo- and hypermagnesaemia) and metabolic acidosis should be corrected as they may cause arrhythmias, reduce the response to treatment, and worsen the prognosis.

Renal failure also influences the response and tolerability of heart failure treatments, namely, digoxin and ACE-inhibitors, angiotensin receptor blocking agents, and spironolactone. Also pre-renal arterial stenosis and post-renal obstruction should be assessed. Administration of ACE-inhibitors is associated with an increased incidence of severe renal failure and hyperkalaemia in patients with concomitant renal failure. An increase in serum creatinine of more than 25-30% and/or achievement of levels >3.5 mg/dL (>266 micromol/L) are relative contraindications to the continuation of ACE-inhibitor treatment.

Moderate-to-severe renal failure [e.g., a serum creatinine >2.5-3 mg/dL (>190-226 micromol/L)] is also associated with a reduced response to diuretics - a significant predictor of mortality in heart failure patients. In such patients, it may be necessary to progressively increase the dose of the loop diuretics and/or add a diuretic with a different mechanism of action (e.g. metolazone). This may, however, be associated with hypokalaemia and a further decline in glomerular filtration rate (GFR).

In patients with severe renal dysfunction and refractory fluid retention, continuous veno-venous hemofiltration (CVVH) may become necessary. Combined with a positive inotropic agent this may increase renal blood blow, improve renal function, and restore diuretic efficiency. This has been associated with an increase in urine output, a reduction in symptoms, and in the left and right ventricular filling pressures and sympathetic stimulation and with an improvement in lung mechanical function, laboratory abnormalities (hyponatremia), and the response to diuretic therapy. Loss of renal function may require dialysis treatment, especially in the presence of hyponatremia, acidosis, and overt uncontrolled fluid retention. The choice between peritoneal dialysis, haemodialysis, or filtration, is usually dependent on technical availability and on baseline blood pressure.

Patients with heart failure are at the highest risk of renal damage after the administration of contrast media. This is ascribed to a decline in renal perfusion and a direct renal tubular damage caused by the contrast media. The most widely used preventive procedure (e.g. pre-procedural and post-procedural hydration) may not be tolerated and the osmotic and volume overload of contrast material may favour pulmonary oedema. Other procedures which may prevent contrast-induced renal failure and which may be better tolerated in the patients with

concomitant heart failure include the use of the smallest amounts of iso-osmotic contrast media, avoidance of nephrotoxic drugs like non-steroidal anti-inflammatory agents, pre-treatment with N-acetylcysteine, and/or the selective DA_1 receptor agonist fenoldopam. Peri-procedural haemodialysis is effective at preventing nephropathy in patients with severe renal dysfunction. All these procedures have been shown to be effective only in small studies and larger trials are needed to confirm their efficacy.

Class IIb recommendation, level of evidence B

Pulmonary Diseases and Bronchoconstriction

When bronchoconstriction is present in patients with AHF, bronchodilators should be used. This is often the case in patients with concomitant lung problems (e.g. asthma, chronic obstructive bronchitis, and lung infections). Bronchodilators may improve cardiac function, but should not be used instead of relevant AHF treatment. Commonly, initial treatment consists of 2.5 mg albuterol (salbutamol) (0.5 mL of a 0.5% solution in 2.5 mL normal saline) by nebulization over 20 min. This may be repeated hourly during the first few hours of therapy and thereafter as part of individual therapy as indicated.

Arrhythmias and AHF

There are no extensive reports on the prevalence of arrhythmias either as a cause or as a complicating factor in decompensated AHF. In the Euroheart Failure Survey, rapid atrial fibrillation was observed at index hospitalization in 9% of patients and 42% had a history of chronic or paroxysmal atrial fibrillation. The prevalence of all atrial tachyarrhythmias was 44%. Life-threatening ventricular arrhythmias were seen at index hospitalization in 2% and in the whole study population they were found as a concomitant early or acute problem in 8% of patients.

Bradyarrhythmias

Bradycardia in AHF patients occurs most often in AMI, particularly with right coronary artery occlusion.

The treatment of bradyarrhythmias is usually initially with atropine 0.25-0.5 mg intravenously, repeated when needed. Isoproterenol 2-20 micrograms/min can be infused in cases of atrioventricular (AV) dissociation with low ventricular response, but should be avoided in ischaemic conditions. Slow ventricular rhythm in atrial fibrillation can be improved by i.v. theophylline 0.2-0.4 mg/kg/h as a bolus and then by infusion. A temporary pacemaker should be inserted if no response is achieved with medical therapy. Ischaemia should be treated as soon as possible before or after inserting a pacemaker as indicated (see table below titled "Treatment of Arrhythmias in AHF").

Class IIa recommendation, level of evidence C

Treatment of Arrhythmias in AHF	
Ventricular	Defibrillate with 200-300-360 joules (preferably by biphasic

Treatment of Arrhythmias in AHF	
fibrillation or pulseless ventricular tachycardia	defibrillation with a maximum of 200 joules). If refractory to initial shocks inject epinephrine 1 mg or vasopressin 40 IU and/or amiodarone 150-300 mg as injection
Ventricular tachycardia	If patient is unstable cardiovert, if stable amiodarone or lidocaine can be given to achieve medical cardioversion

Sinus tachycardia or supraventricular tachycardia	Use beta-blocking agents when clinically and haemodynamically tolerated:
	• Metoprolol 5 mg intravenously as a slow bolus (can be repeated if tolerated)
	• Adenosine may be used to slow AV conduction or to cardiovert re-entrant tachycardia
	• On rare occasions:
	  • Esmolol 0.5-1.0 mg/kg over 1 min, followed by infusion of 50-300 micrograms/kg/min, or
	  • Labetalol 1.2 mg bolus, followed by infusion of 1-2 mg/min (to total 50-200 mg)
	Labetalol also indicated in AHF related to hypertensive crisis or phaeochromocytoma, with 10-mg boluses, to a total dose of 300 mg.

Atrial fibrillation or flutter	Cardiovert if possible. Digoxin 0.125-0.25 mg i.v., or beta-blocking agent, or amiodarone, may be used to slow AV conduction. Amiodarone may induce medical cardioversion without compromising left ventricular haemodynamics. Patient should be heparinized.
Bradycardia	Atropine 0.25-0.5 mg i.v., to total of 1-2 mg. As interim measure, isoproterenol 1 mg in 100 mL NaCl infused to a maximum of 75 mL/hour (2-12 micrograms/minute). If bradycardia is atropine-resistant, transcutaneous or transvenous pacing should be used as an interim measure. Theophylline may be used in AMI patients with atropine-resistant bradycardia with a bolus of 0.25-0.5 mg/kg followed by infusion at 0.2-0.4 mg/kg/h

Supraventricular Tachycardia

Supraventricular tachyarrhythmias (SVTs) may complicate or cause AHF. On rare occasions persistent atrial tachycardias may cause decompensated heart failure requiring hospitalization. Similarly, atrial fibrillation with a rapid ventricular response may be the cause for a dilated cardiomyopathy and AHF.

In CHF or worsening AHF, chronic atrial fibrillation is seen in 10-30% of patients, with the highest prevalence in advanced heart failure. Supraventricular tachycardia, atrial fibrillation, flutter, and paroxysmal tachycardia are seen occasionally in AMI. Late onset (>12 h) is usually related to more severe heart failure (60% of those with Killip Class III or IV).

Recommendations for Treatment of Supraventricular Tachyarrhythmias (SVTs)

The control of the ventricular rate response is important in patients with atrial fibrillation and AHF, particularly in patients with diastolic dysfunction.

Class IIa recommendation, level of evidence A

Patients with restrictive physiology or tamponade, however, may suddenly deteriorate with rapid heart rate reduction. Rapid rate control or cardioversion on clinical demand should be achieved (see table above titled "Treatment of Arrhythmias in AHF"). The therapy of atrial fibrillation depends on the duration of the atrial fibrillation.

Patients with AHF and atrial fibrillation should be anticoagulated. When atrial fibrillation is paroxysmal medical or electrical cardioversion should be considered after initial work-up and stabilization of the patient. If the duration of the atrial fibrillation is more than 48 hours, the patient should be anticoagulated and optimal rate control achieved medically for 3 weeks before cardioversion. If the patient is haemodynamically unstable, urgent cardioversion is clinically mandatory, but atrial thrombus should be excluded by transesophageal echocardiography prior to cardioversion.

Verapamil and diltiazem should be avoided in acute atrial fibrillation as they may worsen heart failure and cause third degree AV block. Amiodarone and beta-blocking agents have been successfully used in atrial fibrillation for rate control and prevention of recurrence.

Class I recommendation, level of evidence A

Rapid digitalization should be considered especially when atrial fibrillation is secondary to AHF. Verapamil can be considered in the treatment of atrial fibrillation or narrow complex supraventricular tachycardia in patients with only slightly reduced ventricular systolic function.

Class I anti-arrhythmic agents should be avoided in patients with low ejection fraction and particularly in patients who have a wide QRS complex. Dofetilide is a new drug with promising results in medical cardioversion (59% cardioverted in dofetilide vs. 34% in placebo group) in one study and prevention of new atrial fibrillation, but further studies are needed to evaluate its safety and efficacy in AHF.

Beta-blocking agents can be tried in supraventricular tachycardias when tolerated. In wide complex tachycardia, i.v. adenosine can be used in an attempt to terminate the arrhythmia. Electrical cardioversion of SVT with sedation should be considered in AHF with hypotension. AHF patients with AMI and heart failure, and patients with diastolic heart failure, do not tolerate rapid supraventricular arrhythmias.

Plasma potassium and magnesium levels should be normalized particularly in patients with ventricular arrhythmias.

Class IIb recommendation, level of evidence B

Treatment of Life-Threatening Arrhythmias

The importance of ventricular tachycardia or fibrillation as a cause of, or related to, AHF is unclear.

Ventricular fibrillation and ventricular tachycardia require immediate cardioversion, with ventilator assistance if required, and in the case of a conscious patient with sedation (see table above titled "Treatment of arrhythmias in AHF").

Amiodarone and beta-blocking agents can prevent repetition of these arrhythmias.

Class I recommendation, level of evidence A

In the case of recurrent ventricular arrhythmias and haemodynamically unstable patients, immediate angiography and electrophysiological testing should be performed. In cases of a localized arrhythmic substrate radiofrequency ablation may eliminate the arrhythmic tendency although the long term effect cannot be ascertained (see table above titled "Treatment of arrhythmias in AHF").

Class IIb recommendation, level of evidence C

Peri-operative AHF

AHF in the peri-operative period is usually related to myocardial ischaemia and the effect of the aging of the general population over the last decade has exacerbated this problem. The incidence of peri-operative cardiac complications including myocardial infarction and death is approximately 5% in patients with at least one of the following cardiovascular risk factors: age >70 years, angina, prior myocardial infarction, congestive heart failure, treatment for ventricular arrhythmias, treatment for diabetes mellitus, limited exercise capacity, hyperlipidaemia, or smoking. The peak incidence occurs within the first 3 days after the operation. Importantly, post-operative instability of coronary artery disease is usually silent, i.e., not associated with chest pain.

Surgical Treatment of AHF

AHF is a severe complication of many cardiac disorders. In some of them surgical therapy improves prognosis if performed urgently or immediately (see table below titled "Cardiac disorders and AHF requiring surgical treatment". Surgical options include coronary revascularization, correction of the anatomic lesions, valve replacement or reconstruction, as well as temporary circulatory support by means of mechanical assist devices. Echocardiography is the most important technique in the diagnostic work-up (see figure 3 of the original guideline document).

Cardiac Disorders and AHF Requiring Surgical Treatment
• Cardiogenic shock after AMI in patients with multi-vessel ischaemic heart disease • Post-infarction ventricular septal defect

Cardiac Disorders and AHF Requiring Surgical Treatment

• Free wall rupture
• Acute decompensation of pre-existing heart valve disease
• Prosthetic valve failure or thrombosis
• Aortic aneurysm or aortic dissection rupture into the pericardial sac
• Acute mitral regurgitation from
  • Ishaemic papillary muscle rupture
  • Ischaemic papillary muscle dysfunction
  • Myxomatous chordal rupture
  • Endocarditis
  • Trauma
• Acute aortic regurgitation from
  • Endocarditis
  • Aortic dissection
  • Closed chest trauma
• Ruptured aneurysm of the sinus of Valsalva
• Acute decompensation of chronic cardiomyopathy requiring support by mechanical assist devices

AHF Related to Complications of AMI

Free Wall Rupture

Free wall rupture is documented in 0.8-6.2% of patients after AMI. Usually sudden death occurs within minutes due to cardiac tamponade and electromechanical dissociation. The diagnosis is rarely established before the patient's death. However, in some cases the presentation of free wall rupture is sub-acute (thrombus or adhesions seal the rupture) giving an opportunity for intervention if the condition is recognized. Most of these patients have signs of cardiogenic shock, sudden hypotension, and/or loss of consciousness. In some patients rupture is preceded by chest pain, nausea, emesis, new ST segment elevation in the infarct related leads, or T-wave changes. All these patients should undergo immediate echocardiography (see Figure 7A in the original guideline document). The clinical presentation, with a pericardial effusion of >1 cm depth and echo densities in the effusion confirm the diagnosis. Temporary haemodynamic stabilization can be obtained by pericardiocentesis, fluids, and positive inotropes. The patient should be immediately transferred to the operating room without any further investigation. Free wall rupture has been also described as a rare complication of dobutamine stress echocardiography after AMI.

Post-Infarction Ventricular Septal Rupture (VSR)

VSR occurs in 1-2% of patients with AMI. Recent data suggest a lower incidence and an earlier presentation in the thrombolytic era. VSR usually occurs in the first 1-5 days after MI. The first sign of VSR is a pansystolic murmur usually at the left lower sternal border in a patient with acute deterioration and signs of AHF/cardiogenic shock after an AMI (see figure 7A of the original guideline document).

Echocardiography will confirm the diagnosis and allow assessment of ventricular function, define the site of the VSR, the size of the left-to-right shunt, and the co-existence of mitral incompetence (see figure 7B of the original guideline document).

Class I recommendation, level of evidence C

PAC oximetry with O_2 step-up will allow estimation of the pulmonary-to-systemic blood flow ratio (usually 2 or more).

Class III recommendation, level of evidence C for PAC for diagnosis if echocardiography is diagnostic

Class IIa recommendation, level of evidence C for PAC for monitoring

Haemodynamically compromised patients should have intra-aortic balloon counter-pulsation, vasodilators, inotropes, and (if necessary) assisted ventilation. Coronary angiography is usually performed because it has been demonstrated in some small retrospective studies that concomitant revascularization may improve late functional status and survival.

Virtually all patients treated medically die. Surgery should be performed soon after the diagnosis in most patients. Hospital mortality is 20-60% in patients undergoing surgical repair. Improvements in surgical technique and myocardial protection improved outcome in recent series.

There is a developing consensus that surgery should be performed as soon as the diagnosis is made, because the rupture can abruptly expand resulting in cardiogenic shock, the most important determinant of adverse outcome. The patients with VSR should be operated on urgently if they are in a haemodynamically stable condition and immediately if they are in cardiogenic shock.

Class I recommendation, level of evidence C

Trans-catheter VSR occlusion has been used to stabilize critically ill patients with good results but more experience is needed before it can be recommended.

Recently, left ventricular outflow tract (LVOT) obstruction with compensatory hyperkinesis of the basal segments of the heart has been described in some patients with apical anterior myocardial infarction as a cause of a new systolic murmur and cardiogenic shock. It persists until appropriate therapy decreases the LVOT obstruction (see Figure 7D in the original guideline document).

<u>Acute Mitral Regurgitation (MR)</u>

Acute severe MR is found in approximately 10% of patients with cardiogenic shock after AMI. The prevalence is uncertain in the general population of patients with AMI. It occurs 1-14 days (usually 2-7 days) after the infarction. In acute MR from complete papillary muscle rupture most of the non-operated patients die in the first 24 hours.

Partial rupture of one or more papillary muscle heads is more common than complete rupture and has a better survival. In most patients the acute MR is secondary to papillary muscle dysfunction rather than to rupture. Endocarditis may also be a cause for severe MR and requires reparatory surgery.

Acute severe MR is manifested by pulmonary oedema and/or cardiogenic shock. The characteristic apical systolic murmur may be absent in patients with severe MR due to the abrupt and severe elevation of left atrial pressure. Chest radiography shows pulmonary congestion (this may be unilateral). Echocardiography will establish the presence and severity of MR and permit assessment of LV function. The left atrium is usually small or slightly enlarged. In some patients transesophageal echocardiography may be needed to establish the diagnosis.

A pulmonary artery catheter can be used to exclude VSR; the PCWP tracing may show large regurgitant V-waves. Ventricular filling pressures can be used to guide patient management (see figure 7C of the original guideline document).

Class IIb recommendation, level of evidence C

Most patients need intra-aortic balloon counterpulsation for stabilization before cardiac catheterization and angiography. When a patient develops acute MR, operation should be done early because many patients deteriorate suddenly or develop other serious complications. The patient with acute severe MR and pulmonary oedema or cardiogenic shock requires emergency surgery (see figure 7E of the original guideline document).

Class I recommendation, level of evidence C

Mechanical Assist Devices and Heart Transplantation

Indication

Temporary mechanical circulatory assistance may be indicated in patients with AHF who are not responding to conventional therapy and where there is the potential for myocardial recovery, or as a bridge to heart transplant or interventions that may result in significant recovery of the heart function (see figure 8 of the original guideline document).

Class IIb recommendation, level of evidence B

Improvement in the design and function of the devices will increase the number of potential candidates for its short- and long-term use in the future.

<u>Intra-Aortic Balloon Counter-Pulsation Pump (IABC)</u>

Counter-pulsation has become a standard component of treatment in patients with cardiogenic shock or severe acute left heart failure that (i) do not respond rapidly to fluid administration, vasodilatation, and inotropic support; (ii) is complicated by significant MR or rupture of the interventricular septum, to obtain haemodynamic stabilization for definitive diagnostic studies or treatment; or (iii)

is accompanied by severe myocardial ischaemia, in preparation for coronary angiography and revascularization.

Synchronized IABC is performed by inflating and deflating a 30-50 mL balloon placed in the thoracic aorta through the femoral artery. The inflation of the balloon in diastole increases aortic diastolic pressure and coronary flow while the deflation during systole decreases afterload and facilitates LV emptying. IABC may dramatically improve haemodynamics but its use should be restricted to patients whose underlying condition may be corrected (by, e.g., coronary revascularization, valve replacement, or heart transplant) or may recover spontaneously (e.g., myocardial stunning very early after AMI or open heart surgery, myocarditis). IABC is contraindicated in patients with aortic dissection or significant aortic insufficiency. It should not be used in patients with severe peripheral vascular disease, uncorrectable causes of heart failure, or multi-organ failure.

Class I recommendation, level of evidence B

Ventricular Assist Devices

Ventricular assist devices are mechanical pumps that partially replace the mechanical work of the ventricle (see table 14 of the original guideline document). They unload the ventricle, thereby decreasing myocardial work, and pump blood into the arterial system increasing peripheral and end-organ flow. Some devices include a system for extra-corporeal oxygenation. New devices intended for the treatment of chronic (rather than acute) failure restrict the progression of ventricular dilatation. Recently, a number of devices have been developed for acute, short-term mechanical circulatory support in patients with acute or acutely decompensated heart failure. Some devices require a median sternotomy and complex surgery. Others simply extract blood from the arterial system pumping the blood again into the arterial or venous vascular system. In some patients, the haemodynamic and clinical improvement may be spectacular.

If recovery from AHF or transplantation is not possible, then the use of ventricular assist devices is unacceptable. The outcome of patients treated with a left ventricular assist devices vs. conventional treatment in a randomized clinical trial improved the prognosis of end-stage heart failure patients compared with conventional care, but was expensive and accompanied by frequent infections and thrombotic complications. Experience is needed for the implantation and service of the pump and these devices should only be used within the framework of an institutional programme. Table 14 of the original guideline document summarizes the more frequently used systems and the main indications.

Class IIa recommendation, level of evidence B

Thromboembolism, bleeding, and infection are the most common complications associated with the use of ventricular assist devices. Haemolysis and device malfunction are also frequent.

Selection of Candidates for Device Therapy

Only patients with severe heart failure-not responding to conventional treatment of AHF including the appropriate use of fluids, diuretics, intravenous inotropics, and vasodilators, as well as IABC and possibly mechanical ventilation -should be considered as potential candidates for mechanical support. Although transient haemodynamic and clinical improvement can be obtained in many cases, only patients with potential recovery of cardiac function should be considered as candidates for ventricular assist devices (see Figure 8 in the original guideline document). These conditions include (i) acute myocardial ischaemia or infarction; (ii) shock after cardiac surgery; (iii) acute myocarditis; (iv) acute valvular dysfunction (particularly in the absence of previous chronic heart failure, when improvement in ventricular function is expected after spontaneous recovery or after appropriate interventions such as revascularization or valve replacement); (v) candidates for heart transplant.

Patients with permanent end-organ dysfunction, including severe systemic disease, severe renal failure, pulmonary disease, hepatic dysfunction, or permanent central nervous injury should not be considered for device therapy.

The selection of the specific device depends on the specific cardiac pathology, device availability, and surgical team experience.

Heart Transplantation

Transplantation can be considered as a possibility in severe AHF known to have poor outcome. This is the case in severe acute myocarditis or in postpuerperal cardiomyopathy or in a patient with major myocardial infarction with an initially poor outcome after revascularization. However, transplantation is not possible until the patient's condition has been stabilized with the aid of devices and artificial pumps.

Summary Comments

The essential principles of the management of AHF are detailed in these guidelines and in the European Society of Cardiology (ESC) Task Force guidelines for the diagnosis and treatment of CHF.

The clinical syndrome of AHF may present as acute *de novo* heart failure or as decompensated CHF with forward, left (backward), or right (backward) dominance in the clinical syndrome. A patient with decompensated AHF failure requires immediate diagnostic evaluation and care, and frequent resuscitative measures to improve symptoms and survival.

Initial diagnostic assessment should include clinical examination supported by the patient's history, ECG, chest x-ray, plasma BNP/NT-proBNP, and other laboratory tests. Echocardiography should be performed in all patients as soon as possible (unless recently done and the result is available).

The initial clinical assessment should include evaluation of preload, afterload, and the presence of MR and other complicating disorders (including other valvular complications, arrhythmia, and concomitant co-morbidities such as infection, diabetes mellitus, respiratory diseases, or renal diseases). Acute coronary

syndromes are a frequent cause of AHF and coronary angiography is often required.

Following initial assessment, an i.v. line should be inserted, and physical signs, ECG, and SpO_2 should be monitored. An arterial line should be inserted when needed.

The initial treatment of AHF consists of:

- Oxygenation with face-mask or by continuous positive airway pressure (SaO_2 target of 94-96%)
- Vasodilatation by nitrate or nitroprusside
- Diuretic therapy by furosemide or other loop diuretic (initially i.v. bolus followed by continuous i.v. infusion, when needed)
- Morphine for relief of physical and psychological distress and to improve haemodynamics
- I.V. fluids if the clinical condition is preload-dependent and there are signs of low filling pressure. This may require testing the response to an aliquot of fluid.
- Other complicating metabolic and organ-specific conditions should be treated on their own merits.
- Patients with acute coronary syndrome or other complicated cardiac disorders should undergo cardiac catheterization and angiography, with a view to invasive intervention including surgery.
- Appropriate medical treatment by beta-blocking agents and other medical therapy should be initiated as described in this report.

Further specific therapies (see figures 5-7 and table 14 of the original guideline document) should be administered based on the clinical and haemodynamic characteristics of the patient who does not respond to initial treatment. This may include the use of inotropic agents or a calcium sensitizer for severe decompensated heart failure, or inotropic agents for cardiogenic shock. The aim of therapy of AHF is to correct hypoxia and increase cardiac output, renal perfusion, sodium excretion, and urine output. Other therapies may be required (e.g., i.v. aminophylline or beta-2-agonist for bronchodilation). Ultrafiltration or dialysis may be prescribed for refractory heart failure.

Patients with refractory AHF or end-stage heart failure should be considered for further support, where indicated (see figures 7 and 8 of the original guideline document) including: intra-aortic balloon pump, artificial mechanical ventilation, or circulatory assist devices as a temporary measure or as a "bridge" to heart transplantation.

The patient with AHF may recover extremely well, depending on the aetiology and the underlying pathophysiology. Prolonged treatment on the ward and expert care are required. This is best delivered by a specialist heart failure team that can rapidly initiate medical management and attend to the information needs of the patient and family.

Definitions:

Levels of Evidence

Level of evidence A: Data derived from multiple randomized clinical trials or meta-analyses

Level of evidence B: Data derived from a single randomized clinical trial or large non-randomized studies

Level of evidence C: Consensus of opinion of the experts and/or small studies, retrospective studies and registries

Classes of Recommendations

Class I: Evidence and/or general agreement that a given diagnostic procedure/treatment is beneficial, useful, and effective

Class II: Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the treatment

- Class IIa: Weight of evidence/opinion is in favour of usefulness/efficacy
- Class IIb: Usefulness/efficacy is less well established by evidence/opinion

Class III*: Evidence or general agreement that the treatment is not useful/effective and in some cases may be harmful

*Use of Class III is discouraged by the European Society of Cardiology (ESC)

CLINICAL ALGORITHM(S)

Clinical algorithms are provided in the original guideline document for:

- The assessment of left ventricular (LV) function in acute heart failure (AHF)
- Immediate goals in treatment of patients with AHF
- The rationale for use of inotropic drugs in AHF
- AHF in acute myocardial infarction (AMI)
- Selection of candidates for LV assist device

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for selected recommendations (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate diagnosis and treatment of acute heart failure (AHF)

POTENTIAL HARMS

- Side effects of vasodilators including hypotension and headache
- Prolonged administration of sodium nitroprusside (SNP) may be associated with toxicity from its metabolites, thiocyanide and cyanide, and should be avoided especially in patients with severe renal or hepatic failure.
- Nesiritide may cause hypotension and some patients are non-responders.
- Although diuretics can be used safely in the majority of patients, secondary effects are frequent and may be life-threatening. These include neurohormonal activation, especially of the angiotensin-aldosterone system and the sympathetic nervous system; hypokalemia, hypomagnesemia and hypochloraemic alkalosis which may lead to severe arrhythmias; nephrotoxicity and aggravation of renal failure. Excessive diuresis may reduce venous pressure, pulmonary wedge pressure, and diastolic filling excessively, leading to a reduction in stroke volume and cardiac output, particularly in patients with severe heart failure and predominant diastolic failure or ischaemic right ventricular dysfunction.
- The use of inotropic agents is potentially harmful as they increase oxygen demand and calcium loading and they should be used with caution.
- Infusion of dobutamine is accompanied by an increased incidence of arrhythmia originating from both ventricles and atria. This effect is dose-related and may be more prominent than with phosphodiesterase inhibitor (PDEI) and should prompt strict potassium compensation during intravenous diuretic use. Tachycardia may also be a limiting parameter, and dobutamine infusion may trigger chest pain in patients with coronary artery disease. In patients with hibernating myocardium, dobutamine appears to increase contractility in the short term at the expense of myocyte necorosis and loss in myocardial recovery.
- Tachycardia and hypotension are described with high-dose levosimendan infusion and it is not currently recommended in patients with systolic blood pressure <85 mmHg. A reduction in the haematocrit, haemoglobin, and plasma potassium, likely secondary to vasodilation and secondary neurohumoral activation, have been described and seem to be dose dependent.

CONTRAINDICATIONS

CONTRAINDICATIONS

- Low-molecular-weight heparin (LMWH) is contraindicated if the creatinine clearance is <30 mL/min or should be used with extreme care with monitoring of the anti-Factor Xa level.
- Calcium antagonists are not recommended in the treatment of acute heart failure (AHF). Diltiazem, and verapamil, and dihydropyridines should be considered contraindicated.
- There has been no study with beta-blocker therapy in AHF targeted to acutely improve the condition. On the contrary, AHF has been considered a contraindication for this treatment. See "Major Recommendations" field concerning use of beta-blockers in AHF.
- Contraindications to the use of cardiac glycosides include bradycardia, second and third degree atrioventricular (AV)-block, sick sinus syndrome, carotid sinus syndrome, Wolff-Parkinson-White syndrome, hypertrophic obstructive cardiomyopathy, hypokalemia, and hypercalcemia.

- Administration of angiotensin-converting enzyme (ACE)-inhibitors is associated with an increased incidence of severe renal failure and hyperkalaemia in patients with concomitant renal failure. An increase in serum creatinine of more than 25-30% and/or achievement of levels >3.5 mg/dL (>226 micromol/L) are relative contraindications to the continuation of angiotensin-converting enzyme-inhibitor treatment.
- Intra-aortic balloon counter-pulsation (IABC) is contraindicated in patients with aortic dissection or significant aortic insufficiency.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Clinical Algorithm
Personal Digital Assistant (PDA) Downloads
Pocket Guide/Reference Cards
Slide Presentation

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Task Force on Acute Heart Failure of the European Society of Cardiology. Guidelines on the diagnosis and treatment of acute heart failure. Sophia Antipolis (FR): European Society of Cardiology; 2005. 36 p. [241 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

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GUIDELINE DEVELOPER(S)

European Society of Cardiology - Medical Specialty Society

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GUIDELINE COMMITTEE

Task Force on Acute Heart Failure of the European Society of Cardiology

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available from the European Society of Cardiology (ESC) Web site.

Print copies: Available from Oxford University Press, Journals Division, Great Clarendon Street, Oxford, OX2 6DP, United Kingdom. Tel: +44 207 424 4422; Fax: +44 207 424 4515.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Guidelines on the diagnosis and treatment of acute heart failure. Executive summary. 2005. Electronic copies: Available in Portable Document Format (PDF) from the European Society of Cardiology (ESC) Web site.
- Guidelines on the diagnosis and treatment of acute heart failure. Pocket guidelines. 2005. An order form for ESC pocket guidelines is available in Portable Document Format (PDF) from the European Society of Cardiology (ESC) Web site. Also available for PDA download from the ESC Web site.
- Guidelines on the diagnosis and treatment of acute heart failure. Slide set. Available from the European Society of Cardiology (ESC) Web site

Print copies: Available from Oxford University Press, Journals Division, Great Clarendon Street, Oxford, OX2 6DP, United Kingdom. Tel: +44 207 424 4422; Fax: +44 207 424 4515.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on April 29, 2005. The information was verified by the guideline developer on July 20, 2005. This summary was updated by ECRI Institute on June 22, 2007 following the U.S. Food and Drug Administration (FDA) advisory on heparin sodium injection. This summary was updated by ECRI Institute on July 12, 2007 following the U.S. Food and Drug Administration (FDA) advisory on Troponin-1 Immunoassay. This summary was updated by ECRI Institute on March 14, 2008 following the updated FDA advisory on heparin sodium injection.

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