Complete Summary

GUIDELINE TITLE

Guidelines for the diagnosis and treatment of chronic heart failure (update 2005).

BIBLIOGRAPHIC SOURCE(S)

Swedberg K, Cleland J, Dargie H, Drexler H, Follath F, Komajda M, Tavazzi L, Smiseth OA, Gavazzi A, Haverich A, Hoes A, Jaarsma T, Korewicki J, Levy S, Linde C, Lopez-Sendon JL, Nieminen MS, Pierard L, Remme WJ. Guidelines for the diagnosis and treatment of chronic heart failure: full text (update 2005): The Task Force for the Diagnosis and Treatment of Chronic Heart Failure of the European Society of Cardiology. Sophia Antipolis (FR): European Society of Cardiology (ESC); 2005. 45 p. [358 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Remme WJ, Swedberg K, Task Force for the Diagnosis and Treatment of Chronic Heart Failure, European Society of Cardiology. Guidelines for the diagnosis and treatment of chronic heart failure. Eur Heart J 2001 Sep;22(17):1527-60.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

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

- August 16, 2007, Coumadin (Warfarin): Updates to the labeling for Coumadin to include pharmacogenomics information to explain that people's genetic makeup may influence how they respond to the drug.
- October 6, 2006, Coumadin (warfarin sodium): Revisions to the labeling for Coumadin to include a new patient Medication Guide as well as a reorganization and highlighting of the current safety information to better inform providers and patients.

COMPLETE SUMMARY CONTENT

** REGULATORY ALERT **
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INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES
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SCOPE

DISEASE/CONDITION(S)

Chronic heart failure (CHF)

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Treatment

CLINICAL SPECIALTY

Cardiology
Family Practice
Internal Medicine
Thoracic Surgery

INTENDED USERS

Advanced Practice Nurses
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To provide updated practical guidelines for the diagnosis, assessment, and treatment of heart failure for use in clinical practice, as well as for epidemiological surveys and clinical trials

TARGET POPULATION

Patients with chronic heart failure (CHF)

INTERVENTIONS AND PRACTICES CONSIDERED

Evaluation/Diagnosis

1. Assessment of signs and symptoms of heart failure
2. Establish severity with New York Heart Association (NYHA) classification and quality of life with Minnesota Living with Heart Failure questionnaire
3. Electrocardiogram (ECG)
4. Chest x-ray
5. Laboratory investigations including haematology and biochemistry
6. Echocardiography (transthoracic Doppler, transoesophageal)
7. Stress echocardiogram
8. Nuclear cardiology (radionuclide angiography [RNA], planar scintigraphy, single photon emission computer tomography [SPECT])
9. Cardiac magnetic resonance imaging (MRI)
10. Measurement of pulmonary function, including forced vital capacity (FVC) measurement, forced expiratory volume (FEV), and peak expiratory flow rate (PEFR)
11. Exercise testing
12. Invasive investigations (coronary angiography, haemodynamic monitoring, endomyocardial biopsy)
13. Measurement of plasma natriuretic peptides including B-type natriuretic peptide (BNP) and N-terminal prohormone B-type natriuretic peptide (NT-proBNP)
14. Holter electrocardiography

Treatment/Management

Non-pharmacological Management

1. General advice and measures including weight control and monitoring; dietary measures such as salt restriction; fluid and alcohol intake reduction; weight control; smoking cessation; advice on traveling, sexual activity, and immunizations; and drug counseling
2. Exercise and exercise training
3. Rest

Pharmacological Therapy

1. Angiotensin-converting enzyme (ACE) inhibitors
2. Diuretics, including loop diuretics, thiazides, and potassium-sparing diuretics
3. Beta-adrenoceptor antagonists
4. Aldosterone receptor antagonists
5. Angiotensin receptor blockers
6. Cardiac glycosides (e.g., digoxin)
7. Vasodilator agents
8. Positive inotropic therapy
9. Antithrombotic agents
10. Antiarrhythmic agents
11. Oxygen therapy (considered, but not recommended)

Devices and Surgery

1. Revascularization procedures (considered, but not recommended)
2. Mitral valve surgery
3. Left ventricular (LV) aneurysmectomy

4. Cardiomyoplasty (considered, but not recommended)
5. Partial left ventriculectomy (Batista operation) (considered, but not recommended)
6. External ventricular restoration (considered, but not recommended)
7. Pacemakers
8. Implantable cardioverter defibrillators
9. Heart transplantation, ventricular assist devices, artificial heart
10. Ultrafiltration

Follow-up Care

Follow-up care including multi-disciplinary approach, discharge planning, intense education and counseling, etc.

Note: Interventions and practices related to treatment of diastolic heart failure, heart failure in the elderly, and heart failure in patients with concomitant arrhythmia, hypertension, or angina are also presented.

MAJOR OUTCOMES CONSIDERED

- Accuracy, sensitivity, and specificity of diagnostic assessments
- Rates of heart failure
- Symptoms of heart failure
- Progression of heart failure, including hospitalization for worsening heart failure
- Mortality, including total mortality, cardiovascular mortality, sudden death, and death due to progression of heart failure
- Quality of life
- Adverse effects

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Searches were performed of the following resources: PubMed, medicals journals by specialty, the Cochrane Library.

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:

A. Data derived from multiple randomized clinical trials or meta-analyses
B. Data derived from a single randomized clinical trial or large non-randomized studies
C. Consensus of opinion of the experts and/or small studies, retrospective studies, 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

This clinical scientific statement represents the consensus of a panel of experts appointed by the European Society of Cardiology (ESC). The writing group comprises cardiovascular specialists and pharmacologists and if necessary surgeons, each having extensive experience with chronic heart failure. The panel focused largely on the management of this complex disease and derived prudent, practical, and contemporary treatment strategies for the many subgroups of patients comprising the broad chronic heart failure disease spectrum.

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 evidence 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

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

This report was drafted by a Writing Group of the Task Force appointed by the Committee for Practice Guidelines (CPG) of the European Society of Cardiology (ESC). The draft was sent to the Committee and the document reviewers and after their input the document was updated, reviewed, and then approved for presentation.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The levels of evidence (A-C) and classes of recommendations (I, II, IIa, IIb, III) are defined at the end of the "Major Recommendations" field.

Diagnosis of Chronic Heart Failure (CHF)

Definition of Chronic Heart Failure

- Heart failure should never be the only diagnosis.

Heart failure is a syndrome in which the patients should have the following features: symptoms of heart failure, typically breathlessness or fatigue, either at rest or during exertion, or ankle swelling and objective evidence of cardiac dysfunction at rest (See Table below titled "Definition of Heart Failure"). The distinctions between cardiac dysfunction, persistent heart failure, heart failure that has been rendered asymptomatic by therapy, and transient heart failure are outlined in Figure 1 in the original guideline document. A clinical response to treatment directed at heart failure alone is not sufficient for diagnosis, although the patient should generally demonstrate some improvement in symptoms and/or signs in response to those treatments in which a relatively fast symptomatic improvement could be anticipated (e.g., diuretic or nitrate administration).

Asymptomatic left ventricular systolic dysfunction is considered as precursor of symptomatic CHF and is associated with high mortality (Wang et al., 2003). It is important when diagnosed and treatment is available, and the condition is therefore included in these Guidelines.

Table. Definition of Heart Failure

I.	Symptoms of heart failure (at rest or during exercise) *and*
II.	Objective evidence (preferably by echocardiography) of cardiac dysfunction (systolic and/or diastolic) (at rest) and (in cases where the diagnosis is in doubt) *and*
III.	Response to treatment directed towards heart failure

Criteria I and II should be fulfilled in all cases.

Possible Methods for the Diagnosis of Heart Failure in Clinical Practice

Symptoms and Signs in the Diagnosis of Heart Failure

- Symptoms and signs are important as they alert the observer to the possibility that heart failure exists. The clinical suspicion of heart failure must be confirmed by more objective tests particularly aimed at assessing cardiac function (See Figure 2 in the original guideline document).

Breathlessness, ankle swelling, and fatigue are the characteristic symptoms and signs of heart failure but may be difficult to interpret, particularly in elderly patients, in obese, and in women. It should be interpreted carefully and different modes (e.g., effort and nocturnal) should be assessed.

Fatigue is also an essential symptom in heart failure. The origins of fatigue are complex including low cardiac output, peripheral hypoperfusion, skeletal muscle deconditioning, and confounded by difficulties in quantifying this symptom.

Peripheral oedema, raised venous pressure, and hepatomegaly are the characteristic signs of congestion of systemic veins (Butman et al., 1993; Stevenson & Perloff, 1989). Clinical signs of heart failure should be assessed in a careful clinical examination, including observing, palpating, and auscultating the patient.

Symptoms and the Severity of Heart Failure

- There is a poor relationship between symptoms and the severity of cardiac dysfunction. (Cleland et al., 2001; Marantz et al., 1988) However, symptoms may be related to prognosis particularly if persisting after therapy. (Adams & Zannad, 1989)

Once a diagnosis of heart failure has been established, symptoms may be used to classify the severity of heart failure and should be used to monitor the effects of therapy. However, as noted subsequently, symptoms cannot guide the optimal titration of neurohormonal blockers. The New York Heart Association (NYHA) classification is in widespread use (See Table 2 in the original guideline document). In other situations, the classification of symptoms into mild, moderate, or severe is used. Patients in NYHA class I would have to have objective evidence of cardiac dysfunction, have a past history of heart failure symptoms, and be receiving treatment for heart failure in order to fulfill the basic definition of heart failure.

Electrocardiogram

- A normal electrocardiogram (ECG) suggests that the diagnosis of CHF should be carefully reviewed.

Electrocardiographic changes are common in patients suspected of having heart failure whether or not the diagnosis proves to be correct. An abnormal ECG, therefore, has little predictive value for the presence of heart failure. On the other hand, if the ECG is completely normal, heart failure, especially due to left ventricular (LV) systolic dysfunction, is unlikely. The presence of pathological Q-waves may suggest myocardial infarction as the cause of cardiac dysfunction. A QRS width >120 ms suggests that cardiac dyssynchrony may be present and a target for treatment.

The Chest X-ray

Chest x-ray should be part of the initial diagnostic work-up in heart failure. It is useful to detect cardiomegaly and pulmonary congestion; however, it has only predictive value in the context of typical signs and symptoms and in abnormal ECG.

Haematology and Biochemistry

Routine diagnostic evaluation of patients with CHF includes complete blood count (Hb, leukocytes, and platelets), S-electrolytes, S-creatinine, S-glucose, S-hepatic enzymes, and urinalysis. Additional tests to evaluate thyroid function should be considered according to clinical findings. In acute exacerbations, acute myocardial infarction is excluded by myocardial specific enzyme analysis.

Natriuretic Peptides

- Plasma concentrations of certain natriuretic peptides or their precursors, especially BNP and NT-proBNP, are helpful in the diagnosis of heart failure.
- A low-normal concentration in an untreated patient makes heart failure unlikely as the cause of symptoms.
- BNP and NT-proBNP have considerable prognostic potential, although evaluation of their role in treatment monitoring remains to be determined.

In considering the use of BNP and NT-proBNP as diagnostic aids, it should be emphasized that a "normal" value cannot completely exclude cardiac disease, but

a normal or low concentration in an untreated patient makes heart failure unlikely as the cause of symptoms.

In clinical practice today, the place of BNP and NT-proBNP is as "rule out" tests to exclude significant cardiac disease, particularly in primary care but also in certain aspects of secondary care (e.g., the emergency room and clinics). The cost-effectiveness of the test suggests that a normal result should obviate the need for further cardiological tests such as in the first instance echocardiography as well as more expensive investigations (Maisel et al., 2002).

Echocardiography

- Echocardiography is the preferred method for the documentation of cardiac dysfunction at rest.
- The most important measurement of ventricular function is the left ventricular ejection fraction (LVEF) for distinguishing patients with cardiac systolic dysfunction from patients with preserved systolic function.

The access to and use of echocardiography is encouraged for the diagnosis of heart failure. Transthoracic Doppler echocardiography (TDE) is rapid, safe, and widely available.

Please refer to the original guideline document for discussion on the assessment of LV diastolic function and diagnostic criteria of diastolic dysfunction.

Additional Non-invasive Tests to be Considered

In patients in whom echocardiography at rest has not provided enough information and in patients with coronary artery disease (e.g., severe or refractory CHF and coronary artery disease), further non-invasive imaging may include stress echocardiography, radionuclide imaging, and cardiac magnetic resonance imaging (CMR).

<u>Cardiac Magnetic Resonance Imaging (CMR)</u>

- CMR is a versatile, highly accurate, and reproducible imaging technique for the assessment of left and right ventricular volumes, global function, regional wall motion, myocardial thickness, thickening, myocardial mass, and cardiac valves (Bellenger et al., 2000; Grothues et al., 2004). The method is well suited for detection of congenital defects, masses and tumours, valvular, and pericardial disease.

Pulmonary Function

- Measurements of lung function are of little value in diagnosing CHF. However, they are useful in excluding respiratory causes of breathlessness. Spirometry can be useful to evaluate the extent of obstructive airways disease which is a common comorbidity in patients with heart failure.

Exercise Testing

- In clinical practice, exercise testing is of limited value for the diagnosis of heart failure. However, a normal maximal exercise test in a patient not receiving treatment for heart failure excludes heart failure as a diagnosis. The main applications of exercise testing in CHF are focused more on functional and treatment assessment and on prognostic stratification.

Invasive Investigation

- Invasive investigation is generally not required to establish the presence of CHF but may be important in elucidating the cause or to obtain prognostic information.

Cardiac Catheterization

Please refer to the original guideline document for a discussion on cardiac catheterization.

Tests of Neuroendocrine Evaluations Other Than Natriuretic Peptides

- Tests of neuroendocrine activation are not recommended for diagnostic or prognostic purposes in individual patients.

Holter Electrocardiography: Ambulatory ECG and Long-time ECG Recording (LTER)

Conventional Holter monitoring is of no value in the diagnosis of CHF, though it may detect and quantify the nature, frequency, and duration of atrial and ventricular arrhythmias which could be causing or exacerbating symptoms of heart failure. Recording LTER should be restricted to patients with CHF and symptoms suggestive of an arrhythmia.

Requirements for the Diagnosis of Heart Failure in Clinical Practice

To satisfy the definition of heart failure, symptoms of heart failure and objective evidence of cardiac dysfunction must be present. (See table above titled "Definition of Heart Failure.") The assessment of cardiac function by clinical criteria alone is unsatisfactory. Cardiac dysfunction should be assessed objectively.

The echocardiogram is the single most effective tool in widespread clinical use. Other conditions may mimic or exacerbate the symptoms and signs of heart failure and therefore need to be excluded. (See table below titled "Assessments to Be Performed Routinely to Establish the Presence and Likely Cause of Heart Failure.") An approach (see Figure 2 in the original guideline document) to the diagnosis of heart failure in symptomatic patients should be performed routinely in patients with suspected heart failure in order to establish the diagnosis. Additional tests (see table below titled "Additional Tests to be Considered to Support the Diagnosis or to Suggest Alternative Diagnoses") should be performed or re-evaluated in cases in which diagnostic doubt persists or clinical features suggest a reversible cause for heart failure.

Figure 2 in the original guideline document represents a simplified plan for the evaluation of a patient presenting with symptoms suggestive of heart failure or signs giving suspicion of left ventricular systolic dysfunction. The table below titled "Management Outline" provides a management outline connecting the diagnosis component of the guidelines with the treatment section.

Table. Assessments to Be Performed Routinely to Establish the Presence and Likely Cause of Heart Failure

Assessments	Diagnosis of heart failure			Suggests alternative or additional diagnosis
	Necessary for	Supports	Opposes	
Appropriate symptoms	+++		+++ (If absent)	
Appropriate signs		+++	+ (If absent)	
Cardiac dysfunction on imaging (usually echocardiography)	+++		+++ (If absent)	
Response of symptoms or signs to therapy		+++	+++ (If absent)	
ECG			+++ (If Normal)	
Chest x-ray		If pulmonary congestion or cardiomegaly	+ (If normal)	Pulmonary disease
Full blood count				Anaemia/secondary polycythaemia
Biochemistry and urinalysis				Renal or hepatic disease/diabetes
Plasma concentration of natriuretic peptides in untreated patients (where available)		+ (If elevated)	+++ (If normal)	Can be normal in treated patients

+ = of some importance; +++ = of great importance

Table. Additional Tests to Be Considered to Support the Diagnosis or to Suggest Alternative Diagnoses

Tests	Diagnosis of heart failure		Suggests alternative or additional diagnosis
	Supports	Opposes	
Exercise test	+ (If impaired)	+++ (If normal)	
Pulmonary function tests			Pulmonary disease
Thyroid function tests			Thyroid disease

Tests	Diagnosis of heart failure		Suggests alternative or additional diagnosis
	Supports	Opposes	
Invasive investigation and angiography			Coronary artery disease, ischaemia
Cardiac output	+++ (If depressed at rest)	+++ (If normal; especially during exercise)	
Left atrial pressure (pulmonary capillary wedge pressure)	+ (If elevated at rest)	+++ (If normal; in absence of therapy)	

+ = of some importance; +++ = of great importance

Table. Management Outline

- Establish that the patient has heart failure (in accordance with the definition presented on page 4, "Definition of CHF" in the original guideline document).
- Ascertain presenting features: pulmonary oedema, exertional breathlessness, fatigue, peripheral oedema.
- Assess severity of symptoms.
- Determine aetiology of heart failure.
- Identify precipitating and exacerbating factors.
- Identify concomitant diseases relevant to heart failure and its management.
- Estimate prognosis based on Table 7 in the original guideline document.
- Assess complicating factors (e.g., renal dysfunction, arthritis).
- Counsel patient and relatives.
- Choose appropriate management.
- Monitor progress and manage accordingly.

Prognostication

- The problem of defining prognosis in heart failure is complex for many reasons: several aetiologies, frequent comorbidities, limited ability to explore the paracrine pathophysiological systems, varying individual progression and outcome (sudden vs. progressive heart failure death), and efficacy of treatments. Moreover, several methodological limitations weaken many prognostic studies. The variables more consistently indicated as independent outcome predictors are reported in Table 7 in the original guideline document.

Treatment of Heart Failure

Aims of Treatment in Heart Failure

i. Prevention--a primary objective
   a. Prevention and/or controlling of diseases leading to cardiac dysfunction and heart failure

b. Prevention of progression to heart failure once cardiac dysfunction is established

ii. Maintenance or improvement in quality of life

iii. Improved survival

Prevention of Heart Failure

- The development of ventricular dysfunction and heart failure may be delayed or prevented by treatment of conditions Leading to heart failure, in particular in patients with hypertension and/or coronary artery disease (Class of recommendation I, Level of evidence A) (Turnbull, 2003).
- The prevention of heart failure should always be a primary objective.

When myocardial dysfunction is already present, the first objective is to remove the underlying cause of ventricular dysfunction if possible (e.g., ischaemia, toxic substances, alcohol, drugs, and thyroid disease), providing the benefits of intervention outweigh the risks. When the underlying cause cannot be corrected treatment should be directed at delaying or preventing left ventricular dysfunction that wilt increase the risk of sudden death and the development of heart failure.

Management of Chronic Heart Failure

The therapeutic approach in patients with CHF that is caused by left ventricular systolic dysfunction includes general advice and other non-pharmacological measures, pharmacological therapy, mechanical devices, and surgery.

Non-pharmacological Management

General Advice and Measures

(Class of recommendation I, level of evidence C for non-pharmacological management unless stated otherwise)

Educating Patients and Family
Patients with CHF and their close relatives should receive general advice.

Weight Monitoring
Patients are advised to weigh on a regular basis to monitor weight gain (preferably as part of a regular daily routine, for instance after morning toilet) and, in case of a sudden unexpected weight gain of >2 kg in 3 days, to alert a health care provider or adjust their diuretic dose accordingly (e.g., to increase the dose if a sustained increase in weight is noted).

Dietary Measures

Sodium. Controlling the amount of salt in the diet is a problem, that is, more relevant in advanced than in mild heart failure.

Fluids. Instructions on fluid control should be given to patients with advanced heart failure, with or without hyponatraemia. The exact amount of fluid restriction

remains unclear, however. In practice, a fluid restriction of 1.5 to 2 L/day is advised in advanced heart failure.

Alcohol. Moderate alcohol intake (one beer, 1 to 2 glasses of wine/day) is permitted other than in case of alcoholic cardiomyopathy when it is prohibited.

Obesity
Treatment of CHF should include weight reduction in obese patients.

Abnormal Weight Loss
Clinical or subclinical malnutrition is present in approximately 50% of patients with severe CHF. The wasting of total body fat and lean body mass that accompanies weight loss is called cardiac cachexia. Cardiac cachexia is an important predictor of reduced survival (Anker et al., 1997).

Smoking
Smoking should always be discouraged. The use of smoking cessation aids should be actively encouraged and may include nicotine replacement therapies.

Travelling
High altitudes or very hot or humid places should be discouraged. In general, short air flights are preferable to long journeys by other means of transport.

Sexual Activity
It is not possible to dictate guidelines about sexual activity counselling. Recommendations are given to reassure the not severely compromised, but frightened patient, to reassure the partner who is often even more frightened, and perhaps refer the couple for specialist counselling. Little is known about the effects of treatments for heart failure on sexual function.

Advice on Immunizations
There is no documented evidence of the effects of immunization in patients with heart failure. Immunization for influenza is widely used.

Drug Counselling
Self-management (when practical) of the dose of the diuretic, based on changes in symptoms and weight (fluid balance), should be encouraged. Within pre-specified and individualized limits, patients are able to adjust their diuretics.

Drugs to Avoid or Beware

The following drugs should be used with caution when co-prescribed with any form of heart failure treatment or avoided:

1. Non-steroidal anti-inflammatory drugs (NSAIDS) and coxibs
2. Class I anti-arrhythmic agents
3. Calcium antagonists (verapamil, diltiazem, and short-acting dihydropyridine derivatives
4. Tricyclic anti-depressants
5. Corticosteroids
6. Lithium

Rest, Exercise, and Exercise Training

Rest
In acute heart failure or destabilization of CHF, physical rest or bed rest is recommended.

Exercise
Exercise improves skeletal muscle function and therefore overall functional capacity. Patients should be encouraged and advised on how to carry out daily physical and leisure time activities that do not induce symptoms. Exercise training programs are encouraged in stable patients in NYHA class Il-Ill. Standardized recommendations for exercise training in heart failure patients by the European Society of Cardiology have been published (Working Group on Cardiac Rehabilitation, 2001).

Pharmacological Therapy

Angiotensin-Converting Enzyme Inhibitors

Angiotensin-converting enzyme (ACE) inhibitors are recommended as first-line therapy in patients with a reduced left ventricular systolic function expressed as a subnormal ejection fraction, i.e., <40-45% with or without symptoms (see non-invasive imaging on page 11 in the original guideline document) (Class of recommendation I, level of evidence A).

ACE-inhibitors should be uptitrated to the dosages shown to be effective in the large, controlled trials in heart failure (Class of recommendation I, level of evidence A), and not titrated based on symptomatic improvement alone (Class of recommendation I, level of evidence C).

ACE Inhibitors in Asymptomatic Left Ventricular Dysfunction

Asymptomatic patients with a documented left ventricular systolic dysfunction should be treated with an ACE-inhibitor to delay or prevent the development of heart failure. ACE-inhibitors also reduce the risk of myocardial infarction and sudden death in this setting (Class of recommendation I, level of evidence A) ("Effect of enalapril on mortality," 1992; Pfeffer et al., 1992; Kober et al., 1995; Jong et al., 2003).

ACE Inhibitors in Symptomatic Heart Failure

- All patients with symptomatic heart failure that is caused by systolic left ventricular dysfunction should receive an ACE inhibitor (Class of recommendation I, level of evidence A). (Flather et al., 2000).
- ACE inhibition improves survival, symptoms, functional capacity, and reduces hospitalization in patients with moderate and severe heart failure and left ventricular systolic dysfunction.
- ACE inhibitors should be given as the initial therapy in the absence of fluid retention. In patients with fluid retention, ACE inhibitors should be given together with diuretics (Class of recommendation I, level of evidence B) (Flather et al., 2000; The CONSENSUS Trial Study Group, 1987).

- ACE inhibition should be initiated in patients with signs or symptoms of heart failure, even if transient, after the acute phase of myocardial infarction, even if the symptoms are transient to improve survival and to reduce reinfarctions and hospitalizations for heart failure (Class of recommendation I, level of evidence A) (Pfeffer et al., 1992; Kober et al., 1995, "Effect of ramipril," 1993).
- Asymptomatic patients with a documented left ventricular systolic dysfunction benefit from long-term ACE inhibitor therapy (Class of recommendation I, level of evidence A) ("Effect of enalapril on mortality," 1992; Pfeffer et al., 1992; Kober et al., 1995; Jong et al., 2003).
- Important adverse effects associated with ACE-inhibitors are cough, hypotension, renal insufficiency, hyperkalaemia, syncope, and angioedema. Angiotensin receptor blockers may be used as an effective alternative in patients who develop cough or angioedema on an ACE-inhibitor (Class of recommendation I, level of evidence A). Changes in systolic and diastolic blood pressure and increases in serum creatinine are usually small in normotensive patients.
- ACE inhibitor treatment is contraindicated in the presence of bilateral renal artery stenosis and angioedema during previous ACE-inhibitor therapy (Class of recommendation III, level of evidence A).

Target maintenance dose ranges of ACE inhibitors shown to be effective in various trials are given in Table 12 in the original guideline document. Recommended initiating and maintenance dosages of ACE-inhibitors which have been approved for the treatment of heart failure in Europe are presented in Table 13 in the original guideline document.

The dose of ACE inhibitors should always be initiated at the lower dose level and titrated to the target dose. The recommended procedures for starting an ACE inhibitor are given in the table below titled "The Recommended Procedure for Starting an ACE Inhibitor or an Angiotensin Receptor Blocker."

Regular monitoring of renal function is recommended: (1) before, 1-2 weeks after each dose increment, and at 3-6 months interval; (2) when the dose of an ACE inhibitor is increased or other treatments, which may affect renal function, are added (e.g., aldosterone antagonist or angiotensin receptor blocker), (3) in patients with past or present renal dysfunction or electrolyte disturbances more frequent measurements should be made, or (4) during any hospitalization.

Table. The Recommended Procedure for Starting an ACE Inhibitor or an Angiotensin Receptor Blocker

• Review the need for and dose of diuretics and vasodilators. • Avoid excessive diuresis before treatment. Consider reducing or withholding diuretics, if being used, for 24 h. • It may be advisable to start treatment in the evening, when supine, to minimize the potential negative effect on blood pressure, although there are no data in heart failure to support this (Level of Evidence C). When initiated in the morning, supervision for several hours with blood pressure control is advisable in risk patients with renal dysfunction or low blood pressure. • Start with a low dose (see Table 13 in the original guideline document) and build-up to maintenance dosages shown to be effective in large trials (see

Table 12 in the original guideline document).

- If renal function deteriorates substantially, stop treatment.
- Avoid potassium-sparing diuretics during initiation of therapy.
- Avoid nonsteroidal anti-inflammatory drugs (NSAIDs) and Cox-2 inhibitors (coxibs).
- Check blood pressure, renal function, and electrolytes
    - 1-2 weeks after each dose increment, at 3 months, and subsequently at 6 regular monthly intervals
- The following patients should be referred for specialist care:
    - Cause of heart failure unknown
    - Systolic blood pressure <100 mmHg
    - Serum creatinine >150 micromoles/L
    - Serum sodium <135 mmol/L
    - Severe heart failure
    - Valve disease as primary cause

Diuretics

Loop Diuretics, Thiazides, and Metolazone

- Diuretics are essential for symptomatic treatment when fluid overload is present and manifest as pulmonary congestion or peripheral oedema. The use of diuretics results in rapid improvement of dyspnoea and increased exercise tolerance (Class of recommendation I, level of evidence A) (Kaddoura et al., 1996, Bayliss et al., 1987).
- There are no controlled randomized trials that have assessed the effect on symptoms or survival of these agents. Diuretics should always be administered in combination with ACE inhibitors and beta-blockers if tolerated (Class of recommendation I, level of evidence C).

Detailed recommendations and major side effects are outlined in Tables 15 and 16 in the original guideline document.

Potassium-sparing Diuretics

- Potassium-sparing diuretics should only be prescribed if hypokalaemia persists despite ACE inhibition, or in severe heart failure despite the combination ACE inhibition and low-dose spironolactone (Class of recommendation I, level of evidence C). In patients who are unable to tolerate even low doses of aldosterone antagonists due to hyperkalaemia and renal dysfunction, amiloride or triamterene may be used (Class of recommendation IIb, level of evidence C).
- Potassium supplements are generally ineffective in this situation (Class of recommendation III, level of evidence C).

The use of all potassium-sparing diuretics should be monitored by repeated measurements of serum creatinine and potassium. A practical approach is to measure serum creatinine and potassium every 5-7 days after initiation of treatment until the values are stable. Thereafter, measurements can be made every 3-6 months.

Beta-adrenoceptor Antagonists

- Beta-blockers should be considered for the treatment of all patients (in NYHA class II-IV) with stable, mild, moderate, and severe heart failure from ischaemic or non-ischaemic cardiomyopathies and reduced LVEF on standard treatment, including diuretics, and ACE- inhibitors, unless there is a contraindication (Class of recommendation I, level of evidence A) (Packer, et al., 1996; "Randomised, placebo-controlled trial of carvedilol," 1997; Packer et al., 2001; "The cardiac insufficiency bisoprolol study II (CIBIS-II)," 1999; "Effect of metoprolol CR/XL," 1999; "Effects of metoprolol CR," 2000; Flather et al., 2005).
- Beta-blocking therapy reduces hospitalizations (all, cardiovascular, and heart failure), improves the functional class, and leads to less worsening of heart failure. This beneficial effect has been consistently observed in subgroups of different age, gender, functional class, LVEF, and ischaemic or non-ischaemic aetiology (Class of recommendation I, Level of evidence A).
- In patients with left ventricular systolic dysfunction, with or without symptomatic heart failure, following an acute myocardial infarction long-term beta-blockade is recommended in addition to ACE inhibition to reduce mortality (Class of recommendation I, level of evidence B). (Dargie, 2001)
- Differences in clinical effects may be present between different beta-blockers in patients with heart failure (The Beta-Blocker Evaluation of Survival Trial Investigators, 2001; Poole-Wilson et al., 2003). Accordingly, only bisoprolol, carvedilol, metoprolol succinate, and nebivolol can be recommended (Class of recommendation I, level of evidence A).

Please refer to the original guideline document for a discussion on initiation of beta-blocker therapy and dose titration.

Aldosterone Receptor Antagonists

- Aldosterone antagonists are recommended in addition to ACE-inhibitors, beta-blockers, and diuretics in advanced heart failure (NYHA III-IV) with systolic dysfunction to improve survival and morbidity (Class of recommendation I, level of evidence B) (Pitt et al., 1999).
- Aldosterone antagonists are recommended in addition to ACE inhibitors and beta-blockers in heart failure after myocardial infarction with left ventricular systolic dysfunction and signs of heart failure or diabetes to reduce mortality and morbidity (Class of recommendation I, level of evidence B) (Pitt et al., 2003).

Administration and dosing considerations for aldosterone antagonists are provided in Table 19 in the original guideline document.

Angiotensin II Receptor Blockers

For patients with left ventricular systolic dysfunction:

- Angiotensin II receptor blockers (ARBs) can be used as an alternative to ACE inhibition in symptomatic patients intolerant to ACE-inhibitors to improve morbidity and mortality (Class of recommendation I, level of evidence B)

(Granger et al., 2003; Pfeffer et al., "Effects of candesartan," 2003; Maggioni et al., 2002; Cohn & Tognoni, 2001).
- ARBs and ACE inhibitors seem to have similar efficacy in CHF on mortality and morbidity (Class of recommendation IIa, level of evidence B).
- In acute myocardial infarction with signs of heart failure or left ventricular dysfunction, ARBs and ACE inhibitors have similar or equivalent effects on mortality (Class of recommendation I, level of evidence B) (Pfeffer et al., "Valsartan, captopril, or both," 2003).
- ARBs can be considered in combination with ACE inhibitors in patients who remain symptomatic, to reduce mortality (Class of recommendation IIa, Level of evidence B) and hospital admissions for heart failure (Class of recommendation I, level of evidence A) (Pfeffer et al., "Effects of candesartan," 2003; McMurray et al., 2003; Jong et al., 2002; Coletta & Cleland, 2003).

In NYHA class III patients remaining symptomatic despite therapy with diuretics, ACE inhibitors, and beta-blockers, there is no definite evidence for the recommendation of next addition; an ARB or an aldosterone antagonist to reduce further heart failure hospitalizations or mortality. Concerns raised by initial studies about a potential negative interaction between ARBs and beta-blockers have not been confirmed by recent studies in post-myocardial infarction or CHF (Class of recommendation I, Level of evidence A) (Pfeffer et al., "Effects of candesartan," 2003; "Valsartan, captopril, or both," 2003).

Dosing
Initiation and monitoring of ARBs, which are outlined in above, are similar to procedures for ACE-inhibitors. Available ARBs and the recommended dose levels are shown in Table 20 in the original guideline document.

Cardiac Glycosides

- Cardiac glycosides are indicated in atrial fibrillation and any degree of symptomatic heart failure, whether or not left ventricular dysfunction is the cause. Cardiac glycosides slow the ventricular rate, which improves ventricular function and symptoms (Class of recommendation I, Level of evidence B) (Khand et al., "Systematic review," 2000).
    - A combination of digoxin and beta-blockade appears superior to either agent alone in patients with atrial fibrillation (Class of recommendation IIa, level of evidence B) (Khand et al., "Digoxin or carvedilol," 2000).
    - Digoxin has no effect on mortality but may reduce hospitalizations and, particularly, worsening heart failure hospitalizations, in the patients with heart failure caused by left ventricular systolic dysfunction and sinus rhythm treated with ACE inhibitors, beta-blockers, diuretics, and, in severe heart failure, spironolactone (Class of recommendation IIa, level of evidence A).

Digoxin
The usual daily dose of oral digoxin is 0.125 to 0.25 mg if serum creatinine is in the normal range (in the elderly 0.0625 to 0.125 mg, occasionally 0.25 mg).

Vasodilator Agents in Chronic Heart Failure

- There is no specific role for direct-acting vasodilator agents in the treatment of CHF (Class of recommendation III, level of evidence A) though they may be used as adjunctive therapy for angina or concomitant hypertension (Class of recommendation I, level of evidence A).

Hydralazine-isosorbide Dinitrate

- In case of intolerance for ACE inhibitors and ARBs, the combination hydralazine/nitrates can be tried to reduce mortality and morbidity and improve quality of life (Class of recommendation IIa, level of evidence B) (Taylor et al., 2004).

Nitrates

- Nitrates may be used for the treatment of concomitant angina or relief of dyspnoea. (Class of recommendation IIa, level of evidence C). Evidence that oral nitrates improve symptoms of heart failure chronically or during an acute exacerbation is lacking.

Alpha-adrenergic Blocking Drugs

- There is no evidence to support the use of alpha-adrenergic blocking drugs in heart failure (Class of recommendation III, level of evidence B) (Cohn et al., 1986).

Calcium Antagonists

- Calcium antagonists are not recommended for the treatment of heart failure caused by systolic dysfunction. Diltiazem- and verapamil-type calcium antagonists, in particular, are not recommended in heart failure because of systolic dysfunction; they are contraindicated in addition to beta-blockade (Class of recommendation III, level of evidence C) (Cohn et al., 1997; Thackray et al., 2000).
- Addition of newer calcium antagonists (felodipine and amlodipine) to standard treatment for heart failure does not improve symptoms and does not impact on survival (Class of recommendation III, level of evidence A) (Cohn et al., 1997; Thackray et al., 2000).

As long-term safety data with felodipine and amlodipine indicate a neutral effect on survival, they may offer a safe alternative for the treatment of concomitant arterial hypertension or angina not controlled by nitrates and beta-blockers.

<u>Positive Inotropic Therapy</u>

- Repeated or prolonged treatment with oral inotropic agents increases mortality and is not recommended in CHF (Class of recommendation III, level of evidence A).
- Intravenous administration of inotropic agents is commonly used in patients with severe heart failure with signs of both pulmonary congestion and peripheral hypoperfusion. However, treatment-related complications may

occur and their effect on prognosis is uncertain. Depending on agent, level of evidence and strength of recommendation varies (Nieminen et al., 2005).

Preliminary data suggests that some calcium sensitizers (e.g., levosimendan) may have beneficial effects on symptoms and end-organ function and are safe. (Follath et al., 2002)

Anti-thrombotic Agents

- In CHF associated with atrial fibrillation, a previous thromboembolic event or a mobile left ventricular thrombus, anti-coagulation is firmly indicated (Class of recommendation I, level of evidence A) (Cleland, Cowburn, & Falk, 1996).
- There is little evidence to show that anti-thrombotic therapy modifies the risk of death or vascular events in patients with heart failure.
- After a prior myocardial infarction, either aspirin or oral anti-coagulants are recommended as secondary prophylaxis (Class of recommendation IIa, level of evidence C) (Antithrombotic Trialists' Collaboration, 2002)
- Aspirin should be avoided in patients with recurrent hospitalization with worsening heart failure (Class of recommendation IIb, level of evidence B).

Because of the potential for increased bleeding complications, anti-coagulant therapy should be administered under the most controlled conditions, planning monitoring in properly managed anti-coagulation clinics.

Anti-arrhythmics

Anti-arrhythmic drugs other than beta-blockers are generally not indicated in patients with CHF. In patients with atrial fibrillation (rarely flutter), non-sustained, or sustained ventricular tachycardia treatment with anti-arrhythmic agents may be indicated.

Class I Anti-arrhythmics

- Class I anti-arrhythmics should be avoided as they may provoke fatal ventricular arrhythmias, have an adverse haemodynamic effect, and reduce survival in heart failure (Class of recommendation III, level of evidence B) ("Preliminary report," 1989).

Class II Anti-arrhythmics

- Beta-blockers reduce sudden death in heart failure (Class of recommendation I, level of evidence A) (see also page 23 in the original guideline document) (Lȯpez-Sendȯn et al., 2004). Beta-blockers may also be indicated alone or in combination with amiodarone or non- pharmacological therapy in the management of sustained or non-sustained ventricular tachyarrhythmias (Class of recommendation IIa, Level of evidence C) (Steinbeck et al., 1992).

Class III Anti-arrhythmics

- Amiodarone is effective against most supraventricular and ventricular arrhythmias (Class of recommendation I, Level of evidence A). It may restore

and maintain sinus rhythm in patients with heart failure and atrial fibrillation even in the presence of enlarged left atria, or improve the success of electrical cardioversion, and amiodarone is the preferred treatment in this condition ("Effect of prophylactic amiodarone," 1997; Levy et al., 1998). Amiodarone is the only anti-arrhythmic drug without clinically relevant negative inotropic effects.

Routine administration of amiodarone in patients with heart failure is not justified (Class of recommendation III, level of evidence A) (Singh et al., 1995; Bardy et al., 2005).

Oxygen Therapy

- Oxygen is used for the treatment of acute heart failure (AHF), but in general has no application in CHF (Class of recommendation III, level of evidence C).

Surgery and Devices

Revascularization Procedures, Mitral Valve Surgery, and Ventricular Restoration

- If clinical symptoms of heart failure are present, surgically correctable pathologies must always be considered (Class of recommendation I, level of evidence C).

Revascularization

- There are no data from multicenter trials to support the use of revascularization procedures for the relief of heart failure symptoms. Single centre, observational studies on heart failure of ischaemic origin suggest that revascularization might lead to symptomatic improvement (Class of recommendation IIb, level of evidence C).
- Until the results of randomized trials are reported, revascularization (surgical or percutaneous) is not recommended as routine management of patients with heart failure and coronary disease (Class of recommendation III, level of evidence C).

Mitral Valve Surgery

- Mitral valve surgery in patients with severe left ventricular systolic dysfunction and severe mitral valve insufficiency due to ventricular insufficiency may lead to symptomatic improvement in selected heart failure patients (Class of recommendation IIb, level of evidence C). This is also true for secondary mitral insufficiency due to left ventricular dilatation.

Left Ventricular Restoration

LV Aneurysmectomy

- LV aneurysmectomy is indicated in patients with large, discrete left ventricular aneurysms who develop heart failure (Class of recommendation I, level of evidence C).

Cardiomyoplasty

- Currently, cardiomyoplasty cannot be recommended for the treatment of heart failure (Class of recommendation III, level of evidence C).
- Cardiomyoplasty cannot be considered a viable alternative to heart transplantation (Class of recommendation III, level of evidence C).

Partial Left Ventriculectomy (Batista Operation)

- Partial left ventriculectomy cannot be recommended for the treatment of heart failure (Class of recommendation I, level of evidence C). Furthermore, the Batista operation should not be considered an alternative to heart transplantation (Class of recommendation III, level of evidence C).

External Ventricular Restoration

- Currently, external ventricular restoration cannot be recommended for the treatment of heart failure. Preliminary data suggest an improvement in LV dimensions and NYHA class with some devices (Class of recommendation IIb, level of evidence C).

Pacemakers

Pacemakers have been used in patients with heart failure to treat bradycardia when conventional indications exist. Pacing only of the right ventricle in patients with systolic dysfunction will induce ventricular dyssynchrony and may increase symptoms (Class of recommendation III, level of evidence A).

- Resynchronization therapy using bi-ventricular pacing can be considered in patients with reduced ejection fraction and ventricular dyssynchrony (QRS width $\geq$120 ms) and who remain symptomatic (NYHA III-IV) despite optimal medical therapy to improve symptoms (Class of recommendation I, level of evidence A), hospitalizations (Class of recommendation I, level of evidence A), and mortality (Class of recommendation I, level of evidence B).

Implantable Cardioverter Defibrillators

- Implantation of an implantable cardioverter defibrillators (ICD) in combination with bi-ventricular pacing can be considered in patients who remain symptomatic with severe heart failure NYHA class lll-IV with LVEF $\leq$ 35% and QRS duration $\geq$120 ms to improve mortality or morbidity (Class of recommendation IIa, level of evidence B) (Bristow et al., 2004).
- ICD therapy is recommended to improve survival in patients who have survived cardiac arrest or who have sustained ventricular tachycardia, which is either poorly tolerated or associated with reduced systolic left ventricular function (Class of recommendation I, level of evidence A) (Moss et al., 1996).
- ICD implantation is reasonable in selected patients with LVEF <30 to 35%, not within 40 days of a myocardial infarction, on optimal background therapy including ACE inhibitor, ARB, beta-blocker, and an aldosterone antagonist, where appropriate, to reduce sudden death (Class of recommendation I, level of evidence A) (Bardy et al., 2005; Moss et al., 2002; Kadish et al., 2004)

Heart Replacement Therapies: Heart Transplantation, Ventricular Assist Devices, and Artificial Heart

Heart Transplantation

- Heart transplantation is an accepted mode of treatment for end stage heart failure. Although controlled trials have never been conducted, it is considered to significantly increase survival, exercise capacity, return to work and quality of life compared with conventional treatment, provided proper selection criteria are applied (Class of recommendation I, level of evidence C).

Patients who should be considered for heart transplantation are those with severe symptoms of heart failure with no alternative form of treatment and with a poor prognosis.

Ventricular Assist Devices and Artificial Heart

- Current indications for left ventricular assist devices and artificial heart include bridging to transplantation, acute severe myocarditis, and in some patients permanent haemodynamic support (Class of recommendation IIa, level of evidence C).
- Left ventricular assist devices are being implanted as a bridge to transplantation. Experience from long-term treatment is accumulating but these devices are not recommended for routine Long-term use (Class of recommendation IIb, level of evidence B) (Rose et al., 2001).

Ultrafiltration

- Ultrafiltration may be used to treat fluid overload (pulmonary or peripheral oedema) refractory to diuretics (Rimondini et al, 1987). However, in most patients with severe heart failure, the relief is temporary (Dormans, Huige, & Gerlag, 1996).

Choice and Timing of Pharmacological Therapy

Please refer to the original guideline document for a discussion of the choice and timing of pharmacological therapy in the various stages of heart failure caused by systolic dysfunction.

Management of Heart Failure with Preserved Left Ventricular Ejection Fraction (PLVEF)

Please refer to the original guideline document for a discussion on the management of heart failure with preserved LVEF.

Pharmacological Therapy of Heart Failure with PLVEF or Diastolic Dysfunction

The following recommendations are largely speculative because of the limited data available in patients with PLVEF or diastolic dysfunction (in general, Class of recommendation IIa, level of evidence C).

There is no clear evidence that patients with primary diastolic heart failure benefit from any specific drug regimen.

1. ACE inhibitors may improve relaxation and cardiac distensibility directly and may have tong-term effects through their anti-hypertensive effects and regression of hypertrophy and fibrosis.
2. Diuretics may be necessary when episodes with fluid overload are present, but should be used cautiously so as not to lower preload excessively and thereby reduce stroke volume and cardiac output.
3. Beta-blockade could be instituted to lower heart rate and increase the diastolic filling period.
4. Verapamil-type calcium antagonists may be used for the same reason (Setaro et al., 1990). Some studies with verapamil have shown a functional improvement in patients with hypertrophic cardiomyopathy (Bonow et al., 1985).
5. A high dose of an ARB may reduce hospitalizations (Yusuf et al., 2003).

Heart Failure Treatment in the Elderly

Please refer to the original guideline document for a discussion of heart failure treatment in the elderly.

Arrhythmias

- It is essential to recognize and correct precipitating factors for arrhythmias, improve cardiac function, and reduce neuro-endocrine activation with beta-blockade, ACE inhibition, and, possibly, aldosterone receptor antagonists (Class of recommendation I, Level of evidence C).

Ventricular Arrhythmias

- In patients with ventricular arrhythmias, the use of anti-arrhythmic agents is only justified in patients with severe, symptomatic, sustained ventricular tachycardias and where amiodarone should be the preferred agent (Class of recommendation IIa, level of evidence B) ("Effect of prophylactic amiodarone," 1997; Singh et al., 1995).
- ICD implantation is indicated in patients with heart failure and with life threatening ventricular arrhythmias (i.e., ventricular fibrillation or sustained ventricular tachycardia) and in selected patients at high risk of sudden death (Class of recommendation I, level of evidence A) (Moss et al., 1996, 2002; "A comparison of antiarrhythmic-drug therapy," 1997; Buxton et al., 1999, Priori et al., 2001).

Atrial Fibrillation

- For persistent (non-self-terminating) atrial fibrillation, electrical cardioversion could be considered, although its success rate may depend on the duration of atrial fibrillation and left atrial size (Class of recommendation IIa, level of evidence B).
- In patients with atrial fibrillation and heart failure and/or depressed left ventricular function, the use of anti-arrhythmic therapy to maintain sinus

rhythm should be restricted to amiodarone (Class of recommendation I, level of evidence C) and, if available, to dofetilide (Class of recommendation IIa, level of evidence B) (Torp-Pederson et al., 1999).
- In asymptomatic patients, beta-blockade, digitalis glycosides, or the combination may be considered for control of ventricular rate (Class of recommendation I, level of evidence B). In symptomatic patients with systolic dysfunction digitalis glycosides are the first choice (Class of recommendation IIa, level of evidence C). In PLVEF, verapamil can be considered (Class of recommendation IIa, level of evidence C).
- Anti-coagulation in persistent atrial fibrillation with warfarin should always be considered unless contraindicated (Class of recommendation I, level of evidence C).
- Management of acute atrial fibrillation is not depending on previous heart failure or not. Treatment strategy is depending on symptoms and haemodynamic stability. For options see Fuster et al., 2001.

Symptomatic Systolic Left Ventricular Dysfunction and Concomitant Angina or Hypertension

Specific recommendations in addition to general treatment for heart failure because of systolic left ventricular dysfunction. If angina is present:

- Optimize existing therapy, e.g., beta-blockade.
- Add long-acting nitrates.
- If not successful, add amlodipine or felodipine.
- Consider coronary revascularization.

If hypertension is present:

- Optimize the dose of ACE inhibitors, beta-blocking agents, and diuretics (Turnbull, 2003).
- Add spironolactone or ARBs if not present already.
- If not successful, try second generation dihydropyridine derivatives.

Care and Follow-up

- An organized system of specialist heart failure care improves symptoms and reduces hospitalizations (Class of recommendation I, level of evidence A) and mortality (Class of recommendation IIa, level of evidence B) of patients with heart failure (Coletta et al., 2003; Rich, 1999; McAlister et al., 2001; Stewart, Pearson, & Horowitz, 1998; Stewart, Marley & Horowitz, 1999; Stromberg et al., 2003).
- It is likely that the optimal model will depend on local circumstances and resources and whether the model is designed for specific sub-groups of patients (e.g., severity of heart failure, age, comorbidity, and left ventricular systolic dysfunction) or the whole heart failure population (Class of recommendation I, level of evidence C) (Weinberger, Oddone, & Henderson, 1996, Jaarsma et al., 1999; Ekman et al., 1998; McAlister et al., 2004).

Table. Recommended Components of Care and Following Programmes (class of recommendation I, level of evidence C

- Use a multi-disciplinary team approach.
- Vigilant follow-up, first follow up within 10 days of discharge
- Discharge planning
- Increased access to health care
- Optimizing medical therapy with guidelines
- Early attention to signs and symptoms (e.g., telemonitoring)
- Flexible diuretic regimen
- Intense education and counselling
- Inpatient and outpatient (home-based)
- Attention to behavioural strategies
- Address barriers to compliance

Definitions:

Levels of Evidence

A. Data derived from multiple randomized clinical trials or meta-analyses.
B. Data derived from a single randomized clinical trial or large non-randomized studies.
C. Consensus of opinion of the experts and/or small studies, retrospective studies, 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 evidence is discouraged by the European Society of Cardiology (ESC)

CLINICAL ALGORITHM(S)

An algorithm is provided in the original guideline document for the diagnosis of heart failure or left ventricular dysfunction.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

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

For the diagnosis, evidence is incomplete and in general based on consensus of expert opinions. As in the 2001 version, it was decided not to use evidence grading in this part.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Accurate diagnosis of chronic heart failure, including establishing the proper epidemiology and prognosis, can aid in optimizing treatment.
- Appropriate treatment of heart failure may prevent disease progression, maintain or improve quality of life, and increase survival.

POTENTIAL HARMS

Angiotensin-converting Enzyme (ACE) Inhibitors

Important adverse effects associated with ACE inhibitors are cough, hypotension, renal insufficiency, hyperkalaemia, syncope, and angioedema.

Diuretics

Major side effects of diuretics are provided in table 16 of the original guideline document and include hypokalaemia, hypomagnesaemia, hyponatraemia, hyperuiricaemia, glucose intolerance, acid-base disturbance, hyperkalaemia, rash, and gynaecomastia.

Beta-blockers

During titration, beta-blockers may reduce heart rate excessively, temporarily induce myocardial depression, and exacerbate symptoms of heart failure.

Positive Inotropic Agents

Repeated or prolonged treatment with oral inotropic agents increases mortality.

Heart Transplantation

Besides shortage of donor hearts, the main problem of heart transplantation is rejection of the allograft, which is responsible for a considerable percentage of deaths in the first postoperative year. The long-term outcome is limited predominantly by the consequences of immuno-suppression (infection,

hypertension, renal failure, malignancy, and by transplant coronary vascular disease).

Heart Failure Treatment in the Elderly

- In elderly patients, hyperkalaemia is more frequently seen with a combination of aldosterone antagonist and ACE inhibitors or nonsteroidal anti-inflammatory drugs (NSAIDs) and Cox-2 inhibitors (coxibs).
- Elderly patients may be more susceptible to adverse effects of digoxin.
- Venodilating drugs, such as nitrates and the arterial dilator hydralazine and the combination of these drugs, should be administered carefully because of the risk of hypotension.

CONTRAINDICATIONS

CONTRAINDICATIONS

- Angiotensin-converting enzyme (ACE) inhibitor treatment is contraindicated in the presence of bilateral renal artery stenosis and angioedema during previous ACE-inhibitor therapy.
- Contraindications to the use of beta-blockers in patients with heart failure include asthma bronchiale, severe bronchial disease, and symptomatic bradycardia or hypotension.
- Relative contraindications for starting a beta-blocker include asymptomatic bradycardia and/or low blood pressure.
- 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 hyperkalaemia.
- Diltiazem- and verapamil-type calcium antagonists are contraindicated in addition to beta-blockade for the treatment of heart failure caused by systolic dysfunction.
- Contraindications for heart transplantation include:
    - Present alcohol and/or drug abuse
    - Lack of proper co-operation
    - Serious mental disease which could not be properly controlled
    - Treated cancer with remission and <5 years follow-up
    - Systemic disease with multi-organ involvement
    - Uncontrolled infection
    - Severe renal failure (creatinine clearance <50 mL min) or creatinine >250 micromoles/L, although some centres accept patients on haemodialysis
    - Fixed high pulmonary vascular resistance (6–8 Wood units and mean transpulmonary gradient >15 mm Hg and pulmonary artery systolic pressure >60 mm Hg)
    - Recent thromboembolic complication
    - Unhealed peptic ulcer
    - Evidence of significant liver impairment
    - Other disease with a poor prognosis

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- National health policy as well as clinical judgement may dictate the order of priority of implementation. It is recognized that some interventions may not be affordable in some countries for all appropriate patients. The recommendations in these guidelines should therefore always be considered in the light of national policies and local regulatory requirements for the administration of any diagnostic procedure, medicine, or device.
- Many definitions of chronic heart failure (CHF) exist, but only selective features of this complex syndrome are highlighted. None is entirely satisfactory. A simple objective definition of CHF is currently impossible as there is no cut-off value of cardiac or ventricular dysfunction or change in flow, pressure, dimension, or volume that can be used reliably to identify patients with heart failure. The diagnosis of heart failure relies on clinical judgment based on a history, physical examination, and appropriate investigations.
- The ESC Guidelines represent the views of the ESC and were arrived at after careful consideration of the available evidence at the time they were written. Health professionals are encouraged to take them fully into account when exercising their clinical judgment. The guidelines do not, however, override the individual responsibility of health professionals to make appropriate decisions in the circumstances of the individual patients, in consultation with that patient, and where appropriate and necessary the patient's guardian or carer. It is also the health professional's responsibility to verify the rules and regulations applicable to drugs and devices at the time of prescription.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Clinical Algorithm
Foreign Language Translations
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

Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Swedberg K, Cleland J, Dargie H, Drexler H, Follath F, Komajda M, Tavazzi L, Smiseth OA, Gavazzi A, Haverich A, Hoes A, Jaarsma T, Korewicki J, Levy S, Linde C, Lopez-Sendon JL, Nieminen MS, Pierard L, Remme WJ. Guidelines for the diagnosis and treatment of chronic heart failure: full text (update 2005): The Task Force for the Diagnosis and Treatment of Chronic Heart Failure of the European Society of Cardiology. Sophia Antipolis (FR): European Society of Cardiology (ESC); 2005. 45 p. [358 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

SOURCE(S) OF FUNDING

European Society of Cardiology

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Within the Task Force, statements of Conflicts of Interests were collected, which are available at the European Society of Cardiology (ESC) Office.

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Remme WJ, Swedberg K, Task Force for the Diagnosis and Treatment of Chronic Heart Failure, European Society of Cardiology. Guidelines for the diagnosis and treatment of chronic heart failure. Eur Heart J 2001 Sep;22(17):1527-60.

GUIDELINE AVAILABILITY

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

Print copies: Available from Oxford University Press, Great Clarendon Street, Oxford, OX2 6DP, UK, Tel: +44 (0) 1865 353263, Fax: +44 (0) 1865 353774, Web site: http://www.eurheartj.org/.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Guidelines for the diagnosis and treatment of chronic heart failure: executive summary (update 2005): The Task Force for the Diagnosis and Treatment of

Chronic Heart Failure of the European Society of Cardiology. Eur Heart J 2005;26:1115-1140. Electronic copies: Available from the European Society of Cardiology (ESC) Web site.

- Diagnosis and treatment of chronic heart failure (update 2005). Pocket guidelines. (Available in English, Italian, Spanish, French, and German). Sophia Antipolis (France): European Society of Cardiology, 2005. Electronic copies: 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 European Society of Cardiology (ESC) Web site.
- ESC guidelines for the diagnosis and treatment of chronic heart failure - 2005. Educational slides. Sophia Antipolis (France): European Society of Cardiology, 2005. Electronic copies: Available in Microsoft PowerPoint from the European Society of Cardiology (ESC) Web site.

PATIENT RESOURCES

None available

NGC STATUS

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