

Editorial / Editöryal Yorum**Diagnosis and treatment of acute and chronic heart failure: What has changed in the New European Society of Cardiology guidelines 2008?**

Akut ve kronik kalp yetersizliği tanı ve tedavisi:

Yeni 2008 Avrupa Kardiyoloji Derneği kılavuzunda neler değişti?

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The most important update of the 2008 European Society of Cardiology (ESC) Heart Failure (HF) Guidelines,^[1] which was absent in the previous guidelines^[2,3] was evaluating chronic and acute heart failure (AHF) together as one disease with different processes.

A new classification is currently being established taking into consideration time and prognosis of heart failure. Accordingly, heart failure is being classified into three groups including new onset, transient and chronic. As anticipated, new onset HF is the initial clinic presentation of HF as depicted from its name, whereas transient HF refers to symptomatic HF within a certain time period. On the other hand, chronic HF may be stable, or decompensated following occasional worsening episodes. The major abnormality is not heart disease in cases of high cardiac output and the disease can be reversed by appropriate treatment. It is more appropriate to classify such conditions as secondary HF associated with high cardiac output in the circulation. Diagnosis of such conditions is important since they can be treated and as they should be excluded in the diagnosis of HF.

The latest guidelines stress on the importance of natriuretic peptides in the algorithm for the diagnosis of HF and recommend measuring natriuretic peptides (particularly in the primary health care services) in patients with suspected HF by clinical electrocardiography (ECG), teleradiography and echocardiography. The recommended algorithm cut-off values for brain

natriuretic peptide (BNP) and NT-proBNP have been provided (Figure 1). According to the latest guidelines, a BNP level of >400 pg/mL and NT-proBNP level of >2000 pg/mL increase the risk of HF, whereas a BNP level of <100 pg/mL and NT-proBNP level of <400 pg/mL exclude the possibility of HF in patients who do not receive treatment for HF.

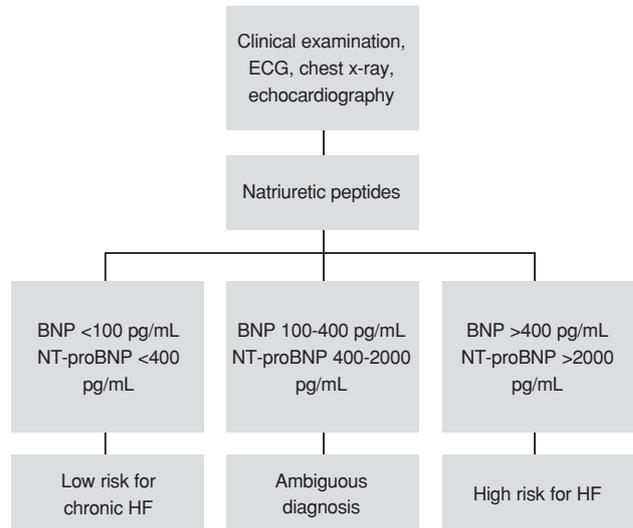


Figure 1. Flow chart for the diagnosis of HF using natriuretic peptide analysis in patients with symptoms suggestive of HF

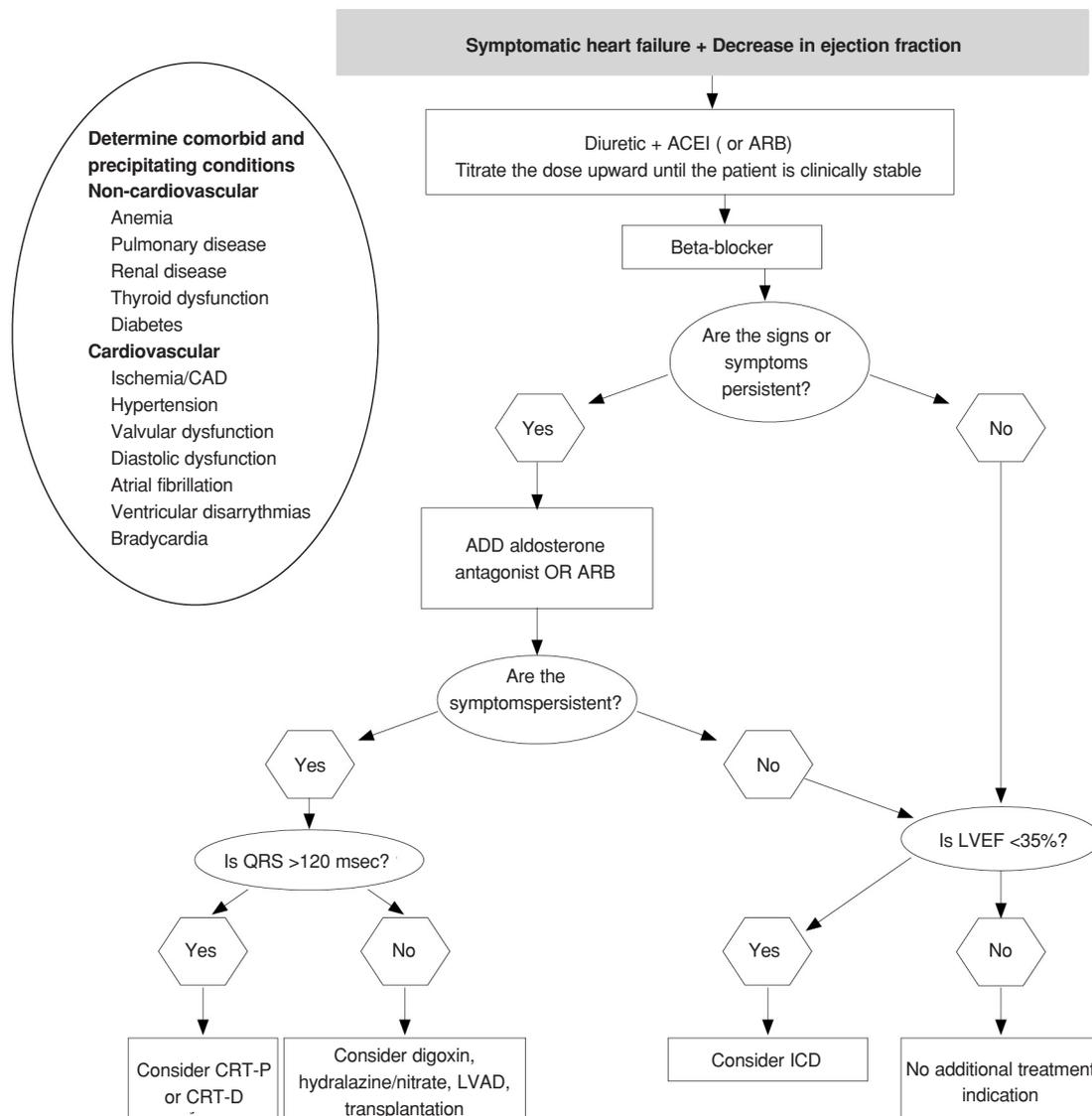


Figure 2. Treatment algorithm for patients with systolic and symptomatic heart failure (HF)

The AHA/ACC/ESC has established new indications for endocardial biopsy, which were not included in the previous guidelines,^[4] and suggested that endocardial biopsy should be considered in patients with acute or fulminant HF of unknown etiology, whose condition worsens with ventricular arrhythmia and/or atrioventricular heart block or in patients unresponsive to conventional HF treatment. In addition, endomyocardial biopsy may be performed in patients with suspected infiltrative processes such as amyloidosis, sarcoidosis and hemochromatosis or in patients with eosinophilic myocarditis and restrictive cardiomyopathy of unknown origin.

The importance of self-care in the treatment of heart failure is especially being emphasized. Guidelines recommend a new algorithm for the pharmacologic treatment of systolic and symptomatic HF (Figure 2). Management of precipitating or comorbid conditions should also be considered during the treatment of HF. No dramatic update is available in the guidelines regarding the pharmacologic treatment of HF including angiotensin converting enzyme inhibitor, beta-blocker, angiotensin receptor blocker, aldosterone antagonists, hydralazine and isosorbide dinitrate, digoxin, diuretics, anticoagulants and antithrombotics. The main updates comprehensively mentioned include indications, war-

Table 1. Treatment recommendations for heart failure (HF) patients with some valvular heart disease

Valvular heart disease	Indication	Class	Level of Evidence
Aortic stenosis (AS)	Severe AS with HF symptoms	I	C
	Severe asymptomatic AS with EF of <50%	I	C
	Left ventricular dysfunction with highly reduced valvular area	IIb	C
Aortic regurgitation (AR)	Severe AR with HF symptoms	I	B
	Severe asymptomatic AR with moderately impaired EF ($\leq 50\%$)	IIa	C
Organic mitral regurgitation (MR)	Severe symptomatic MR with EF of >30%	I	C
	Severe MR with EF of <30% with inadequate pharmacologic treatment and low risk profile	IIb	C
Functional MR	Severe MR with low degree of EF with inadequate pharmacologic treatment	IIb	C
	Biventricular pacing in patients who are suitable for CRT	IIa	B
Ischemic MR	Severe MR with EF of >30% in patients scheduled for ACBG	I	C
	Moderate MR in patients scheduled for ABCG	IIa	C
Tricuspid regurgitation (TR)	In conditions of systemic congestion where medical treatment is inadequate in cases of isolated functional TR	III	C

ABCG: Coronary artery bypass graft surgery; EF: ejection fraction

ning/precautions and contraindications with more information. In addition and contrary to the previous guidelines, the latest guidelines recommend statin treatment in elderly patients with symptomatic chronic HF and systolic dysfunction due to coronary artery disease in order to minimize the hospitalization rate due to cardiovascular events (Class of Recommendation: IIb, Level of Evidence: B).

The European Society of Cardiology (ESC) Guidelines for the Management of Valvular Heart Disease are recommended in treatment of HF patients with aortic stenosis and regurgitation, mitral regurgitation (organic, functional and ischemic) and tricuspid regurgitation (Table 1).^[5]

Traditional indications for pacemaker implementation are available in patients with HF.^[6] However, certain factors should be considered during pacemaker implantation in patients with HF: DDD pacing should be preferred to VVI pacing in patients with HF. In addition, indications for ICD, biventricular pacing (CRT-P) or a combination of ICD and biventricular pacing (CRT-D) device should be established and assessed before pacemaker implantation for atrioventricular conduction defect in patients with HF. Right ventricular pacing may cause desynchronization, leading to worsening of symptoms.

Table 2. Data on recommendations for cardiac resynchronization therapy (CRT) and implantable cardioverter-defibrillator (ICD) in patients with heart failure (HF)

Procedure	Indication	Class	Level of Evidence
CRT-P	Symptomatic NYHA class III-IV patients with EF of $\leq 35\%$ and QRS of ≥ 120 msec despite optimal pharmacologic treatment	I	A
ICD	Secondary prevention: in patients with documented VT leading to hemodynamic dysfunction, patients who survived from VF, patients with VT and concomitant syncope, and patients with >1-year life expectancy with EF of $\leq 40\%$ and a good functional status	I	A
	Primary prevention (ischemic): Patients with MI of >40 days, patients with EF of $\leq 35\%$, and NYHA class II-III patients with more than one year life expectancy while under optimal medical treatment	I	A
	Primary prevention (non-ischemic): patients with EF of $\leq 35\%$, and NYHA class II-III patients with more than one year life expectancy under optimal medical treatment	I	A
	Patients with more than one year life expectancy following CRT	I	A

EF: Ejection fraction; CRT-P: Biventricular pacing; VF: Ventricular fibrillation; VT: Ventricular tachycardia.

Apart from traditional indications, pacing is not recommended for the initiation of treatment with beta-blocker or for dose adjustment. Indications for ICD also include primary prevention in non-ischemic heart failure (Class of Recommendation: I, Level of Evidence: B). The addition of ICD to the therapy is recommended for patients who underwent cardiac resynchronization therapy (CRT) and patients with a life expectancy of more than one year (Class of Recommendation: I, Level of Evidence: A). Recommendations for CRT and ICD procedures in the latest guidelines are given in Table 2.

Contrary to previous guidelines, the latest guidelines include recommendations on patient groups suitable for HF treatment and their treatments. The ESC Guidelines for hypertension are recommended in management of hypertension in patients with HF.^[7] Pharmacologic treatment in these patients should include angiotensin converting enzyme inhibitors or angiotensin receptor blockers. Management of hypertension in patients with HF with preserved systolic function should be aggressive. One third of all patients with HF have diabetes mellitus (DM). Recommendations of the ESC/EASD Guidelines for the management of diabetes mellitus are appropriate for the majority of patients with HF.^[8] Thiazolidinedione has been reported to increase peripheral edema and symptomatic HF. The risk of edema with thiazolidinedione treatment is dose-dependent and the risk increases in patients with

concomitant insulin therapy. Therefore, patients in NYHA class III-IV should not be treated with thiazolidinediones, whereas patients in NYHA class I-II may receive low doses with close monitoring.

The latest guidelines also include some recommendations for cachexia, defined as the non-edematous weight loss of >6% of total body weight within 6-12 months. Cachexia is associated with increased mortality. No consensus has been reached on the prevention of cachexia due to HF and whether treatment is necessary for these patients. Hypercaloric diets, appetizers, physical activity and anabolic medications (insulin, anabolic steroids) are recommended alternatives.

Acute heart failure

Definition of acute heart failure (AHF) has been revised in the latest guidelines. The updated guidelines define AHF as a rapid onset or change in the signs and symptoms of HF, resulting in the need for urgent therapy. AHF may either be a new HF or worsening of a pre-existing chronic HF. The clinical presentation of AHF reflects a spectrum of conditions since AHF is a syndrome. The latest guidelines present six clinical categories based on clinical presentation. Five of these categories are the same in the previous and new guidelines, whereas one of the categories is different in the latter. AHF due to acute coronary syndrome has been replaced by AHF with a high level of cardiac output.

Table 3. Recommendations on acute heart failure (AHF) based on clinical presentations

Clinical AHF class	Recommendation
Decompensated chronic HF	Initiate vasodilator therapy and loop diuretics High dose diuretics in patients with renal failure or patients regularly using diuretics should be preferred Inotropic support for hypotension and hypoperfusion
Pulmonary edema	Morphine is often necessary Oxygenation should be provided Initiate vasodilator therapy if there is adequate SBP; use diuretics in congestive conditions; inotropic support is necessary in hypoperfusion
Hypertensive HF	Initiate vasodilator therapy Low dose diuretics are recommended in patients with congestion or pulmonary edema
Cardiogenic shock	Fluid, inotropic, vasodepressor, IABP and support devices should be administered respectively to reach target level of SBP (>90 mmHg) Intubation often required
Right HF	Ineffective fluid perfusion Avoid mechanical ventilation Inotropic support is recommended in the presence of hypoperfusion Investigate the presence of pulmonary embolism or right ventricular myocardial infarction
HF secondary to ACS	Early revascularization is required Investigate mechanical complications by ECG IABP and immediate revascularization should be performed in case of cardiogenic shock

ACS: acute coronary syndrome; IABP: intraaortic balloon pump; HF: heart failure; SBP: systolic blood pressure

Furthermore, the latest guidelines include diagnostic algorithms similar to the definition in the previous guidelines. However, as previously mentioned, cut-off values of natriuretic peptides used in the diagnosis have been revised.

Treatment goals for clinical, laboratory and hemodynamic morbidity and mortality are recommended in the previous guidelines, whereas the latest guidelines recommend similar treatment goals with the assessment of immediate-, intermediate- and long-term effects of the disease. Various drugs are used in the treatment of acute heart failure; however there is limited data from clinical studies. As a result, empirical treatment is often followed. Algorithm for empirical treatment recommended is similar to that in the previous guidelines, but more simplified. Contrary to the previous guidelines, the latest version recommends individual treatment based on the clinical presentation of AHF. Recommendations on acute heart failure based on clinical presentation are given in Table 3.

Similar to previous guidelines, the latest version also recommends an arterial oxygen saturation of $\geq 95\%$ ($>90\%$ in COAH patients), delivering oxygen therapy in the early stages in patients with hypoxemia (Class of Recommendation: I, Level of Evidence: C). Increased FIO₂ with airway mask, noninvasive ventilation (CPAP=continuous positive airway pressure or NIPPV=noninvasive positive pressure ventilation) followed by intubation and mechanical ventilation are used to reach target level of arterial oxygen saturation. However, no statement on whether CPAP or NIPPV should be used is made in the latest guidelines.

Diuretic dose is another main issue in the latest guidelines recommending an initial dose of furosemide 20-40 mg I.V. during hospitalization. The dose may be increased and continuous infusion may also be administered following the initial dose in patients with excessive volume overload. The maximum dose of furosemide should not exceed 100 mg within the first 6 hours and 240 mg within the first 24 hours. In addition, the latest guidelines include similar recommendations for the indications and doses of vasodilators: the lower limit of systolic blood pressure where vasodilators are not recommended is 85 mmHg in the previous guidelines; while in the latest guidelines this has been changed to a systolic blood pressure of 90 mmHg. Norepinephrine is also the only recommended vasopressor. Epinephrine administration is not recommended as inotropic or vasopressor in the presence of cardiogenic shock, in the latest guidelines. It is only recommended as a resuscitation treatment in the presence of cardiac arrest.

Moreover, both guidelines include identical indications for inotropic agents (class of recommendation: IIa). However, the level of evidence has been elevated from C to B in the study with levosimendan trials. As a result, inotropic agents should be used in AHF patients with low cardiac output presenting with hypoperfusion or congestion despite vasodilator and/or diuretic administration to relief symptoms, they should also be administered in patients with dilated or hypokinetic ventricle. A systolic blood pressure of 90 mmHg is recommended instead of 85 mmHg in the latest guidelines as the limit of the hazardous effect of vasodilator therapy. Dobutamine, dopamine, milrinone, enoximone and levosimendan are recommended as inotropic agents. Dopamine in low doses together with higher dobutamine doses, is particularly recommended, while a lower bolus dose of levosimendan (I.V.) compared to the previous guidelines is recommended. As a result, the bolus dose of levosimendan (3-12 μ g/kg for 10 minutes) may be administered followed by a continuous infusion (0.05-0.2 μ g/kg/min for 24 hours). The infusion rate may also be accelerated in the presence of stability. Infusion should be initiated without bolus injection to prevent hypotension in patients with a systolic blood pressure of <100 mmHg.

Management programs in patients with heart failure

Several management programs have been developed including patient education, optimization of pharmacologic treatment, psychosocial support and increased accessibility to health care services. The latest guidelines support the development of such programs, with strong recommendations. Management programs for heart failure are recommended to patients who have recently been hospitalized due to HF and others at high risk (Class of Recommendation: I, Level of Evidence: A). Heart Failure Management Programs have been organized as a multidisciplinary approach which coordinates the various stages involved in the development of heart failure and the chain of services provided by various health services. The multidisciplinary team may include nurses, cardiologists, primary health care physicians, physiotherapists, dieticians, social service workers, psychologists, pharmacists, geriatrists and other health care professionals for the treatment of HF. The content and structure of the treatment programs may vary dramatically in different countries with different health care system and programs should be adapted to local conditions.

REFERENCES

1. Task Force for Diagnosis and Treatment of Acute and Chronic Heart Failure 2008 of European Society of Cardiology, Dickstein K, Cohen-Solal A, Filippatos G, McMurray JJ, Ponikowski P, Poole-Wilson PA, et al. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2008: the Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2008 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association of the ESC (HFA) and endorsed by the European Society of Intensive Care Medicine (ESICM). *Eur Heart J* 2008; 29:2388-442.
2. Swedberg K, Cleland J, Dargie H, Drexler H, Follath F, Komajda M, et al. 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;26:1115-40.
3. Nieminen MS, Böhm M, Cowie MR, Drexler H, Filippatos GS, Jondeau G, et al. Executive summary of the guidelines on the diagnosis and treatment of acute heart failure: the Task Force on Acute Heart Failure of the European Society of Cardiology. *Eur Heart J* 2005; 26:384-416.
4. Cooper LT, Baughman KL, Feldman AM, Frustaci A, Jessup M, Kuhl U, et al. The role of endomyocardial biopsy in the management of cardiovascular disease: a scientific statement from the American Heart Association, the American College of Cardiology, and the European Society of Cardiology. *Circulation* 2007; 116:2216-33.
5. Vahanian A, Baumgartner H, Bax J, Butchart E, Dion R, Filippatos G, et al. Guidelines on the management of valvular heart disease: The Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology. *Eur Heart J* 2007;28:230-68.
6. Vardas PE, Auricchio A, Blanc JJ, Daubert JC, Drexler H, Ector H, et al. Guidelines for cardiac pacing and cardiac resynchronization therapy: The Task Force for Cardiac Pacing and Cardiac Resynchronization Therapy of the European Society of Cardiology. Developed in collaboration with the European Heart Rhythm Association. *Eur Heart J* 2007;28:2256-95.
7. Mancia G, De Backer G, Dominiczak A, Cifkova R, Fagard R, Germano G, et al. 2007 Guidelines for the management of arterial hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *Eur Heart J* 2007; 28:1462-536.
8. Rydén L, Standl E, Bartnik M, Van den Berghe G, Betteridge J, de Boer MJ, et al. Guidelines on diabetes, pre-diabetes, and cardiovascular diseases: executive summary. The Task Force on Diabetes and Cardiovascular Diseases of the European Society of Cardiology (ESC) and of the European Association for the Study of Diabetes (EASD). *Eur Heart J* 2007;28:88-136.