ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

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Definition（過去現在未來）

- HF is a clinical syndrome characterized by typical symptoms (e.g. breathlessness, ankle swelling and fatigue) that may be accompanied by signs (e.g. elevated jugular venous pressure, pulmonary crackles and peripheral oedema) caused by a structural and/or functional cardiac abnormality, resulting in a reduced cardiac output and/ or elevated intracardiac pressures at rest or during stress

precursor

- Because they are related to poor outcomes , and starting treatment at the precursor stage may reduce mortality in patients with asymptomatic systolic LV dysfunction

Table 3.1 Definition of heart failure with preserved (HFpEF), mid-range (HFmrEF) and reduced ejection fraction (HFrEF)

Type of HF		HFrEF	HFmrEF	HFpEF
CRITERIA	1	Symptoms ± Signs[a]	Symptoms ± Signs[a]	Symptoms ± Signs[a]
	2	LVEF <40%	LVEF 40–49%	LVEF ≥50%
	3	–	1. Elevated levels of natriuretic peptides[b]; 2. At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE), b. diastolic dysfunction (for details see Section 4.3.2).	1. Elevated levels of natriuretic peptides[b]; 2. At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE), b. diastolic dysfunction (for details see Section 4.3.2).

BNP = B-type natriuretic peptide; HF = heart failure; HFmrEF = heart failure with mid-range ejection fraction; HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction; LAE = left atrial enlargement; LVEF = left ventricular ejection fraction; LVH = left ventricular hypertrophy; NT-proBNP = N-terminal pro-B type natriuretic peptide.

[a]Signs may not be present in the early stages of HF (especially in HFpEF) and in patients treated with diuretics.

[b]BNP>35 pg/ml and/or NT-proBNP>125 pg/mL.

定義

- A treated patient with symptoms and signs that have remained generally unchanged for at least 1 month is said to be ‘stable
- If chronic stable HF deterior ates->‘decompensated’ suddenly or slowly, often leading to admission, an event of considerable prognostic importance

- Congestive HF' is a term that is sometimes used, and may describe acute or chronic HF with evidence of volume overload
- advanced HF' is used to characterize patients with severe symptoms + recurrent decompensation + severe cardiac dysfunction

流行病學

- 1–2% of the adult
- >70 y/o ->rising to ≥10%
- >65 Y/O with D.O.E, one in six will have unrecognized HF (mainly HFpEF)
- lifetime risk of HF at age 55 years is 33% for men and 28% for women

HPrEF vs HPpEF

- HFpEF are older, more often women and more commonly have a history of hypertension and atrial fibrillation (AF),
- ->Less history of MI myocardial infarction

outcome

- (ESC-HF pilot study)->12-month
- hospitalized and stable/ambulatory HF
- all-cause mortality : 17% and 7%,
- hospitalization rates : 44% and 32%.

Essential initial investigations(背)

- 1.BNP
- 2.ECG
- 3.TTE

NPs（背35-125;100-300）

- below the cutpoint for the exclusion of important cardiac dysfunction do not require echocardiography
- acute setting, higher values should be used [BNP <100 pg/mL, NT-proBNP<300 pg/mL and mid-regional pro A-type natriuretic peptide (MR-proANP)<120 pmol/L].
- negative predictive values are very high (0.94–0.98)

- positive predictive values are lower both in the non-acute setting (0.44–0.57) and in the acute setting (0.66–0.67)
- AF, age and renal failure ,obesity ->the most important interpretation of NP measurements

Table 12.3 Causes of elevated concentrations of natriuretic peptides[522–524]

Cardiac	Heart failure Acute coronary syndromes Pulmonary embolism Myocarditis Left ventricular hypertrophy Hypertrophic or restrictive cardiomyopathy Valvular heart disease Congenital heart disease Atrial and ventricular tachyarrhythmias Heart contusion Cardioversion, ICD shock Surgical procedures involving the heart Pulmonary hypertension
Non-cardiac	Advanced age Ischaemic stroke Subarachnoid haemorrhage Renal dysfunction Liver dysfunction (mainly liver cirrhosis with ascites) Paraneoplastic syndrome Chronic obstructive pulmonary disease Severe infections (including pneumonia and sepsis) Severe burns Anaemia Severe metabolic and hormone abnormalities (e.g. thyrotoxicosis, diabetic ketosis)

HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction; ICD = implantable cardioverter defibrillator.

背

ECG

- provide information on aetiology (e.g. myocardial infarction)
- for therapy (e.g. anticoagulation for AF, pacing for bradycardia, CRT if broadened QRS complex
- HF is unlikely in patients presenting with a completely normal ECG (sensitivity 89%)

Echocardiography

- establish the diagnosis and treatment
- chamber volumes,
- ventricular systolic and diastolic function,
- wall thickness,
- valve function
- Pulmonary hypertension

Table 4.1 Symptoms and signs typical of heart failure

Symptoms	Signs
Typical	**More specific**
Breathlessness Orthopnoea Paroxysmal nocturnal dyspnoea Reduced exercise tolerance Fatigue, tiredness, increased time to recover after exercise Ankle swelling	Elevated jugular venous pressure Hepatojugular reflux Third heart sound (gallop rhythm) Laterally displaced apical impulse
Less typical	**Less specific**
Nocturnal cough Wheezing Bloated feeling Loss of appetite Confusion (especially in the elderly) Depression Palpitations Dizziness Syncope Bendopnea[53]	Weight gain (>2 kg/week) Weight loss (in advanced HF) Tissue wasting (cachexia) Cardiac murmur Peripheral oedema (ankle, sacral, scrotal) Pulmonary crepitations Reduced air entry and dullness to percussion at lung bases (pleural effusion) Tachycardia Irregular pulse Tachypnoea Cheyne Stokes respiration Hepatomegaly Ascites Cold extremities Oliguria Narrow pulse pressure

Table 3.4 Aetiologies of heart failure

DISEASED MYOCARDIUM		
Ischaemic heart disease	Myocardial scar	
	Myocardial stunning/hibernation	
	Epicardial coronary artery disease	
	Abnormal coronary microcirculation	
	Endothelial dysfunction	
Toxic damage	Recreational substance abuse	Alcohol, cocaine, amphetamine, anabolic steroids.
	Heavy metals	Copper, iron, lead, cobalt.
	Medications	Cytostatic drugs (e.g. anthracyclines), immunomodulating drugs (e.g. interferons monoclonal antibodies such as trastuzumab, cetuximab), antidepressant drugs, antiarrhythmics, non-steroidal anti-Inflammatory drugs, anaesthetics.
	Radiation	
Immune-mediated and inflammatory damage	Related to infection	Bacteria, spirochaetes, fungi, protozoa, parasites (Chagas disease), rickettsiae, viruses (HIV/AIDS).
	Not related to infection	Lymphocytic/giant cell myocarditis, autoimmune diseases (e.g. Graves' disease, rheumatoid arthritis, connective tissue disorders, mainly systemic lupus erythematosus), hypersensitivity and eosinophilic myocarditis (Churg–Strauss).
Infiltration	Related to malignancy	Direct infiltrations and metastases.
	Not related to malignancy	Amyloidosis, sarcoidosis, haemochromatosis (iron), glycogen storage diseases (e.g. Pompe disease), lysosomal storage diseases (e.g. Fabry disease).
Metabolic derangements	Hormonal	Thyroid diseases, parathyroid diseases, acromegaly, GH deficiency, hypercortisolaemia, Conn's disease, Addison disease, diabetes, metabolic syndrome, phaeochromocytoma, pathologies related to pregnancy and peripartum.
	Nutritional	Deficiencies in thiamine, L-carnitine, selenium, iron, phosphates, calcium, complex malnutrition (e.g. malignancy, AIDS, anorexia nervosa), obesity.
Genetic abnormalities	Diverse forms	HCM, DCM, LV non-compaction, ARVC, restrictive cardiomyopathy (for details see respective expert documents), muscular dystrophies and laminopathies.

ABNORMAL LOADING CONDITIONS		
Hypertension		
Valve and myocardium structural defects	Acquired	Mitral, aortic, tricuspid and pulmonary valve diseases.
	Congenital	Atrial and ventricular septum defects and others (for details see a respective expert document).
Pericardial and endomyocardial pathologies	Pericardial	Constrictive pericarditis Pericardial effusion
	Endomyocardial	HES, EMF, endocardial fibroelastosis.
High output states		Severe anaemia, sepsis, thyrotoxicosis, Paget's disease, arteriovenous fistula, pregnancy.
Volume overload		Renal failure, iatrogenic fluid overload.
ARRHYTHMIAS		
Tachyarrhythmias		Atrial, ventricular arrhythmias.
Bradyarrhythmias		Sinus node dysfunctions, conduction disorders.

ARVC = arrhythmogenic right ventricular cardiomyopathy; DCM = dilated cardiomyopathy; EMF = endomyocardial fibrosis; GH = growth hormone; HCM = hypertrophic cardiomyopathy; HES = hypereosinophilic syndrome; HIV/AIDS = human immunodeficiency virus/acquired immune deficiency syndrome; LV = left ventricular.

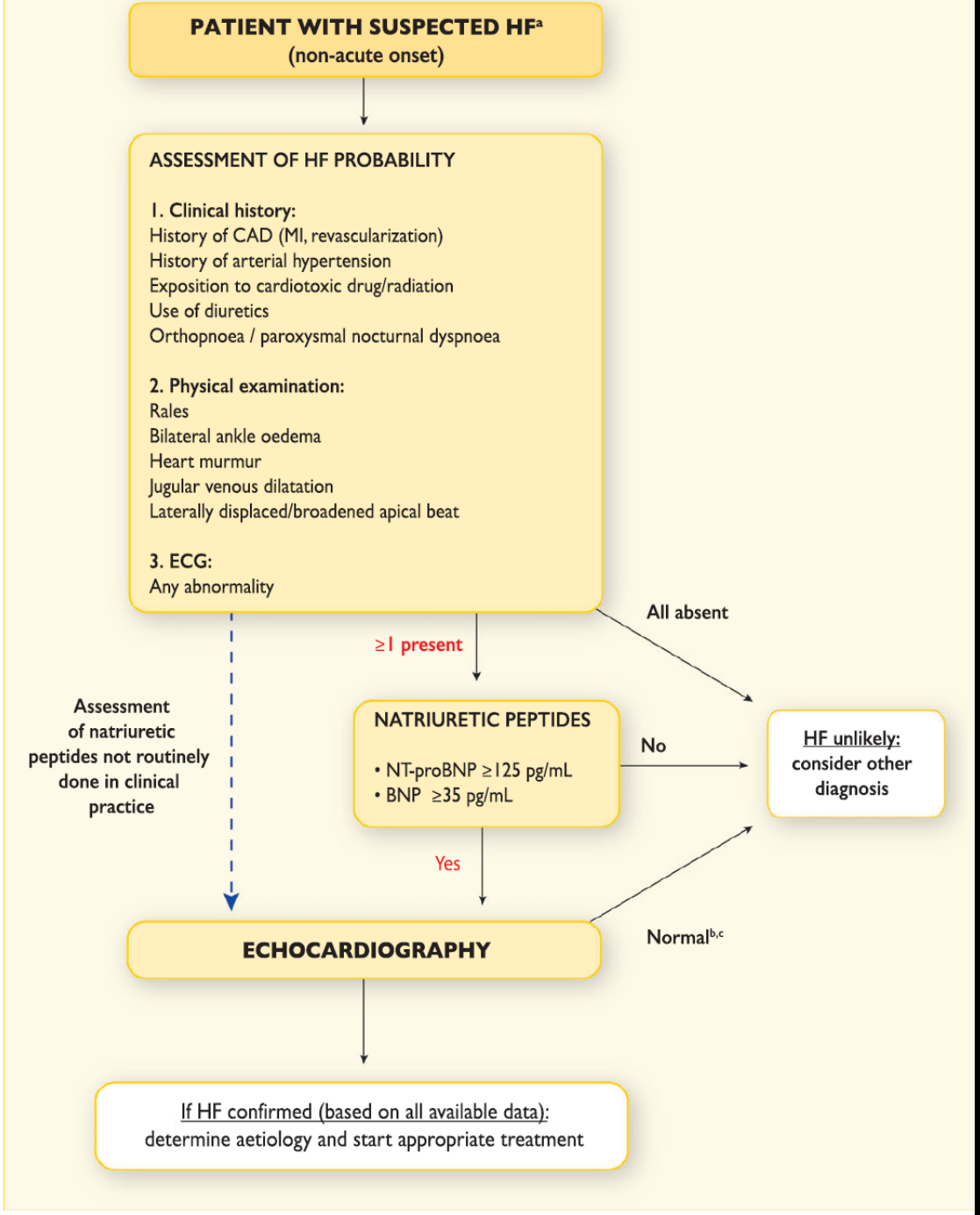

Figure 4.1 Diagnostic algorithm for a diagnosis of heart failure of non-acute onset

echo

- Key structural alterations are a
- left atrial volume index (LAVI) .34 mL/m2 or a left ventricular mass index (LVMI) ≥115 g/m2 for males and ≥95 g/m2 for females.
- Key functional alterations are an E/e′ ≥13 and a mean e’ septal and lateral wall ,9
- Other (indirect) echocardiographically derived measurements are longitudinal strain or tricuspid regurgitation velocity (TRV).

echo

- Exercise-induced increases in E/e′ beyond diagnostic cut-offs(i.e. .13), but also other indirect measures of systolic and diastolic function, such as longitudinal strain or TRV, are used

right ventricular function

- tricuspid annular plane systolic excursion (TAPSE; abnormal TAPSE ,17 mm indicates RV systolic dysfunction) and tissue Doppler-derived tricuspid lateral annular systolic velocity (s′) (s′ velocity ,9.5 cm/s indicates RV systolic dysfunction).

TTE indication

TTE is recommended for the assessment of myocardial structure and function in subjects with suspected HF in order to establish a diagnosis of either HFrEF, HFmrEF or HFpEF.	I	C
TTE is recommended to assess LVEF in order to identify patients with HF who would be suitable for evidence-based pharmacological and device (ICD, CRT) treatment recommended for HFrEF.	I	C
TTE is recommended for the assessment of valve disease, right ventricular function and pulmonary arterial pressure in patients with an already established diagnosis of either HFrEF, HFmrEF or HFpEF in order to identify those suitable for correction of valve disease.	I	C
TTE is recommended for the assessment of myocardial structure and function in subjects to be exposed to treatment which potentially can damage myocardium (e.g. chemotherapy).	I	C
Other techniques (including systolic tissue Doppler velocities and deformation indices, i.e. strain and strain rate), should be considered in a TTE protocol in subjects at risk of developing HF in order to identify myocardial dysfunction at the preclinical stage.	IIa	C

CXR

- most useful in identifying an alternative, pulmonary explanation
- It is important to note that significant LV dysfunction may be present without cardiomegaly on the chest X-ray

背Transoesophageal echocardiography (TOE)

- aortic dissection,
- suspected endocarditis or
- congenital heart disease
- and for ruling out intracavitary thrombi in AF patients requiring cardioversion

Stress echocardiography

- inducible ischaemia and/or myocardium viability
- dynamic mitral regurgitation,
- low-flow–low-gradient aortic stenosis
- diastolic dysfunction

Cardiac magnetic resonance

- gold standard for the measurements of volumes, mass and EF of both the left and right ventricles
- Nondiagnostic echocardiographic studies (right heart)
- Complex congenital heart diseases
- myocardial fibrosis using late gadolinium enhancement (LGE)
- myocarditis,amyloidosis, sarcoidosis, Chagas disease, Fabry disease non-compaction cardiomyopathy and haemochromatosis
- GFR<30 mL/min/1.73m2, may trigger nephrogenic systemic fibrosis

CMR is recommended for the assessment of myocardial structure and function (including right heart) in subjects with poor acoustic window and patients with complex congenital heart diseases (taking account of cautions/contra-indications to CMR).	I	C
CMR with LGE should be considered in patients with dilated cardiomyopathy in order to distinguish between ischaemic and non-ischaemic myocardial damage in case of equivocal clinical and other imaging data (taking account of cautions/contra-indications to CMR).	IIa	C
CMR is recommended for the characterization of myocardial tissue in case of suspected myocarditis, amyloidosis, sarcoidosis, Chagas disease, Fabry disease non-compaction cardiomyopathy, and haemochromatosis (taking account of cautions/contra-indications to CMR).	I	C
Non-invasive stress imaging (CMR, stress echocardiography, SPECT, PET) may be considered for the assessment of myocardial ischaemia and viability in patients with HF and CAD (considered suitable for coronary revascularization) before the decision on revascularization.	IIb	B

SPECT /PET

- Single-photon emission CT (SPECT) and Positron emission tomography (PET)
- assess ischaemia and viability

Coronary angiography

- HF with angina pectoris recalcitrant to medical therapy, provided the patient is otherwise suitable for coronary revascularization
- history of symptomatic ventricular arrhythmia or aborted cardiac arrest

Invasive coronary angiography is recommended in patients with HF and angina pectoris recalcitrant to pharmacological therapy or symptomatic ventricular arrhythmias or aborted cardiac arrest (who are considered suitable for potential coronary revascularization) in order to establish the diagnosis of CAD and its severity.	I	C
Invasive coronary angiography should be considered in patients with HF and intermediate to high pre-test probability of CAD and the presence of ischaemia in non-invasive stress tests (who are considered suitable for potential coronary revascularization) in order to establish the diagnosis of CAD and its severity.	IIa	C
Cardiac CT may be considered in patients with HF and low to intermediate pre-test probability of CAD or those with equivocal non-invasive stress tests in order to rule out coronary artery stenosis.	IIb	C

Right heart catheterization with a pulmonary artery catheter:		
- is recommended in patients with severe HF being evaluated for heart transplantation or mechanical circulatory support;	I	C
- should be considered in patients with probable pulmonary hypertension assessed by echocardiography in order to confirm pulmonary hypertension and its reversibility before the correction of valve/structural heart disease;	IIa	C
- may be considered in order to adjust therapy in patients with HF who remain severely symptomatic despite initial standard therapies and whose haemodynamic status is unclear.	IIb	C
EMB should be considered in patients with rapidly progressive HF despite standard therapy when there is a probability of a specific diagnosis which can be confirmed only in myocardial samples and specific therapy is available and effective.	IIa	C
Thoracic ultrasound may be considered for the confirmation of pulmonary congestion and pleural effusion in patients with AHF.	IIb	C
Ultrasound measurement of inferior vena cava diameter may be considered for the assessment of volaemia status in patients with HF.	IIb	C

Genetic testing in heart failure

- definite clinical diagnosis of HF, there is no confirmatory role for routine genetic testing to establish the diagnosis.
- Genetic counselling is recommended in patients with HCM, idiopathic DCM and ARVC.（背）
- Restrictive cardiomyopathy and isolated non-compaction cardiomyopathies also be considered for genetic testing

MOGE(S) classification

- For inherited cardiomyopathies
- morphofunctional phenotype (M),
- organ(s) involvement (O),
- genetic inheritance pattern (G),
- aetiological annotation (E), including genetic defect or underlying disease/substrate, and the
- functional status (S)

Before s/sx

- Delaying or preventing the development of overt heart failure or preventing death before the onset of symptoms

SPRINT study（背）

- treating hypertension to a lower goal
- SBP<120 mmHg vs. ,140 mmHg] in ≥75 y/o or high-risk hypertensive patients reduces the risk of cardiovascular disease, death and hospitalization for HF.

Treatment of hypertension is recommended to prevent or delay the onset of HF and prolong life.	I	A

OHA（背）

- empaglifozin (an inhibitor of sodium-glucose cotransporter 2), has been shown to improve outcomes (including the reduction of mortality and HF hospitalizations) in patients with type 2 diabetes

Treating other risk factors of HF (e.g. obesity, dysglycaemia) should be considered in order to prevent or delay the onset of HF.	IIa	C
Empagliflozin should be considered in patients with type 2 diabetes in order to prevent or delay the onset of HF and prolong life.	IIa	B

smoking cessation

- Although smoking cessation has not been shown to reduce the risk of developing HF, the epidemiological associations with the development of cardiovascular disease suggest that such advice, if followed, would be beneficial

alcohol intake

- risk of developing de novo HF is U-shaped, with the lowest risk with modest alcohol consumption (up to 7 drinks/week)
- Greater alcohol intake may trigger the development of toxic cardiomyopathy, and when present, complete abstention from alcohol is recommended

- ≥40 y/o with either cardiovascular risk factors or cardiovascular disease (but neither asymptomatic LV dysfunction nor overt HF), BNP-driven collaborative care between the primary care physician and the specialist cardiovascular centre may reduce the combined rates of LV systolic dysfunction and overt HF

Statin in HFrEF

- Statins reduce the rate of cardiovascular events and mortality; there is also reasonable evidence that they prevent or delay the onset of HF

Treatment with statins is recommended in patients with or at high-risk of CAD whether or not they have LV systolic dysfunction, in order to prevent or delay the onset of HF and prolong life.	I	A

ACEi(必用)

- CAD, without LV systolic dysfunction or HF, ACEIs prevent or delay the onset of HF and reduce cardiovascular and all cause mortality.
- Up-titration of ACEi/ARB and beta-blockers to maximum tolerated dosages may improve outcomes, including HF, in high NPs.
- asymptomatic chronically reduced LVEF, regardless of its aetiology, an ACEI can reduce the risk of HF requiring hospitalization.
- This has not yet been shown for beta-blockers or MRAs

STEMI

- primary PCI for STEMI reduce infarct size decreases the risk of developing a substantial reduction in LVEF and subsequent development of HFrEF
- ACEI, a beta-blocker and an MRA immediately after MI, especially with LV systolic dysfunction, reduces the rate of hospitalization for HF and as do statins

ACE-I is recommended in patients with asymptomatic LV systolic dysfunction and a history of myocardial infarction in order to prevent or delay the onset of HF and prolong life.	I	A
ACE-I is recommended in patients with asymptomatic LV systolic dysfunction without a history of myocardial infarction, in order to prevent or delay the onset of HF.	I	B
ACE-I should be considered in patients with stable CAD even if they do not have LV systolic dysfunction, in order to prevent or delay the onset of HF.	IIa	A
Beta-blocker is recommended in patients with asymptomatic LV systolic dysfunction and a history of myocardial infarction, in order to prevent or delay the onset of HF or prolong life.	I	B

ICD

- asymptomatic LV systolic dysfunction (LVEF<30%) of ischaemic origin who are ≥40 days after an AMI, an implantable cardioverter-defibrillator (ICD) is recommended to prolong life

ICD is recommended in patients: a) with asymptomatic LV systolic dysfunction (LVEF ≤30%) of ischaemic origin, who are at least 40 days after acute myocardial infarction, b) with asymptomatic non-ischaemic dilated cardiomyopathy (LVEF ≤30%), who receive OMT therapy, in order to prevent sudden death and prolong life.	I	B

Symptomatic EFrHF

Pharmacological treatments indicated in patients with symptomatic (NYHA Class II-IV) heart failure with reduced ejection fraction

Recommendations	Class [a]	Level [b]	Ref [c]
An ACE-I[d] is recommended, in addition to a beta-blocker, for symptomatic patients with HFrEF to reduce the risk of HF hospitalization and death.	I	A	2, 163 –165
A beta-blocker is recommended, in addition an ACE-I[d], for patients with stable, symptomatic HFrEF to reduce the risk of HF hospitalization and death.	I	A	167– 173
An MRA is recommended for patients with HFrEF, who remain symptomatic despite treatment with an ACE-I[d] and a beta-blocker, to reduce the risk of HF hospitalization and death.	I	A	174, 175

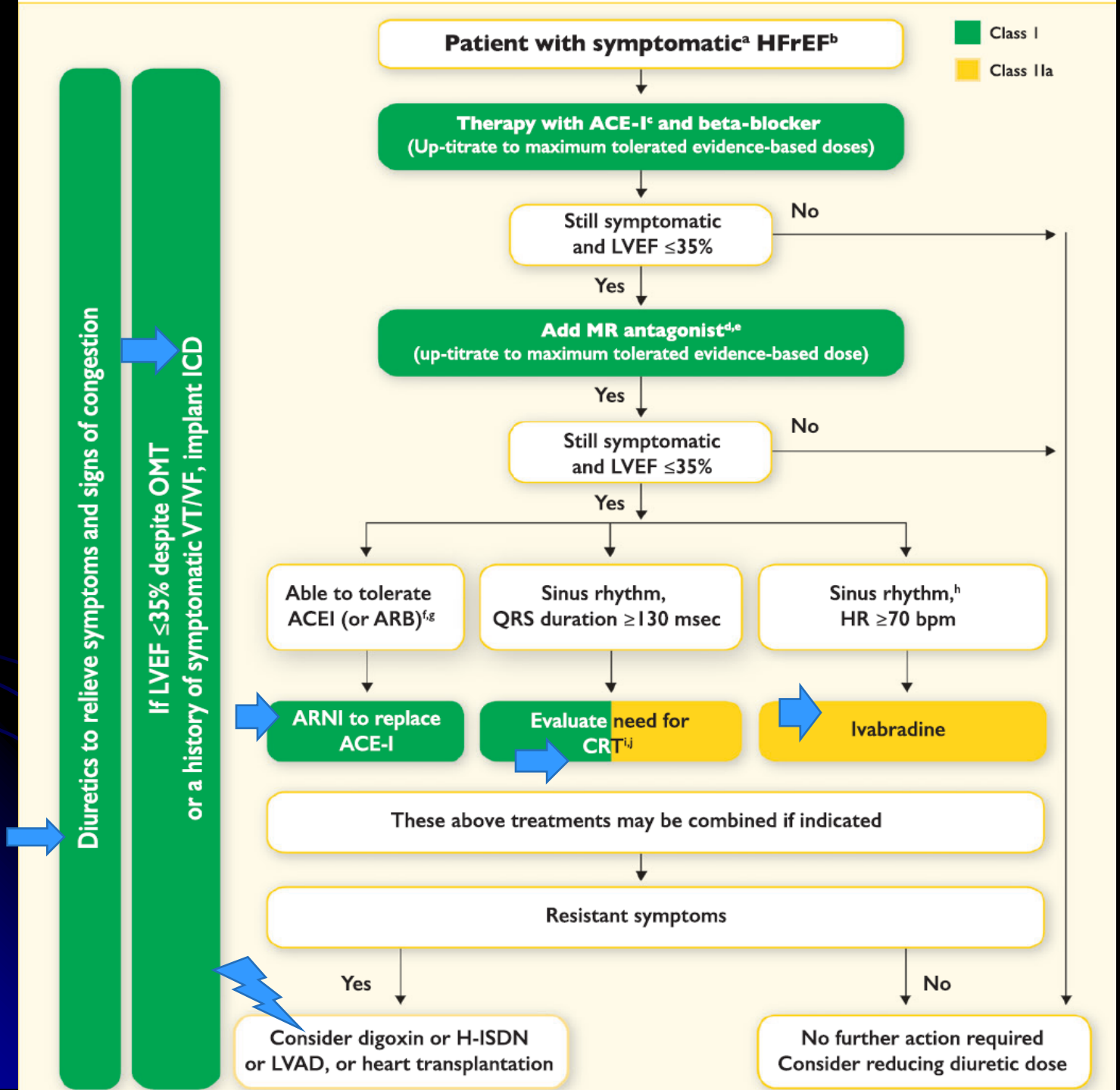
Class I
Class IIa
Patient with symptomatic[a] HFrEF[b]
Therapy with ACE-I[c] and beta-blocker
(Up-titrate to maximum tolerated evidence-based doses)
Still symptomatic and LVEF ≤35%
No
Yes
Add MR antagonist[d,e]
(up-titrate to maximum tolerated evidence-based dose)
Yes
Still symptomatic and LVEF ≤35%
No
Yes
Diuretics to relieve symptoms and signs of congestion
If LVEF ≤35% despite OMT or a history of symptomatic VT/VF, implant ICD
Able to tolerate ACEI (or ARB)[f,g]
Sinus rhythm, QRS duration ≥130 msec
Sinus rhythm,[h] HR ≥70 bpm
ARNI to replace ACE-I
Evaluate need for CRT[i,j]
Ivabradine
These above treatments may be combined if indicated
Resistant symptoms
Yes
No
Consider digoxin or H-ISDN or LVAD, or heart transplantation
No further action required
Consider reducing diuretic dose

Table 7.2 Evidence-based doses of disease-modifying drugs in key randomized trials in heart failure with reduced ejection fraction (or after myocardial infarction)

	Starting dose (mg)	Target dose (mg)
ACE-I		
Captopril[a]	6.25 *t.i.d.*	50 *t.i.d.*
Enalapril	2.5 *b.i.d.*	10–20 *b.i.d.*
Lisinopril[b]	2.5–5.0 *o.d.*	20–35 *o.d.*
Ramipril	2.5 o.d.	10 *o.d.*
Trandolapril[a]	0.5 *o.d.*	4 *o.d.*
Beta-blockers		
Bisoprolol	1.25 *o.d.*	10 *o.d.*
Carvedilol	3.125 *b.i.d.*	25 *b.i.d.*[d]
Metoprolol succinate (CR/XL)	12.5–25 *o.d.*	200 o.d.
Nebivolol[c]	1.25 *o.d.*	10 *o.d.*
ARBs		
Candesartan	4–8 *o.d.*	32 *o.d.*
Valsartan	40 *b.i.d.*	160 *b.i.d.*
Losartan[b,c]	50 *o.d.*	150 *o.d.*
MRAs		
Eplerenone	25 *o.d.*	50 *o.d.*
Spironolactone	25 *o.d.*	50 *o.d.*
ARNI		
Sacubitril/valsartan	49/51 *b.i.d.*	97/103 *b.i.d.*
I_f-channel blocker		
Ivabradine	5 *b.i.d.*	7.5 *b.i.d.*

ARNI ; Coralan

Angiotensin receptor neprilysin inhibitor		
Sacubitril/valsartan is recommended as a replacement for an ACE-I to further reduce the risk of HF hospitalization and death in ambulatory patients with HFrEF who remain symptomatic despite optimal treatment with an ACE-I, a beta-blocker and an MRA[d]	I	B
If-channel inhibitor		
Ivabradine should be considered to reduce the risk of HF hospitalization or cardiovascular death in symptomatic patients with LVEF ≤35%, in sinus rhythm and a resting heart rate ≥70 bpm despite treatment with an evidence-based dose of beta-blocker (or maximum tolerated dose below that), ACE-I (or ARB), and an MRA (or ARB).	IIa	B
Ivabradine should be considered to reduce the risk of HF hospitalization and cardiovascular death in symptomatic patients with LVEF ≤35%, in sinus rhythm and a resting heart rate ≥70 bpm who are unable to tolerate or have contra-indications for a beta-blocker. Patients should also receive an ACE-I (or ARB) and an MRA (or ARB).	IIa	C

Hydralazine and isosorbide dinitrate		
Hydralazine and isosorbide dinitrate should be considered in self-identified black patients with LVEF ≤35% or with an LVEF <45% combined with a dilated LV in NYHA Class III–IV despite treatment with an ACE-I a beta-blocker and an MRA to reduce the risk of HF hospitalization and death.	IIa	B
Hydralazine and isosorbide dinitrate may be considered in symptomatic patients with HFrEF who can tolerate neither an ACE-I nor an ARB (or they are contra-indicated) to reduce the risk of death.	IIb	B
Other treatments with less-certain benefits		
Digoxin		
Digoxin may be considered in symptomatic patients in sinus rhythm despite treatment with an ACE-I (or ARB), a beta-blocker and an MRA, to reduce the risk of hospitalization (both all-cause and HF-hospitalizations).	IIb	B
N-3 PUFA		
An n-3 PUFA[e] preparation may be considered in symptomatic HF patients to reduce the risk of cardiovascular hospitalization and cardiovascular death.	IIb	B

digoxin

- Controversial in Af
- only recommended for HFrEF + AF with RVR when other therapeutic options cannot be pursued
- strict rate control might be deleterious.
- Rest HR 70–90 bpm is recommended based on current opinion, although one trial ->up to 110 bpm might still be acceptable
- Digitalis should always be prescribed under specialist supervision.
- Caution in females, in the elderly and in reduced renal function.

Statin

- not effective in HFrEF
- underlying CAD or/and hyperlipidaemia, a continuation of this therapy should be considered

Oral anticoagulants and antiplatelet therapy

- Except AF (both HFrEF and HFpEF), there is no evidence that an oral anticoagulant reduces mortality/morbidity compared with placebo or aspirin
- HFrEF with anticoagulation in AF or risk of venous thromboembolism should continue anticoagulation
- no evidence on the benefits of antiplatelet drugs (including aspirin) in HF without accompanying CAD

Renin inhibitors:DRI

- Aliskiren (direct renin inhibitor) failed to improve outcomes for patients hospitalized for HF at 6 months or 12 months in one study and is not presently recommended as an alternative to an ACEI or ARB.

Contra-indication in symptomatic EFrHF

- Thiazolidinediones (glitazones)
- NSAIDs or COX-2 inhibitors
- Diltiazem or verapamil
- ->increase the risk of HF worsening and HF hospitalization
- ARB (or renin inhibitor) + ACE-I and an MRA ->increased risk of renal dysfunction and hyperkalaemia.

CCB

- There is only evidence on safety for amlodipine and Felodipine in patients with HFrEF, and they can be used only if there is a compelling indication in patients with HFrEF

ICD

Recommendations for implantable cardioverter-defibrillator in patients with heart failure

Recommendations	Class [a]	Level [b]	Ref [c]
Secondary prevention An ICD is recommended to reduce the risk of sudden death and all-cause mortality in patients who have recovered from a ventricular arrhythmia causing haemodynamic instability, and who are expected to survive for >1 year with good functional status.	I	A	223–226
Primary prevention An ICD is recommended to reduce the risk of sudden death and all-cause mortality in patients with symptomatic HF (NYHA Class II–III), and an LVEF ≤35% despite ≥3 months of OMT, provided they are expected to survive substantially longer than one year with good functional status, and they have:			
• IHD (unless they have had an MI in the prior 40 days – see below).	I	A	149, 156, 227
• DCM.	I	B	156, 157, 227
ICD implantation is not recommended within 40 days of an MI as implantation at this time does not improve prognosis.	III	A	158, 228
ICD therapy is not recommended in patients in NYHA Class IV with severe symptoms refractory to pharmacological therapy unless they are candidates for CRT, a ventricular assist device, or cardiac transplantation.	III	C	229–233
Patients should be carefully evaluated by an experienced cardiologist before generator replacement, because management goals and the patient's needs and clinical status may have changed.	IIa	B	234–238
A wearable ICD may be considered for patients with HF who are at risk of sudden cardiac death for a limited period or as a bridge to an implanted device.	IIb	C	239–241

CRT

Recommendations for cardiac resynchronization therapy implantation in patients with heart failure

Recommendations	Class [a]	Level [b]	Ref [c]
CRT is recommended for symptomatic patients with HF in sinus rhythm with a QRS duration ≥150 msec and LBBB QRS morphology and with LVEF ≤35% despite OMT in order to improve symptoms and reduce morbidity and mortality.	I	A	261–272
CRT should be considered for symptomatic patients with HF in sinus rhythm with a QRS duration ≥150 msec and non-LBBB QRS morphology and with LVEF ≤35% despite OMT in order to improve symptoms and reduce morbidity and mortality.	IIa	B	261–272
CRT is recommended for symptomatic patients with HF in sinus rhythm with a QRS duration of 130–149 msec and LBBB QRS morphology and with LVEF ≤35% despite OMT in order to improve symptoms and reduce morbidity and mortality.	I	B	266, 273
CRT may be considered for symptomatic patients with HF in sinus rhythm with a QRS duration of 130–149 msec and non-LBBB QRS morphology and with LVEF ≤35% despite OMT in order to improve symptoms and reduce morbidity and mortality.	IIb	B	266, 273
CRT rather than RV pacing is recommended for patients with HFrEF regardless of NYHA class who have an indication for ventricular pacing and high degree AV block in order to reduce morbidity. This includes patients with AF (see Section 10.1).	I	A	274–277
CRT should be considered for patients with LVEF ≤35% in NYHA Class III–IV[d] despite OMT in order to improve symptoms and reduce morbidity and mortality, if they are in AF and have a QRS duration ≥130 msec provided a strategy to ensure bi-ventricular capture is in place or the patient is expected to return to sinus rhythm.	IIa	B	275, 278–281
Patients with HFrEF who have received a conventional pacemaker or an ICD and subsequently develop worsening HF despite OMT and who have a high proportion of RV pacing may be considered for upgrade to CRT. This does not apply to patients with stable HF.	IIb	B	282
CRT is contra-indicated in patients with a QRS duration < 130 msec.	III	A	266, 283–285