

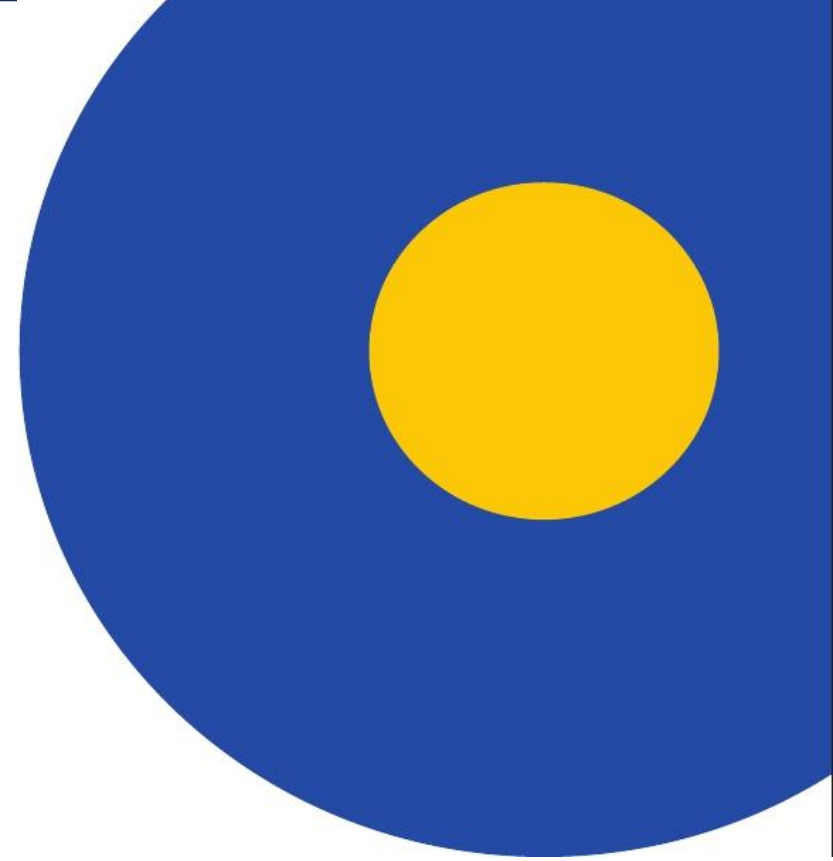
Heart Failure – Part 2

According to 2021 ESC guidelines

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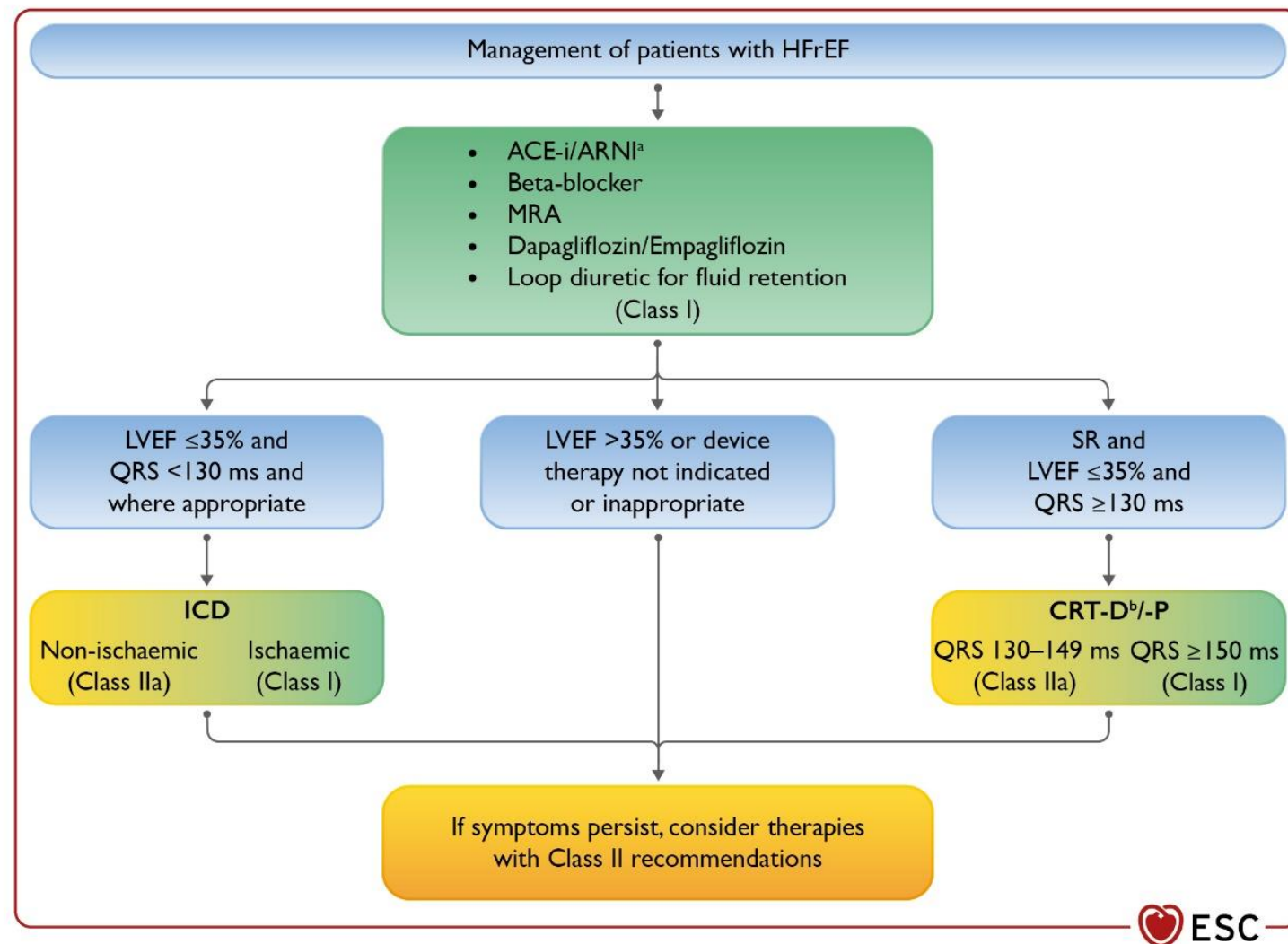


Therapeutic algorithm of Class I Therapy Indications for a patient with heart failure with reduced ejection fraction

ACE-I = angiotensin-converting enzyme inhibitor; ARNI = angiotensin receptor-neprilysin inhibitor; CRT-D = cardiac resynchronization therapy with defibrillator; CRT-P = cardiac resynchronization therapy pacemaker; ICD = implantable cardioverter-defibrillator; HFrEF = heart failure with reduced ejection fraction; MRA = mineralocorticoid receptor antagonist; QRS = Q, R, and S waves of an ECG; SR = sinus rhythm.

^aAs a replacement for ACE-I.

^bWhere appropriate. Class I=green. Class IIa=Yellow.



Pharmacological treatments indicated in patients with (NYHA class II-IV) heart failure with reduced ejection fraction (LVEF \leq 40%)



Recommendations	Class	Level
An ACE-I is recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.	I	A
A beta-blocker is recommended for patients with stable HFrEF to reduce the risk of HF hospitalization and death.	I	A
An MRA is recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.	I	A
Dapagliflozin or empagliflozin are recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.	I	A
Sacubitril/valsartan is recommended as a replacement for an ACE-I in patients with HFrEF to reduce the risk of HF hospitalization and death.	I	B

ACE-I = angiotensin-converting enzyme inhibitor; HF = heart failure; HFrEF = heart failure with reduced ejection fraction; LVEF = left ventricular ejection fraction; MRA = mineralocorticoid receptor antagonist; NYHA= New York Heart Association.

Other pharmacological treatments indicated in selected patients with NYHA class II-IV heart failure with reduced ejection fraction (LVEF $\leq 40\%$) (1)

Recommendations	Class	Level
Loop diuretics		
Diuretics are recommended in patients with HFrEF with signs and/or symptoms of congestion to alleviate HF symptoms, improve exercise capacity, and reduce HF hospitalizations.	I	C
ARB		
An ARB ^a is recommended to reduce the risk of HF hospitalization and CV death in symptomatic patients unable to tolerate an ACE-I or ARNI (patients should also receive a beta-blocker and an MRA).	I	B

ACE-I = angiotensin-converting enzyme inhibitor; ARB = angiotensin-receptor blocker; ARNI = angiotensin receptor-neprilysin inhibitor; CV = cardiovascular; HF = heart failure; HFrEF = heart failure with reduced ejection fraction; MRA = mineralocorticoid receptor antagonist; NYHA = New York Heart Association.

^aThe ARBs with evidence in HFrEF are candesartan, losartan, and valsartan.

Other pharmacological treatments indicated in selected patients with NYHA class II-IV heart failure with reduced ejection fraction (LVEF $\leq 40\%$) (2)

Recommendations	Class	Level
I_f-channel inhibitor		
Ivabradine should be considered in symptomatic patients with LVEF $\leq 35\%$, in SR and a resting heart rate ≥ 70 b.p.m. despite treatment with an evidence-based dose of beta-blocker (or maximum tolerated dose below that), ACE-I/(or ARNI), and an MRA, to reduce the risk of HF hospitalization and CV death.	IIa	B
Ivabradine should be considered in symptomatic patients with LVEF $\leq 35\%$, in SR and a resting heart rate ≥ 70 b.p.m. who are unable to tolerate or have contraindications for a beta-blocker to reduce the risk of HF hospitalization and CV death. Patients should also receive an ACE-I (or ARNI) and an MRA.	IIa	C

ACE-I = angiotensin-converting enzyme inhibitor; ARNI = angiotensin receptor-neprilysin inhibitor; b.p.m. = beats per minute; CV = cardiovascular; HF = heart failure; LVEF = left ventricular ejection fraction; MRA = mineralocorticoid receptor antagonist; NYHA = New York Heart Association; SR = sinus rhythm.

Other pharmacological treatments indicated in selected patients with NYHA class II-IV heart failure with reduced ejection fraction (LVEF \leq 40%) (3)

Recommendations	Class	Level
Soluble guanylate cyclase stimulator		
Vericiguat may be considered in patients in NYHA class II-IV who have had worsening HF despite treatment with an ACE-I (or ARNI), a beta-blocker and an MRA to reduce the risk of CV mortality or HF hospitalization.	IIb	B
Hydralazine and isosorbide dinitrate		
Hydralazine and isosorbide dinitrate should be considered in self-identified black patients with LVEF \leq 35% or with an LVEF $<$ 45% combined with a dilated left ventricle in NYHA class III-IV despite treatment with an ACE-I (or ARNI), 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 patients with symptomatic HFrEF who cannot tolerate any of an ACE-I, an ARB, or ARNI (or they are contraindicated) to reduce the risk of death.	IIb	B

ACE-I = angiotensin-converting enzyme inhibitor; ARNI = angiotensin receptor-neprilysin inhibitor; CV = cardiovascular; HF = heart failure; LVEF = left ventricular ejection fraction; MRA = mineralocorticoid receptor antagonist; NYHA= New York Heart Association.

Other pharmacological treatments indicated in selected patients with NYHA class II-IV heart failure with reduced ejection fraction (LVEF \leq 40%) (4)



Recommendations

Class Level

Digoxin

Digoxin may be considered in patients with symptomatic HFrEF in sinus rhythm despite treatment with an ACE-I (or ARNI), a beta-blocker and an MRA, to reduce the risk of hospitalization (both all-cause and HF hospitalizations).

IIb

B

ACE-I = angiotensin-converting enzyme inhibitor; ARNI = angiotensin receptor-neprilysin inhibitor; HF = heart failure; HFrEF = heart failure with reduced ejection fraction; MRA = mineralocorticoid receptor antagonist.

Management of HFrEF

To reduce mortality - for all patients

ACE-I/ARNI

BB

MRA

SGLT2i

To reduce HF hospitalization/mortality - for selected patients

Volume overload

Diuretics

SR with LBBB ≥ 150 ms

CRT-P/D

SR with LBBB 130–149 ms or non LBBB ≥ 150 ms

CRT-P/D

Ischaemic aetiology

ICD

Non-ischaemic aetiology

ICD

Atrial fibrillation

Anticoagulation

Atrial fibrillation

Digoxin

PVI

Coronary artery disease

CABG

Iron deficiency

Ferric carboxymaltose

Aortic stenosis

SAVR/TAVI

Mitral regurgitation

TEE MV Repair

Heart rate SR >70 bpm

Ivabradine

Black Race

Hydralazine/ISDN

ACE-I/ARNI intolerance

ARB

For selected advanced HF patients

Heart transplantation

MCS as BTT/BTC

Long-term MCS as DT

To reduce HF hospitalization and improve QOL - for all patients

Exercise rehabilitation

Multi-professional disease management

Strategic phenotypic overview of the management of heart failure with reduced ejection fraction

ACE-I = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; ARNI = angiotensin receptor-neprilysin inhibitor; BB = beta-blocker; b.p.m. = beats per minute; BTC = bridge to candidacy; BTT = bridge to transplantation; CABG = coronary artery bypass graft; CRT-D = cardiac resynchronization therapy with defibrillator; CRT-P = cardiac resynchronization therapy pacemaker; DT = destination therapy; HF = heart failure; HFrEF = heart failure with reduced ejection fraction; ICD = implantable cardioverter-defibrillator; ISDN = isosorbide dinitrate; LBBB = left bundle branch block; MCS = mechanical circulatory support; MRA = mineralocorticoid receptor antagonist; MV = mitral valve; PVI = pulmonary vein isolation; QOL = quality of life; SAVR = surgical aortic valve replacement; SGLT2i = sodium-glucose co-transporter 2 inhibitor; SR = sinus rhythm; TAVI = transcatheter aortic valve replacement; TEE = transcatheter edge to edge. Colour code for classes of recommendation: Green for Class of recommendation I; Yellow for Class of recommendation IIa (see Table 1 for further details on classes of recommendation).

The Figure shows management options with Class I and IIa recommendations. See the specific Tables for those with Class IIb recommendations.

Recommendations for an implantable cardioverter-defibrillator in patients with heart failure (1)

Recommendations	Class	Level
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, in the absence of reversible causes or unless the ventricular arrhythmia has occurred <48 h after a MI.	I	A
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) of an ischaemic aetiology (unless they have had a MI in the prior 40 days—see below), and an LVEF ≤35% despite ≥3 months of OMT, provided they are expected to survive substantially longer than 1 year with good functional status.	I	A

HF = heart failure; ICD = implantable cardioverter-defibrillator; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NYHA = New York Heart Association; OMT = optimal medical therapy.

Recommendations for an implantable cardioverter-defibrillator in patients with heart failure (2)

Recommendations	Class	Level
Primary prevention (continued)		
An ICD should be considered to reduce the risk of sudden death and all-cause mortality in patients with symptomatic HF (NYHA class II-III) of a non-ischaemic aetiology, and an LVEF \leq 35% despite \geq 3 months of OMT, provided they are expected to survive substantially longer than 1 year with good functional status.	IIa	A
Patients should be carefully evaluated by an experienced cardiologist before generator replacement, because management goals, the patient's needs and clinical status may have changed.	IIa	B
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	B

HF = heart failure; ICD = implantable cardioverter-defibrillator; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; OMT = optimal medical therapy.

Recommendations for an implantable cardioverter-defibrillator in patients with heart failure (3)

Recommendations	Class	Level
Primary prevention (continued)		
ICD implantation is not recommended within 40 days of a MI as implantation at this time does not improve prognosis.	III	A
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 VAD, or cardiac transplantation.	III	A

CRT = cardiac resynchronization therapy; ICD = implantable cardioverter-defibrillator; NYHA =New York Heart Association; VAD = ventricular assist device.

Recommendations for cardiac resynchronization therapy implantation in ESC patients with heart failure (1)

Recommendations	Class	Level
CRT is recommended for symptomatic patients with HF in SR with a QRS duration ≥ 150 ms and LBBB QRS morphology and with LVEF $\leq 35\%$ despite OMT in order to improve symptoms and reduce morbidity and mortality.	I	A
CRT should be considered for symptomatic patients with HF in SR with a QRS duration of 130–149 ms and LBBB QRS morphology and with LVEF $\leq 35\%$ despite OMT in order to improve symptoms and reduce morbidity and mortality.	IIa	B
CRT should be considered for symptomatic patients with HF in SR with a QRS duration ≥ 150 ms and non-LBBB QRS morphology and with LVEF $\leq 35\%$ despite OMT in order to improve symptoms and reduce morbidity and mortality.	IIa	B
CRT may be considered for symptomatic patients with HF in SR with a QRS duration of 130–149 ms and non-LBBB QRS morphology and with LVEF $\leq 35\%$ despite OMT in order to improve symptoms and reduce morbidity and mortality.	IIb	B

AF = atrial fibrillation; AV = atrio-ventricular; CRT = cardiac resynchronization therapy; HF = heart failure; HFrEF = heart failure with reduced ejection fraction; ICD = implantable cardioverter-defibrillator; LBBB = left bundle branch block; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; OMT = optimal medical therapy (class I recommended medical therapies for at least 3 months); QRS = Q, R, and S waves of an ECG; RV = right ventricular; SR = sinus rhythm.

Recommendations for cardiac resynchronization therapy implantation in ESC patients with heart failure (2)

Recommendations	Class	Level
CRT rather than RV pacing is recommended for patients with HFrEF regardless of NYHA class or QRS width who have an indication for ventricular pacing for high degree AV block in order to reduce morbidity. This includes patients with AF.	I	A
Patients with an LVEF $\leq 35\%$ who have received a conventional pacemaker or an ICD and subsequently develop worsening HF despite OMT and who have a significant proportion of RV pacing should be considered for 'upgrade' to CRT.	IIa	B
CRT is not recommended in patients with a QRS duration < 130 ms who do not have an indication for pacing due to high degree AV block.	III	A

AF = atrial fibrillation; AV = atrio-ventricular; CRT = cardiac resynchronization therapy; HF = heart failure; HFrEF = heart failure with reduced ejection fraction; ICD = implantable cardioverter-defibrillator; LBBB = left bundle branch block; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; OMT = optimal medical therapy (class I recommended medical therapies for at least 3 months); QRS = Q, R, and S waves of an ECG; RV = right ventricular; SR = sinus rhythm.

Pharmacological treatments to be considered in patients with (NYHA class II-IV) heart failure with mildly reduced ejection fraction

Recommendations	Class	Level
Diuretics are recommended in patients with congestion and HFmrEF in order to alleviate symptoms and signs.	I	C
An ACE-I may be considered for patients with HFmrEF to reduce the risk of HF hospitalization and death.	IIb	C
An ARB may be considered for patients with HFmrEF to reduce the risk of HF hospitalization and death.	IIb	C
A beta-blocker may be considered for patients with HFmrEF to reduce the risk of HF hospitalization and death.	IIb	C
An MRA may be considered for patients with HFmrEF to reduce the risk of HF hospitalization and death.	IIb	C
Sacubitril/valsartan may be considered for patients with HFmrEF to reduce the risk of HF hospitalization and death.	IIb	C

ACE-I = angiotensin-converting enzyme inhibitor; ARB = angiotensin-receptor blocker; HF = heart failure; HFmrEF = heart failure with mildly reduced ejection fraction; MRA = mineralocorticoid receptor antagonist; NYHA = New York Heart Association.

Recommendations for the treatment of patients with heart failure with preserved ejection fraction

Recommendations	Class	Level
Screening for, and treatment of, aetiologies, and cardiovascular and non-cardiovascular comorbidities is recommended in patients with HFpEF (see relevant sections of this document).	I	C
Diuretics are recommended in congested patients with HFpEF in order to alleviate symptoms and signs.	I	C

HFpEF = heart failure with preserved ejection fraction.

Recommendations for the primary prevention of heart failure in patients with risk factors for its development ESC

Recommendations	Class	Level
Treatment of hypertension is recommended to prevent or delay the onset of HF, and to prevent HF hospitalizations.	I	A
Treatment with statins is recommended in patients at high risk of CV disease or with CV disease in order to prevent or delay the onset of HF, and to prevent HF hospitalizations.	I	A
SGLT2 inhibitors (canagliflozin, dapagliflozin, empagliflozin, ertugliflozin, sotagliflozin) are recommended in patients with diabetes at high risk of CV disease or with CV disease in order to prevent HF hospitalizations.	I	A
Counselling against sedentary habit, obesity, cigarette smoking, and alcohol abuse is recommended to prevent or delay the onset of HF.	I	C

CV=cardiovascular; HF=heart failure; SGLT2=sodium-glucose co-transporter 2.

Recommendations for the treatment of patients with advanced heart failure (1)

Recommendations	Class	Level
Patients being considered for long-term MCS must have good compliance, appropriate capacity for device handling and psychosocial support.	I	C
Heart transplantation is recommended for patients with advanced HF, refractory to medical/ device therapy and who do not have absolute contraindications.	I	C
Long-term MCS should be considered in patients with advanced HFrEF despite optimal medical and device therapy, not eligible for heart transplantation or other surgical options, and without severe right ventricular dysfunction, to reduce the risk of death and improve symptoms.	IIa	A
Long-term MCS should be considered in patients with advanced HFrEF refractory to optimal medical and device therapy as a bridge to cardiac transplantation in order to improve symptoms, reduce the risk of HF hospitalization and the risk of premature death.	IIa	B

HF = heart failure; HFrEF = heart failure with reduced ejection fraction; MCS = mechanical circulatory support.

Recommendations for the treatment of patients with advanced heart failure (2)

Recommendations	Class	Level
Renal replacement therapy should be considered in patients with refractory volume overload and end-stage kidney failure	IIa	C
Continuous inotropes and/or vasopressors may be considered in patients with low cardiac output and evidence of organ hypoperfusion as bridge to MCS or heart transplantation.	IIb	C
Ultrafiltration may be considered in refractory volume overload unresponsive to diuretic treatment.	IIb	C

MCS = mechanical circulatory support.