

# **Insuffisance Cardiaque**

## **Recommandations ESC 2021**

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**ESC GUIDELINES**

# **2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure**

**Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)**

**With the special contribution of the Heart Failure Association (HFA) of the ESC**

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# ESC Classes of recommendations

Classes of recommendations

Definition		Wording to use
<b>Class I</b>	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	Is recommended or is indicated
<b>Class II</b>	Conflicting evidence and/or a divergence of opinion about the usefulness/ efficacy of the given treatment or procedure.	
Class IIa	Weight of evidence/opinion is in favour of usefulness/efficacy.	Should be considered
Class IIb	Usefulness/efficacy is less well established by evidence/opinion.	May be considered
<b>Class III</b>	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.	Is not recommended

# ESC Classes of recommendations

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

# Definition of heart failure with reduced ejection fraction, mildly reduced ejection fraction and preserved ejection fraction

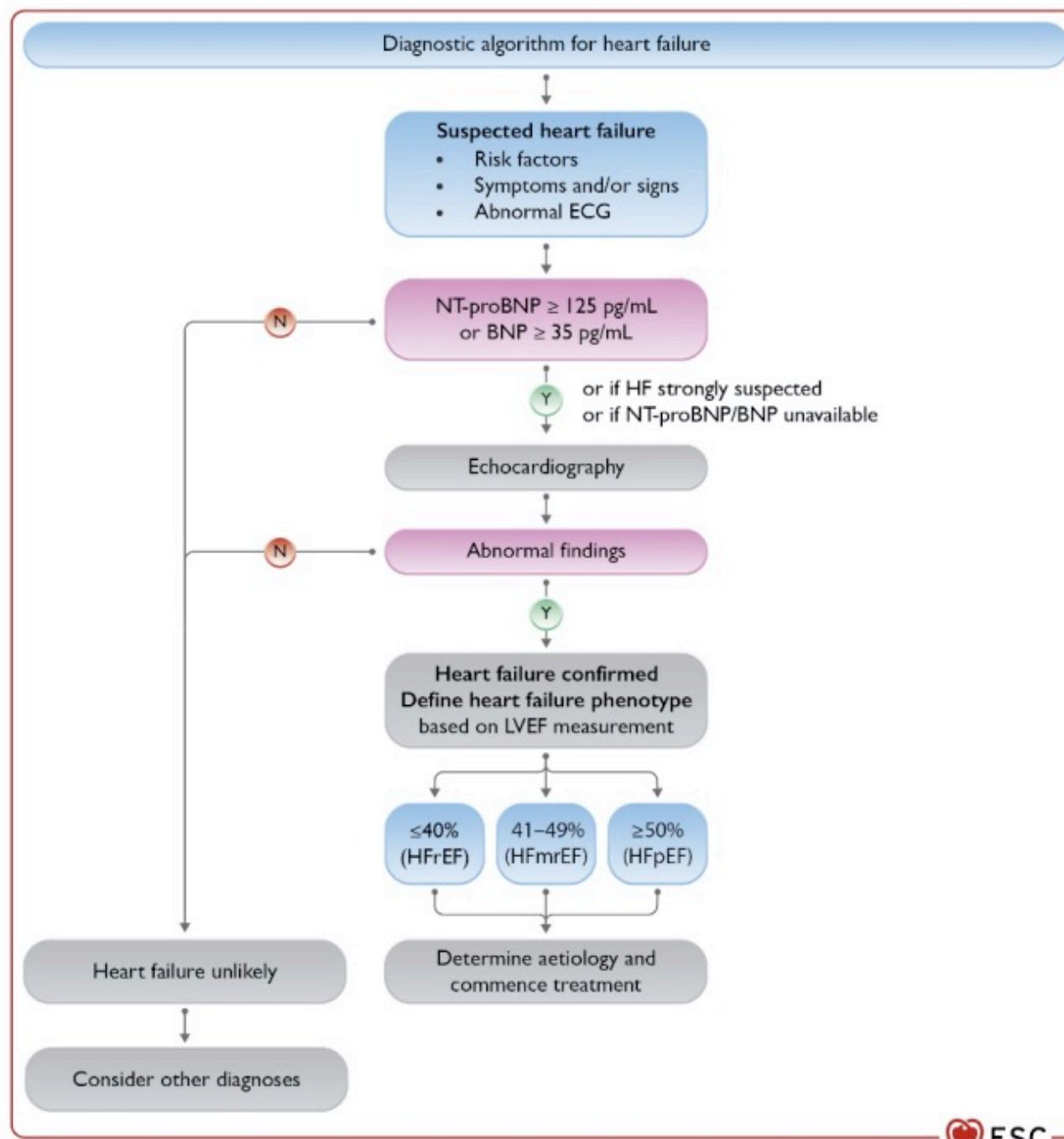
Type of HF		HFrEF	HFmrEF	HFpEF
CRITERIA	1	Symptoms ± Signs <sup>a</sup>	Symptoms ± Signs <sup>a</sup>	Symptoms ± Signs <sup>a</sup>
	2	LVEF ≤40%	LVEF 41–49% <sup>b</sup>	LVEF ≥50%
	3	-	-	Objective evidence of cardiac structural and/or functional abnormalities consistent with the presence of LV diastolic dysfunction/raised LV filling pressures, including raised natriuretic peptides <sup>c</sup>

HF = heart failure; HFmrEF = heart failure with mildly reduced ejection fraction; HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction; LV = left ventricle; LVEF = left ventricular ejection fraction.

<sup>a</sup>Signs may not be present in the early stages of HF (especially in HFpEF) and in optimally treated patients.

<sup>b</sup>For the diagnosis of HFmrEF, the presence of other evidence of structural heart disease (e.g. increased left atrial size, LV hypertrophy or echocardiographic measures of impaired LV filling) makes the diagnosis more likely.

<sup>c</sup>For the diagnosis of HFpEF, the greater the number of abnormalities present, the higher the likelihood of HFpEF.





# Recommended diagnostic tests in all patients with suspected chronic heart failure

Recommendations	Class	Level
BNP/NT-proBNP <sup>a</sup>	I	B
12-lead ECG	I	C
Transthoracic echocardiography	I	C
Chest radiography (X-ray)	I	C
Routine blood tests for comorbidities, including full blood count, urea and electrolytes, thyroid function, fasting glucose and HbA1c, lipids, iron status (TSAT and ferritin)	I	C

BNP = B-type natriuretic peptide; ECG = electrocardiogram; HbA1c = glycated haemoglobin; NT-proBNP = N-terminal pro-B-type natriuretic peptide; TSAT = transferrin saturation.

<sup>a</sup>References are listed in section 4.2 for this item.

# Recommendations for specialised diagnostic tests for selected patients with chronic heart failure to detect reversible/treatable causes of heart failure (1)

Recommendations	Class	Level
<b>CMR</b>		
CMR is recommended for the assessment of myocardial structure and function in those with poor echocardiogram acoustic windows.	<b>I</b>	<b>C</b>
CMR is recommended for the characterization of myocardial tissue in suspected infiltrative disease, Fabry disease, inflammatory disease (myocarditis), LV non-compaction, amyloid, sarcoidosis, iron overload/haemochromatosis.	<b>I</b>	<b>C</b>
CMR with LGE should be considered in DCM to distinguish between ischaemic and non-ischaemic myocardial damage.	<b>IIa</b>	<b>C</b>

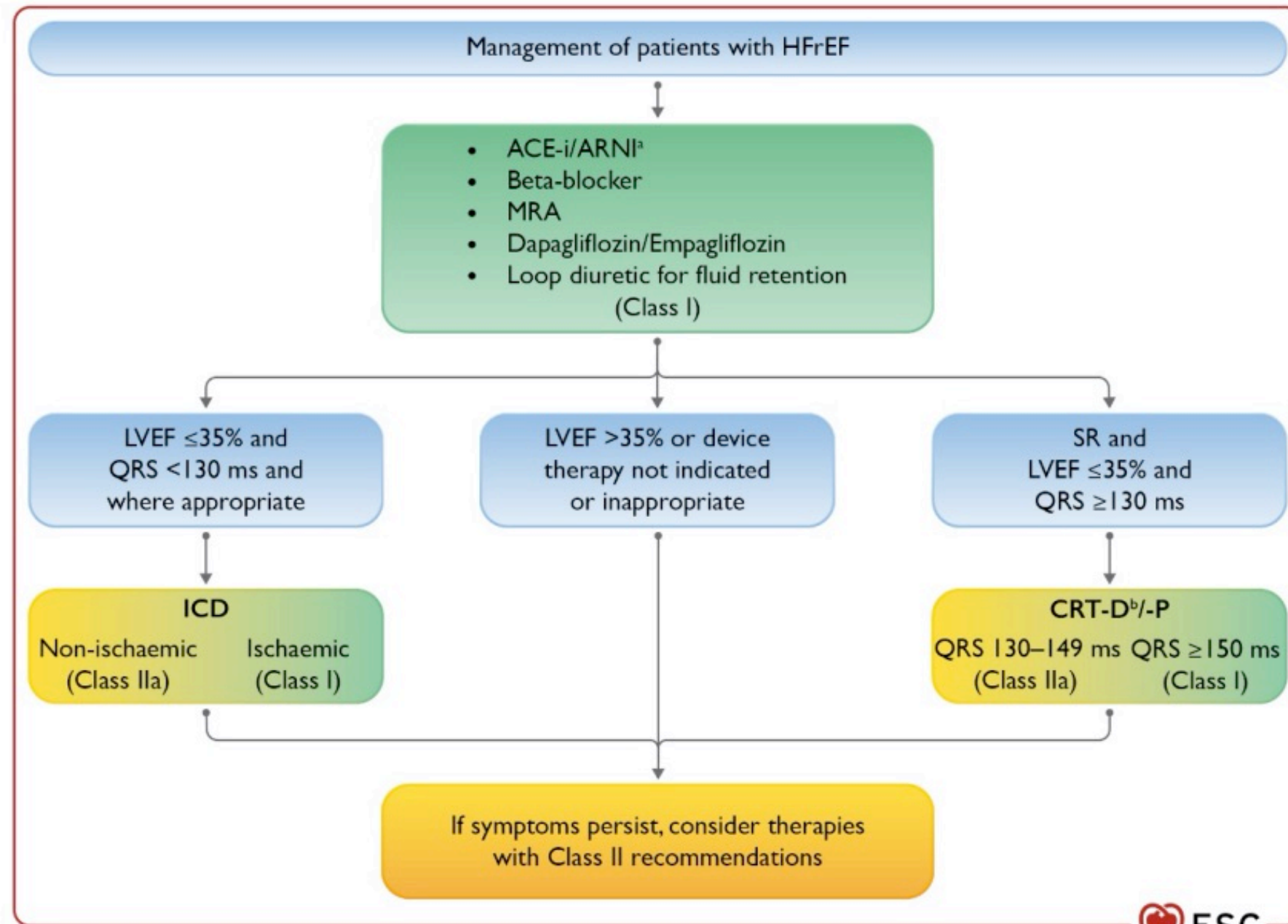
CMR = cardiac magnetic resonance; DCM = dilated cardiomyopathy; LGE = late gadolinium enhancement; LV = left ventricular.



## Recommendations for specialised diagnostic tests for selected patients with chronic heart failure to detect reversible/treatable causes of heart failure (4)

Recommendations	Class	Level
<b>Cardiopulmonary exercise testing</b>		
Cardiopulmonary exercise testing is recommended as a part of the evaluation for heart transplantation and/or MCS.	I	C
Cardiopulmonary exercise testing should be considered to optimize prescription of exercise training.	IIa	C
Cardiopulmonary exercise testing should be considered to identify the cause of unexplained dyspnoea and/or exercise intolerance.	IIa	C

MCS = mechanical circulatory support.



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

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.

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



## 5.2.2 General principles of pharmacotherapy for heart failure with reduced ejection fraction

Modulation of the renin-angiotensin-aldosterone (RAAS) and sympathetic nervous systems with angiotensin-converting enzyme inhibitors (ACE-I) or an angiotensin receptor-neprilysin inhibitor (ARNI), beta-blockers, and mineralocorticoid receptor antagonists (MRA) has been shown to improve survival, reduce the risk of HF hospitalizations, and reduce symptoms in patients with HFrEF. These drugs serve as the foundations of pharmacotherapy for patients with HFrEF. The triad of an ACE-I/ARNI, a beta-blocker, and an MRA is recommended as cornerstone therapies for these patients, unless the drugs are contraindicated or not tolerated.<sup>103–105</sup> They should be uptitrated to the doses used in the clinical trials (or to maximally tolerated doses if that is not possible). This guideline still recommends the use of ARNI as a replacement for ACE-I in suitable patients who remain symptomatic on ACE-I, beta-blocker, and MRA therapies; however, an ARNI may be considered as a first-line therapy instead of an ACE-I.<sup>106,107</sup> The recommended doses of these drugs are given in *Table 8*. Angiotensin-receptor blockers (ARBs) still have a role in those who are intolerant to ACE-I or ARNI.

The sodium-glucose co-transporter 2 (SGLT2) inhibitors dapagliflozin and empagliflozin added to therapy with ACE-I/ARNI/beta-blocker/MRA reduced the risk of CV death and worsening HF in patients with HFrEF.<sup>108,109</sup> Unless contraindicated or not tolerated, dapagliflozin or empagliflozin are recommended for all patients with HFrEF already treated with an ACE-I/ARNI, a beta-blocker, and an MRA, regardless of whether they have diabetes or not.

# Evidence-based doses of disease-modifying drugs in key randomized trials in patients with heart failure with reduced ejection fraction (1)

	Starting dose	Target dose
<b>ACE-I</b>		
Captopril <sup>a</sup>	6.25 mg <i>t.i.d.</i>	50 mg <i>t.i.d.</i>
Enalapril	2.5 mg <i>b.i.d.</i>	10–20 mg <i>b.i.d.</i>
Lisinopril <sup>b</sup>	2.5–5 mg <i>o.d.</i>	20–35 mg <i>o.d.</i>
Ramipril	2.5 mg <i>b.i.d.</i>	5 mg <i>b.i.d.</i>
Trandolapril <sup>a</sup>	0.5 mg <i>o.d.</i>	4 mg <i>o.d.</i>
<b>ARNI</b>		
Sacubitril/valsartan	49/51 mg <i>b.i.d.</i> <sup>c</sup>	97/103 mg <i>b.i.d.</i>

ACE-I = angiotensin-converting enzyme inhibitor; ARNI = angiotensin receptorneprilysin inhibitor; b.i.d. = bis in die; o.d. = omne in die (once daily); t.i.d. = ter in die (three times a day).

<sup>a</sup>Indicates an ACE-I where the dosing target is derived from post-myocardial infarction trials.

<sup>b</sup>Indicates drugs where a higher dose has been shown to reduce morbidity/mortality compared with a lower dose of the same drug, but there is no substantive randomized, placebo-controlled trial and the optimum dose is uncertain. <sup>c</sup>Sacubitril/valsartan may have an optional lower starting dose of 24/26 mg b.i.d. for those with a history of symptomatic hypotension.



# Evidence-based doses of disease-modifying drugs in key randomized trials in patients with heart failure with reduced ejection fraction (2)

	Starting dose	Target dose
<b>Beta-blockers</b>		
Bisoprolol	1.25 mg <i>o.d.</i>	10 mg <i>o.d.</i>
Carvedilol	3.125 mg <i>b.i.d.</i>	25 mg <i>b.i.d.</i> <sup>e</sup>
Metoprolol succinate (CR/XL)	12.5–25 mg <i>o.d.</i>	200 mg <i>o.d.</i>
Nebivolol <sup>d</sup>	1.25 mg <i>o.d.</i>	10 mg <i>o.d.</i>
<b>MRA</b>		
Eplerenone	25 mg <i>o.d.</i>	50 mg <i>o.d.</i>
Spironolactone	25 mg <i>o.d.</i> <sup>f</sup>	50 mg <i>o.d.</i>

b.i.d. = bis in die (twice daily); CR = controlled release; MRA = mineralocorticoid receptor antagonist; o.d. = omne in die (once daily); XL = extended release.

<sup>d</sup>Indicates a treatment not shown to reduce CV or all-cause mortality in patients with heart failure (or shown to be non-inferior to a treatment that does).

<sup>e</sup>A maximum dose of 50 mg twice daily can be administered to patients weighing over 85 kg.

<sup>f</sup>Spironolactone has an optional starting dose of 12.5 mg in patients where renal status or hyperkalaemia warrant caution.



# Evidence-based doses of disease-modifying drugs in key randomized trials in patients with heart failure with reduced ejection fraction (3)

	Starting dose	Target dose
<b>SGLT2 inhibitor</b>		
Dapagliflozin	10 mg <i>o.d.</i>	10 mg <i>o.d.</i>
Empagliflozin	10 mg <i>o.d.</i>	10 mg <i>o.d.</i>
<b>Other agents</b>		
Candesartan	4 mg <i>o.d.</i>	32 mg <i>o.d.</i>
Losartan	50 mg <i>o.d.</i>	150 mg <i>o.d.</i>
Valsartan	40 mg <i>b.i.d.</i>	160 mg <i>b.i.d.</i>
Ivabradine	5 mg <i>b.i.d.</i>	7.5 mg <i>b.i.d.</i>
Vericiguat	2.5 mg <i>o.d.</i>	10 mg <i>o.d.</i>

b.i.d. = bis in die (twice daily); o.d. = omne in die (once daily); SGLT2 = sodium-glucose co-transporter 2; t.i.d. = ter in die (three times a day).

# 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
<b>Loop diuretics</b>		
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.	<b>I</b>	<b>C</b>
<b>ARB</b>		
An ARB <sup>a</sup> 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).	<b>I</b>	<b>B</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.

<sup>a</sup>The ARBs with evidence in HFrEF are candesartan, losartan, and valsartan.

# 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  $\geq 150$  ms

CRT-P/D

SR with LBBB 130–149 ms or non LBBB  $\geq 150$  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

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

Recommendations	Class	Level
<b>Secondary prevention</b>		
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
<b>Primary prevention</b>		
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
<b>Primary prevention (continued)</b>		
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.	<b>IIa</b>	<b>A</b>
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.	<b>IIa</b>	<b>B</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.	<b>IIb</b>	<b>B</b>

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

# 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 $\geq 150$ ms and LBBB QRS morphology and with LVEF $\leq 35\%$ despite OMT in order to improve symptoms and reduce morbidity and mortality.	<b>I</b>	<b>A</b>
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.	<b>I</b>	<b>B</b>
CRT should be considered for symptomatic patients with HF in SR with a QRS duration $\geq 150$ ms and non-LBBB QRS morphology and with LVEF $\leq 35\%$ despite OMT in order to improve symptoms and reduce morbidity and mortality.	<b>IIa</b>	<b>B</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.	<b>IIb</b>	<b>B</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 (combination of three of the graphical deflections); RV = right ventricular; SR = sinus rhythm.

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# 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.	<b>I</b>	<b>A</b>
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.	<b>IIa</b>	<b>B</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.	<b>III</b>	<b>A</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 (combination of three of the graphical deflections); RV = right ventricular; SR = sinus rhythm.

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

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
Screening for, and treatment of, aetiologies, and cardiovascular and non-cardiovascular comorbidities is recommended in patients with HFpEF (see relevant sections of this document).	<b>I</b>	<b>C</b>
Diuretics are recommended in congested patients with HFpEF in order to alleviate symptoms and signs. <sup>137</sup>	<b>I</b>	<b>C</b>

# 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 anaemia and iron deficiency in patients with heart failure

Recommendations	Class	Level
It is recommended that all patients with HF be periodically screened for anaemia and iron deficiency with a full blood count, serum ferritin concentration, and TSAT.	I	C
Intravenous iron supplementation with ferric carboxymaltose should be considered in symptomatic patients with LVEF <45% and iron deficiency, defined as serum ferritin <100 ng/mL or serum ferritin 100–299 ng/mL with TSAT <20%, to alleviate HF symptoms, improve exercise capacity and QOL.	IIa	A
Intravenous iron supplementation with ferric carboxymaltose should be considered in symptomatic HF patients recently hospitalized for HF and with LVEF <50% and iron deficiency, defined as serum ferritin <100 ng/mL or serum ferritin 100–299 ng/mL with TSAT <20%, to reduce the risk of HF hospitalization.	IIa	B

HF = heart failure; LVEF = left ventricular ejection fraction; QOL= quality of life; TSAT = transferrin saturation.

# Multidisciplinary interventions recommended for the management of chronic heart failure

Recommendations	Class	Level
It is recommended that HF patients are enrolled in a multidisciplinary HF management programme to reduce the risk of HF hospitalization and mortality	I	A
Self-management strategies are recommended to reduce the risk of HF hospitalization and mortality.	I	A
Either home-based and/or clinic-based programmes improve outcomes and are recommended to reduce the risk of HF hospitalization and mortality.	I	A
Influenza and pneumococcal vaccinations should be considered in order to prevent HF hospitalizations.	IIa	B

HF=heart failure.

# Recommendations for exercise rehabilitation in patients with chronic heart failure

Recommendations	Class	Level
Exercise is recommended for all patients who are able in order to improve exercise capacity, QOL, and reduce HF hospitalization. <sup>a</sup>	I	A
A supervised, exercise-based, cardiac rehabilitation programme should be considered in patients with more severe disease, frailty, or with comorbidities.	IIa	C

HF = heart failure; QOL= quality of life.

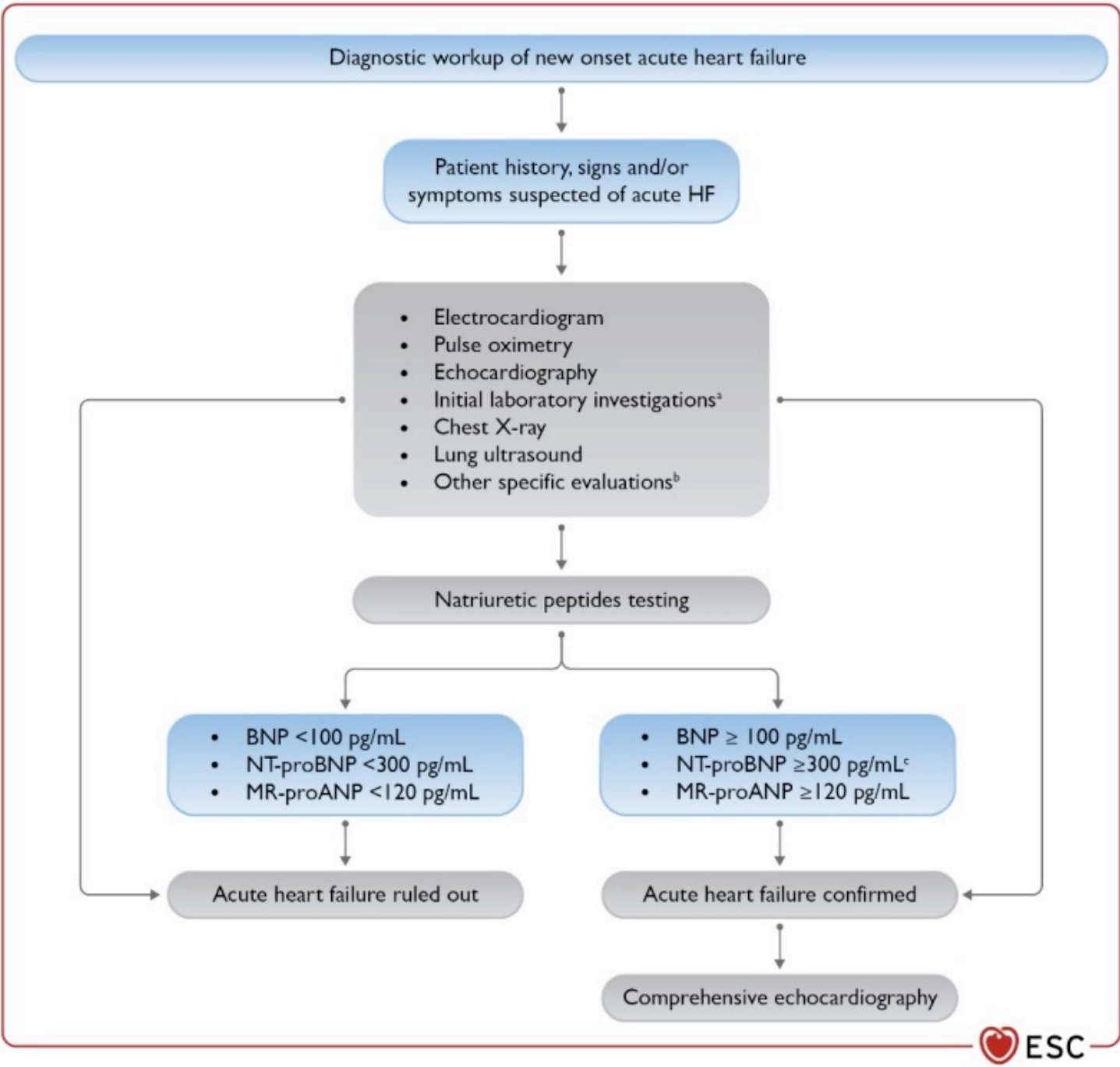
<sup>a</sup>In those who are able to adhere to the exercise programme.

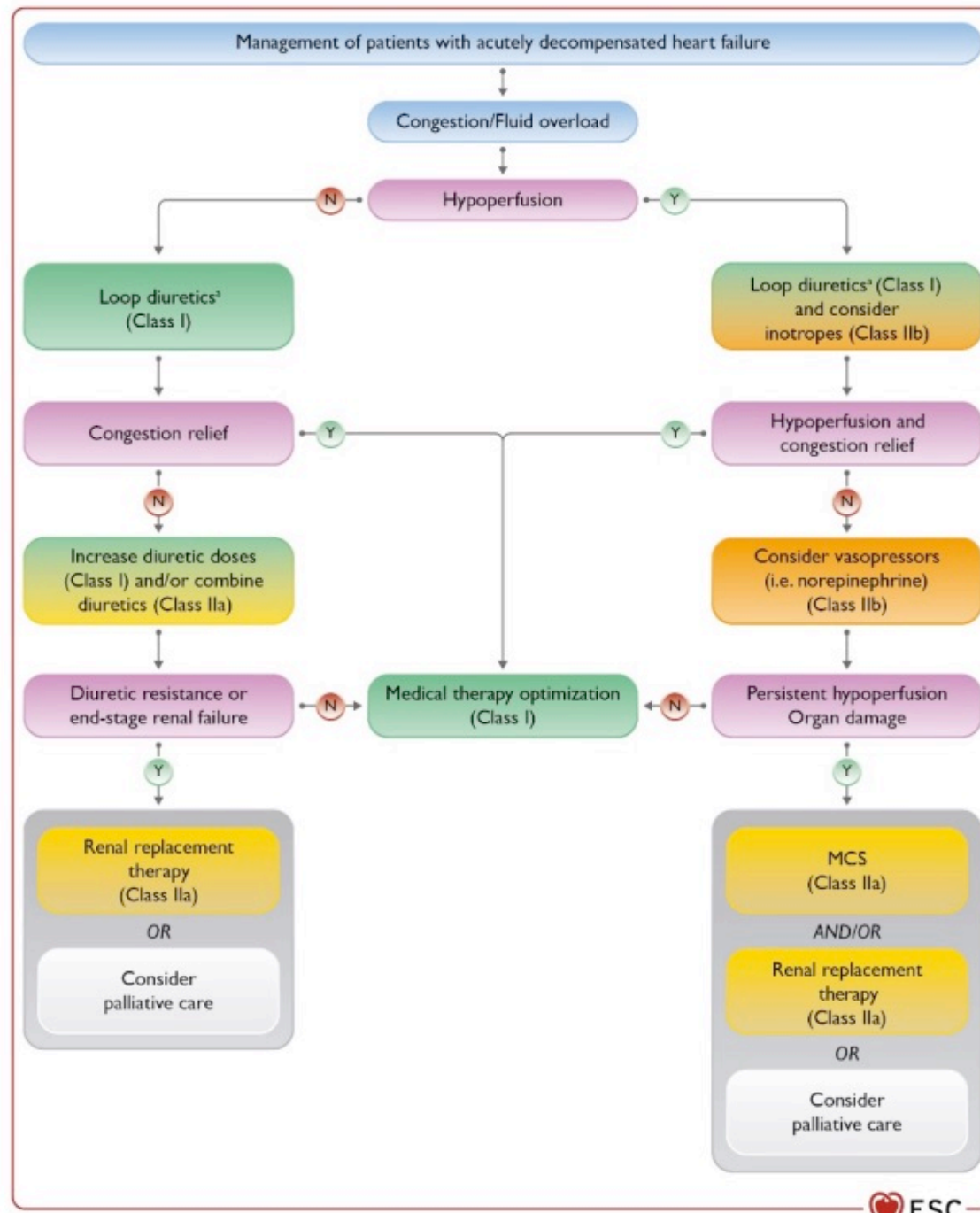


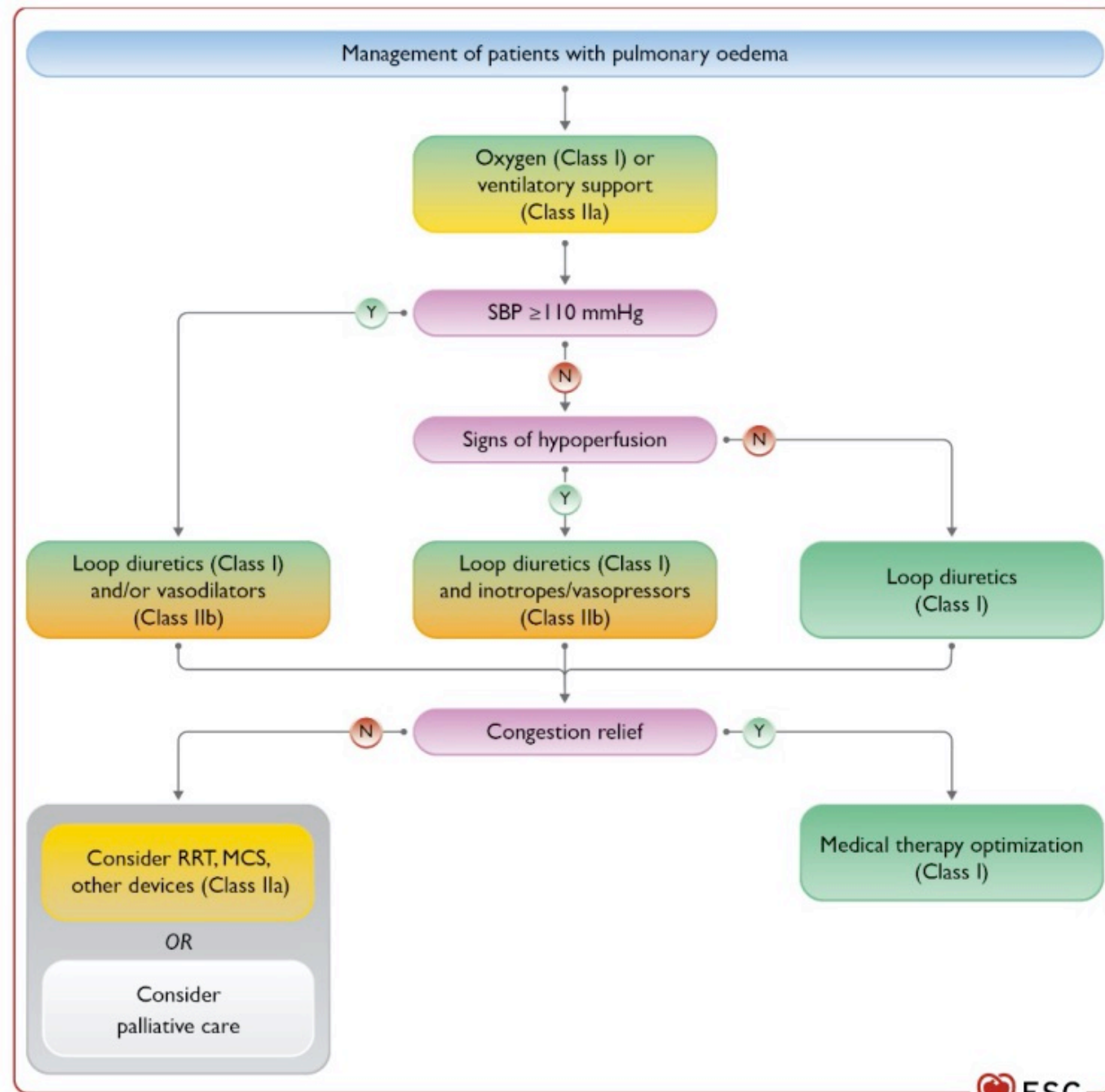
# Recommendations for telemonitoring

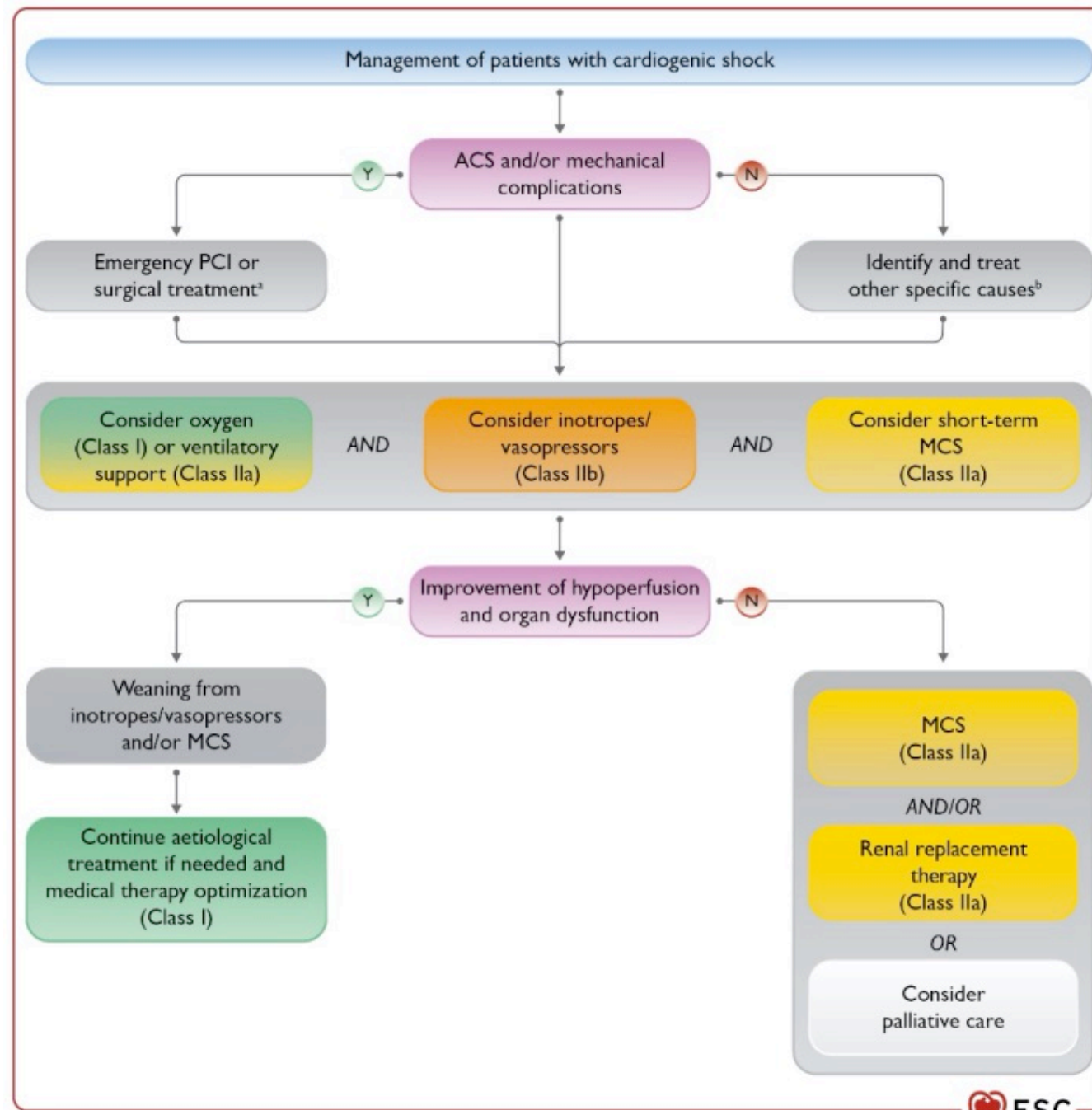
Recommendations	Class	Level
Non-invasive HTM may be considered for patients with HF in order to reduce the risk of recurrent CV and HF hospitalizations and CV death.	<b>IIb</b>	<b>B</b>
Monitoring of pulmonary artery pressure using a wireless haemodynamic monitoring system may be considered in symptomatic patients with HFrEF (LVEF $\leq 35\%$ ) in order to improve clinical outcomes.	<b>IIb</b>	<b>B</b>

CV = cardiovascular; HF = heart failure; HFrEF = heart failure with reduced ejection fraction; HTM= home telemonitoring; LVEF = left ventricular ejection fraction.









# Conclusions

- Des recommandations « déroutantes » pour l'insuffisance cardiaque chronique à FEVG abaissée
- 4 molécules d'emblée pour tous... 5 si diurétique
- « Tapis rouge » pour les glifozines
- DAI en retrait pour les CMD non-ischémiques (IIa)
- Insuffisance cardiaque à fraction d'éjection modérément abaissée ???
- Insuffisance cardiaque aiguë: des données peu robustes dans la littérature, des recommandations de faible niveau