ESC European Society of Cardiology

European Heart Journal (2026) **00**, 1–112
https://doi.org/10.1093/eurheartj/ehag100

ESC GUIDELINES

2026 ESC Guidelines for the management of heart failure

Developed by the task force for the management of heart failure of the European Society of Cardiology (ESC)

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

Endorsed by the European Association for Cardio-Thoracic Surgery (EACTS)

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All experts involved in the development of these guidelines have submitted declarations of interest which are reported in a supplementary document to the guidelines. See the *European Heart Journal* online or https://www.escardio.org/Guidelines for supplementary documents as well as evidence tables.

Keywords Guidelines • European Society of Cardiology (ESC) • Heart failure • Heart failure with reduced ejection fraction (HFrEF) • Heart failure with preserved ejection fraction (HFpEF) • Decompensated heart failure • Advanced heart failure • Stages of heart failure • Heart failure phenotypes • Treatment • Prevention • Pharmacotherapy • Foundational medical therapy • Additional medical therapy • Guideline directed interventional therapy • Cardiac resynchronization therapy • Implantable cardioverter-defibrillator • Aetiology • Diagnosis • Comorbidities • Cardiac amyloidosis

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Abbreviations and acronyms

18F-FDG-PET	18F-fluorodeoxyglucose-positron emission tomography
ACC	American College of Cardiology
ACE-I	Angiotensin-converting enzyme inhibitor
ACHD	Adult congenital heart disease
AF	Atrial fibrillation
AHA	American Heart Association
AL-CA	Immunoglobulin light chain cardiac amyloidosis
AMT	Additional medical therapy
APO	Acute pulmonary oedema
ARB	Angiotensin II receptor blocker
ARNI	Angiotensin receptor–neprilysin inhibitor
ARVC	Arrhythmogenic right ventricular cardiomyopathy
ASCVD	Atherosclerotic cardiovascular disease
ASV	Adaptive servo-ventilation
ATTR	Transthyretin amyloidosis
ATTR-CA	Transthyretin cardiac amyloidosis
BMI	Body mass index
BNP	B-type natriuretic peptide
CA	Cardiac amyloidosis
CABG	Coronary artery bypass grafting
CAD	Coronary artery disease
CI	Confidence interval
CIED	Cardiac implantable electronic device
CKD	Chronic kidney disease
CMR	Cardiac magnetic resonance
COPD	Chronic obstructive pulmonary disease
CPAP	Continuous positive airway pressure
CPET	Cardiopulmonary exercise testing
CRT	Cardiac resynchronization therapy
CRT-D	Cardiac resynchronization therapy with defibrillator
CRT-P	Cardiac resynchronization therapy with pacemaker
CS	Cardiogenic shock
CSA	Central sleep apnoea
CSP	Conduction system pacing
CT	Computed tomography
CTCA	Computed tomography coronary angiography
CV	Cardiovascular
CVD	Cardiovascular disease
DCM	Dilated cardiomyopathy
DHF	Decompensated heart failure
DPD	3,3-Diphosphono-1,2-propanodicarboxylic acid
ECG	Electrocardiogram
ECLS	Extracorporeal life support
ECV	Extracellular volume
eGFR	Estimated glomerular filtration rate
ESC	European Society of Cardiology
FITT	Frequency, intensity, time, type
FMT	Foundational medical therapy
GDIT	Guideline-directed interventional therapy
GDMT	Guideline-directed medical therapy
GFR	Glomerular filtration rate
GIP	Glucose-dependent insulinotropic peptide
GLP-1 RA	Glucagon-like peptide-1 receptor agonist
HCM	Hypertrophic cardiomyopathy
HF	Heart failure
HFA	Heart Failure Association
HFH	Heart failure hospitalization
HF-MDT	Heart failure multidisciplinary team
HFmrEF	Heart failure with mildly reduced ejection fraction
HFpEF	Heart failure with preserved ejection fraction
HFrEF	Heart failure with reduced ejection fraction
HR	Hazard ratio

i.v.	Intravenous
IABP	Intra-aortic balloon pump
ICA	Invasive coronary angiography
ICD	Implantable cardioverter-defibrillator
ID	Iron deficiency
INTERMACS	Interagency Registry for Mechanically Assisted Circulatory Support
KCCQ	Kansas City Cardiomyopathy Questionnaire
KDIGO	Kidney Disease: Improving Global Outcomes
LBBB	Left bundle branch block
LGE	Late gadolinium enhancement
LV	Left ventricular
LVAD	Left ventricular assist device
LVEF	Left ventricular ejection fraction
MCS	Mechanical circulatory support
MI	Myocardial infarction
MR	Mitral regurgitation
MRA	Mineralocorticoid receptor antagonist
MR-proANP	Mid-regional pro-atrial natriuretic peptide
NT-proBNP	N-terminal pro-B-type natriuretic peptide
NYHA	New York Heart Association
OSA	Obstructive sleep apnoea
PaO_2	Partial pressure of oxygen
PCI	Percutaneous coronary intervention
PVC	Premature ventricular contraction
QoL	Quality of life
RCT	Randomized controlled trial
RHC	Right heart catheterization
RV	Right ventricular
SCAI	Society for Cardiovascular Angiography and Interventions
SCD	Sudden cardiac death
SDB	Sleep-disordered breathing
SGLT2	Sodium–glucose co-transporter 2
SGLT2-I	Sodium–glucose co-transporter 2 inhibitor
SHARC	Shock Academic Research Consortium
S-ICD	Subcutaneous implantable cardioverter-defibrillator
SpO_2	Oxygen saturation
T2DM	Type 2 diabetes mellitus
TAVI	Transcatheter aortic valve implantation
TEER	Transcatheter edge-to-edge repair
TR	Tricuspid regurgitation
TSAT	Transferrin saturation
TTR	Transthyretin
UACR	Urine albumin-to-creatinine ratio
uNa^+	Urinary sodium
WHF	Worsening heart failure
WHO	World Health Organization

For acronyms of studies and trials, see Supplementary data online, *Table S1*.

1. Preamble

Guidelines evaluate and summarize available evidence with the aim of assisting health professionals in proposing the best diagnostic or therapeutic approach for an individual patient with a given condition. ESC Guidelines are intended for use by health professionals but do not override their individual responsibility to make appropriate and accurate decisions in consideration of each patient's health condition and in consultation with the patient or the patient's caregiver where appropriate and/or necessary. It is also the health professional's responsibility to verify the rules and regulations applicable in each country to drugs and devices at the time of prescription and to respect the ethical rules of their profession.

ESC Guidelines represent the official position of the ESC on a given topic. Guideline topics are selected for updating after annual expert review of new evidence conducted by the ESC Clinical Practice Guidelines (CPG) Committee. ESC Policies and Procedures for formulating and issuing ESC Guidelines can be found on the ESC website (https://www.escardio.org/Guidelines/Clinical-Practice-Guidelines/Guidelines-development/Writing-ESC-Guidelines).

This guideline updates and replaces the previous version from 2021. This Task Force was selected by the ESC to include professionals involved with the medical care of patients with this pathology and to include patient representatives and methodologists. The selection procedure included an open call for authors and aimed to include members from across the entire ESC region and from relevant ESC Subspecialty Communities. Consideration was given to diversity and inclusion.

Guidelines Task Forces perform a critical review and evaluation of the published literature on diagnostic and therapeutic approaches including assessment of the risk–benefit ratio. Recommendations are based on major randomized trials and relevant systematic reviews and meta-analyses, when available. Systematic literature searches are conducted in cases of controversy or uncertainty to ensure that all key studies are considered. For recommendations related to diagnosis and prognosis, additional types of evidence are included, such as diagnostic accuracy studies and studies focused on the development and validation of prognostic models. The strength of each recommendation and the level of evidence supporting it are weighed and scored according to predefined criteria. The criteria for grading the strength of recommendations are described in *Table 1*. A new system for grading levels of evidence for ESC Guidelines has been published[1,2] and utilized for the first time in 2026 ESC Guidelines. For therapy and prevention, the framework includes consideration of study type and the number of studies supporting a recommendation, as well as whether a study is adequately powered, shows substantial evidence against the play of chance, and is free of major sources of bias. This is described in *Table 2*. A separate grading system has also been developed for diagnostic tests and prediction models, which is described in *Table 3*.

Patient-Reported Outcome Measures (PROMs) and Patient-Reported Experience Measures (PREMs) are also evaluated when available as the basis for recommendations and/or discussion in these guidelines.

Evidence tables summarizing key information from relevant studies are generated to facilitate the formulation of recommendations, to enhance comprehension of recommendations after publication, and to reinforce transparency in the guidelines development process. The tables are published in their own section of ESC Guidelines and reference specific recommendation tables.

After an iterative process of deliberations, a first Task Force vote on all recommendations is conducted prior to the initiation of rounds of review. A second Task Force vote on all recommendations is conducted after the final round of review and revision. For each vote, the Task Force follows ESC voting procedures: to achieve quorum, at least two-thirds of the Task Force must vote agree or disagree, and to be approved all recommendations require at least 75% of votes in favour, excluding abstentions. Restrictions on voting and on participation in task force deliberations are applied as needed based on declarations of interest.

The writing and reviewing panels provide declaration of interest forms for all relationships that might be perceived as real or potential sources of conflicts of interest. Their declarations of interest are reviewed according to the ESC declaration of interest rules, which can be found on the ESC website (http://www.escardio.org/doi) and are compiled in a report published in a supplementary document with the guidelines. Funding for the development of ESC Guidelines is derived entirely from the ESC with no involvement of the healthcare industry.

The CPG Committee supervises and coordinates the preparation of new guidelines and approves their publication. In addition to review by the CPG Committee, ESC Guidelines undergo multiple rounds of double-blind peer review on a dedicated online review platform. The review is conducted by a panel of 70 or more topic experts including members from ESC National Cardiac Societies and from relevant ESC Subspecialty Communities. Reviewers critically assess and comment on the content of the Guidelines and grade their comments as major and minor. Guideline Task Forces consider all review comments and are required to respond on the online platform to all those classified as major. The review comments inform revisions after each round. After the final review round and the second Task Force vote on all recommendations, the Task Force and the CPG Committee members approve the final document for publication in the *European Heart Journal*.

Unless otherwise stated, ESC Guidelines content refers to sex, understood as the biological condition of being male or female, defined by genes, hormones, and sexual organs. Off-label use of medication may be presented in this guideline if a sufficient level of evidence shows that it can be considered medically appropriate for a given condition. However, decisions on off-label use must be made by the responsible health professional giving special consideration to ethical rules concerning healthcare, the specific situation of the patient, patient consent, and country-specific health regulation.

Table 1 Classes of recommendations

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

Table 2 Levels of evidence—therapy and prevention

Level of evidence	Definition
A	Conclusive evidence, usually from at least two adequately powered randomized controlled trials[a] free of major bias, with substantial evidence against the play of chance when combined in a meta-analysis (e.g., P <0.005 for superiority).[b]
B1	Suggestive evidence from at least one adequately powered randomized controlled trial free of major bias, or a meta-analysis of such randomized controlled trials, with some evidence against the play of chance (e.g., P <0.05 for superiority).[c]
B2	Limited evidence from at least two adequately powered non-randomized studies with careful control of major sources of bias and substantial evidence against the play of chance (e.g., P <0.005 for superiority),[b] or from a meta-analysis of small, underpowered randomized controlled trials with some evidence against the play of chance (e.g., P <0.05 for superiority).[c]
C	Preliminary evidence from non-randomized studies without careful control of major sources of bias, a single small, underpowered randomized controlled trial, or expert consensus.

[a]Exceptionally, level of evidence A can be considered if (1) there is a single very large randomized controlled trial that provides convincing evidence across a wide range of patients that is already widely accepted by most practitioners, or (2) the effects of the intervention are clinically obvious; in either case, over 90% of voting guideline task force members need to agree with level of evidence A.
[b]Studies do not need to individually show substantial evidence against the play of chance (e.g. a P-value of <.005 for superiority) if a meta-analysis of these studies provides such evidence.
[c]Studies do not need to individually show some evidence against the play of chance (e.g. a P-value of <.05 for superiority) if a meta-analysis of these studies provides such evidence.

Table 3 Levels of evidence—diagnostic tests and prediction models

Level of evidence	Diagnostic test	Prediction model (including diagnostic and prognostic models)
A	Conclusive evidence of adequate diagnostic ability from at least two high-quality studies	Conclusive evidence of adequate predictive ability from at least one high-quality derivation study, and two or more external validation studies of at least moderate quality.
B	Suggestive evidence of adequate diagnostic ability from a single high-quality or at least two moderate-quality studies.	Suggestive evidence of adequate predictive ability from one or more derivation and one or more external validation studies of at least moderate quality.
C	Preliminary evidence of adequate diagnostic ability from a single moderate-quality study, any number of low-quality studies, or expert consensus.	Preliminary evidence of adequate predictive ability from a derivation study of at least moderate quality, but with external validation absent or in a low-quality study, or a derivation study of low quality (irrespective of external validation).

2. Introduction

In these guidelines, we have redefined the classification of heart failure (HF) compared with the definition used in the *2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure*,[3] and provided a simple definition that we believe will translate into everyday clinical practice. As early detection of HF is increasingly important, we have, in alignment with the *2022 AHA/ACC/HFSA Guideline for the management of heart failure*,[4] also included risk factors and early signs of HF into the staging of HF. An updated classification for the treatment of HF has also been added, which emphasizes foundational and additional medical therapies, as well as interventional therapies. *Figure 1* provides an overview of current management recommendations for HF. Since the publication of the *2021 ESC Guidelines for the diagnosis and treatment of acute and*

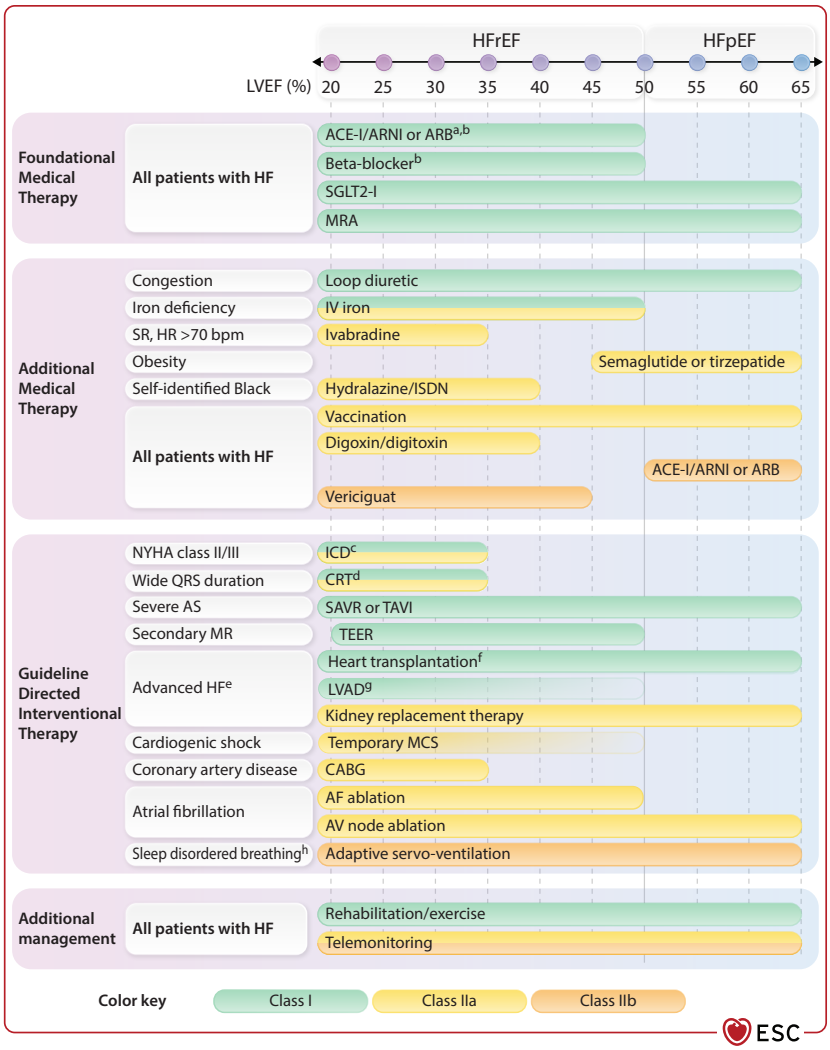

Figure 1 Central illustration. Management of heart failure. ACE-I, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; ARB, angiotensin II receptor blocker; ARNI, angiotensin receptor–neprilysin inhibitor; AS, aortic stenosis; AV, atrioventricular; CABG, coronary artery bypass grafting; CRT, cardiac resynchronization therapy; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; HR, heart rate; ICD, implantable cardioverter-defibrillator; ISDN, isosorbide dinitrate; IV, intravenous; LVAD, left ventricular assist device; LVEF, left ventricular ejection fraction; MCS, mechanical circulatory support; MR, mitral regurgitation; MRA, mineralocorticoid receptor antagonist; TEER, transcatheter edge-to-edge repair; NYHA, New York Heart Association; SAVR, surgical aortic valve replacement; SGLT2-I, sodium–glucose co-transporter 2 inhibitor; SR, sinus rhythm; TAVI, transcatheter aortic valve implantation. Green colour refers to Class I recommendation. Yellow colour refers to Class IIa recommendation. Orange colour refers to Class IIb recommendation. [a]An ARB is recommended in patients with symptomatic HFrEF if they are unable to tolerate an ACE-I or ARNI. [b]No large prospective randomized controlled trial has been performed on the use of beta-blockers, ACE-I/ARNI/ARB exclusively in patients with LVEF 41%–49%. [c]Class of recommendation for ICD differs according to ischaemic vs non-ischaemic aetiology. [d]Class of recommendation for CRT differs according to QRS duration and morphology (see *Figure 10* and *Recommendation Table 7*). [e]Criteria for advanced HF are listed in *Table 14*. [f]Indications and contraindications for heart transplantation are listed in *Table 17*. [g]Indications and contraindications for LVAD implantation are listed in *Table 16*. [h]Predominantly obstructive sleep apnoea.

chronic heart failure[3] and the *2023 Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure*,[5] new guidance for interpretation of evidence has been published by the ESC.[1,2] Consequently, all recommendations, new and old, have been regraded to comply with the revised ESC evidence grading system. For recommendations with more than one outcome, e.g. cardiovascular (CV) death and HF hospitalization (HFH), the wording reflects whether both outcomes were individually significant ('AND') or the outcome was a composite ('OR').

For each topic, we have considered age and sex differences and included these in the recommendations, if deemed clinically relevant.

Since the publication of the *2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure*,[3] several relevant guidelines on specific topics, such as cardio-oncology,[6]

pregnancy,[7] myocarditis,[8] valvular heart disease,[9] and chronic coronary syndrome,[10] have been published. In the current guidelines, these topics are not addressed in detail, and we refer to the specific guidelines for each topic.

2.1. What is new

In the *2026 ESC Guidelines for the management of heart failure*, some new concepts compared with the 2021 version are introduced in addition to the recommendations listed below. These changes will have impact on some recommendations, specifically concerning guideline-recommended treatment of HF because we have changed the classification of HF based on left ventricular ejection fraction (LVEF). For details of the new concepts, see *Sections 3*, *6*, and *7*. *Table 4* provides an overview of new concepts. *Table 5* highlights the new recommendations and *Table 6* the revised recommendations, included in this document.

Table 4 New concepts

New concepts
HFrEF has been expanded to include LVEF up to 50%
HFmrEF has been removed
HFpEF includes LVEF from 50% and above
Decompensated HF replaces acute HF
Stages of HF (A–D) ranging from risk factors to advanced HF have been adopted
New classifications for medical and interventional therapy have been introduced

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; LVEF, left ventricular ejection fraction.

Table 5 New recommendations

Recommendations	Class[a]	Level[b]
Prevention of heart failure—*Section 4*		
Counselling on healthy lifestyle choices including maintaining a healthy weight, consuming a well-balanced diet, avoiding sedentary behaviour, abstaining from smoking and heavy alcohol consumption, as well as counselling against the use of drugs such as cocaine, amphetamines, and anabolic steroids, is recommended for all patients with stage A or B HF to reduce the risk of HF progression.	I	C
A GLP-1 RA should be considered in patients with T2DM and at least one other additional CV risk factor to reduce the risk of HF or CV death.	IIa	A
An ACE-I or ARB (if intolerant to ACE-I) is recommended in patients with stage B HF and LVEF ≤40% to reduce the risk of HFH and death.	I	A
A beta-blocker is recommended in patients with stage B HF and LVEF <50% to reduce the risk of HFH or death.	I	B1
Eplerenone is recommended in patients after myocardial infarction with LVEF ≤40% with signs of HF or diabetes to reduce the risk of HFH or death.	I	B1
Diagnosis of chronic heart failure—*Section 5*		
Initial diagnostic testing with serum and urine immunofixation, serum free light chains assay, and DPD/PYP/HMDP bone scintigraphy is recommended in patients with HF and a suspicion of cardiac amyloidosis.	I	B
Genetic testing is recommended in patients fulfilling diagnostic criteria for cardiomyopathy in cases where it enables diagnosis, prognostication, therapeutic stratification, or reproductive management of the patient, or where it enables cascade genetic evaluation of their relatives who would otherwise be enrolled into long-term surveillance.	I	C
18F-FDG-PET scanning should be considered for the diagnostic work-up in patients with cardiomyopathy in whom cardiac sarcoidosis is suspected.	IIa	C
Review of the proportion of RV pacing should be considered in all patients with CIED and de novo or worsening HFrEF.	IIa	C
Electrical cardioversion as a diagnostic tool may be considered in patients with persistent AF where there is uncertainty about the value of sinus rhythm restoration on symptoms or to assess improvement in left ventricular function.	IIb	C
Management of chronic heart failure—*Section 6*		
Uptitration of FMT at least every 1–2 weeks in patients with HF, guided by symptoms, vital signs, and laboratory findings, to achieve optimal target doses shown to be efficacious in RCTs is recommended to reduce the risk of HFH or death.	I	C
Continuation of FMT at the highest tolerated doses is recommended in all patients with HF, including those who become asymptomatic or with LVEF improvement, in order to reduce the risk of HFH and death.	I	C
Gradual discontinuation of FMT under frequent clinical, laboratory, and imaging surveillance may be considered in highly selected patients who are asymptomatic with complete normalization of LV function and volume as well as natriuretic peptide levels after specific treatment of reversible causes of HF, in order to accommodate patient preference.	IIb	C
ACE-I/ARB/ARNI may be considered in patients with symptomatic HFpEF to reduce the risk of HFH.	IIb	C
Initiation of FMT and planning for CRT implantation may be considered simultaneously in patients with symptomatic HFrEF, an LBBB with QRS ≥150 ms, and LVEF ≤35% to improve symptoms and reduce morbidity and death, although reassessment of LVEF should be conducted prior to CRT implantation.	IIb	C

Continued

Decompensated heart failure—*Section 7*		
Urinary Na^+-guided diuretic therapy may be considered during the first days of treatment of patients with DHF to improve natriuresis and diuresis.	IIb	B1
In-hospital initiation of SGLT2-I is recommended in patients with DHF after initial stabilization to improve QoL and congestion symptoms and reduce the risk of HFH.	I	B1
A multidisciplinary Shock Team is recommended in potential candidates for temporary MCS to guide the device selection (modality and type) based on patient and HF characteristics.	I	C
Temporary MCS with a microaxial flow pump should be considered in selected patients with cardiogenic shock caused by ST-elevation MI with LV systolic dysfunction and no risk of hypoxic brain injury in order to reduce the risk of death.	IIa	B1
Temporary MCS should be considered in patients with mechanical complications related to MI as a bridge to definitive treatment.	IIa	C
Temporary MCS is not recommended in unselected patients with cardiogenic shock caused by acute MI, due to risk of harm.	III	B1
Advanced heart failure—*Section 8*		
Early consultation with an advanced HF centre is recommended in patients with advanced HF or at risk of advanced HF, who are motivated and do not have absolute contraindications for heart transplantation or durable MCS, in order to evaluate candidacy.	I	A
Downtitration or discontinuation of beta-blockers or ivabradine should be considered in selected patients with advanced HFrEF and evidence of organ hypoperfusion, despite initial treatment, to increase cardiac output and improve symptoms.	IIa	C
Histopathological examination of explanted heart tissue from LVAD or heart transplantation surgery should be considered in patients with non-ischaemic HF to identify an aetiological diagnosis that may be treatable or facilitate family screening.	IIa	C
Cardiovascular comorbidities—*Section 9*		
Atrioventricular node ablation combined with CRT should be considered in patients with severely symptomatic permanent AF and poor rate control despite medical therapy and at least one HFH to reduce symptoms, physical limitations, recurrent HFH and death.	IIa	B1
Intravenous amiodarone or digoxin may be considered in haemodynamically unstable patients with HFrEF and AF to stabilize the patient and achieve acute control of heart rate.	IIb	C
Non-cardiovascular comorbidities—*Section 10*		
Semaglutide or tirzepatide should be considered for patients with symptomatic HF, LVEF ≥45%, and BMI ≥30 kg/m^2, regardless of diabetes status, to reduce body weight, and improve exercise capacity and QoL.	IIa	B1
Bariatric surgery may be considered in obese patients with HF and a BMI ≥35 kg/m^2 to reduce body weight when repetitive and structured lifestyle changes combined with weight-reducing medications do not result in maintained weight loss.	IIb	C
Adaptive servo-ventilation may be considered in patients with HFrEF and sleep-disordered breathing with predominant obstructive sleep apnoea to improve sleep quality, health-related QoL, and symptoms.	IIb	C
Assessment of anxiety, depression and frailty should be considered in patients with HF to support the development of personalized care plans and to identify factors that may contribute to adverse outcomes.	IIa	C
Multidisciplinary management of heart failure—*Section 11*		
Personalized exercise training, in the context of multidisciplinary exercise-based cardiac rehabilitation, is recommended for all stable patients, unless there are specific contraindications, in order to improve exercise capacity, and QoL, and reduce the risk of all-cause hospitalization.	I	B1
Personalized exercise training outside exercise-based cardiac rehabilitation is recommended for all stable patients on a long-term basis, unless there are specific contraindications, in order to improve exercise capacity and QoL, and reduce the risk of all-cause hospitalization.	I	B2
Cardiac rehabilitation is recommended in patients with an LVAD to improve functional capacity and QoL.	I	B1
Cardiac rehabilitation should be considered in patients with DHF, as soon as safely possible, to improve functional capacity and QoL.	IIa	B1
Proactive discussion regarding HF trajectory, goals of care, and advance care planning is recommended in patients with advanced HF to facilitate communication on end of life and QoL.	I	B1
Access to an integrated HF palliative care multidisciplinary team is recommended for patients in an advanced HF stage to improve QoL and reduce symptom burden.	I	B2

Continued

Specific conditions—*Section 12*		
Pre-conception care and counselling is recommended for patients with HF to facilitate decision-making surrounding HF treatments, pregnancy, contraception, pre-implantation genetic screening, and assisted reproductive therapies.	I	C
In pregnant women with HFrEF, it is recommended that non-selective beta-blockers are switched to beta$_1$-selective blockers (metoprolol, bisoprolol) with close mother and foetus monitoring to reduce the risk of adverse foetal events and a lower birth weight.	I	C
ACE-Is, ARBs, ARNIs, MRAs, ivabradine, and SGLT2-Is are not recommended during pregnancy due to the risk of foetotoxicity or teratogenicity.	III	C

18F-FDG-PET, 18F-fluorodeoxyglucose-positron emission tomography; ACE-I, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; ARB, angiotensin II receptor blocker; ARNI, angiotensin receptor–neprilysin inhibitor; BMI, body mass index; BTB, bridge to bridge; BTC, bridge to candidacy; BTD, bridge to decision; BTR, bridge to recovery; BTT, bridge to transplantation; CIED, cardiac implantable electronic device; CRT, cardiac resynchronization therapy; CV, cardiovascular; DHF, decompensated heart failure; DPD, 3,3-diphosphono-1,2-propanodicarboxylic acid; FMT, foundational medical therapy; GLP-1 RA, glucagon-like peptide-1 receptor agonist; HF, heart failure; HFH, heart failure hospitalization; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; HMDP, hydroxymethylene diphosphonate; LBBB, left bundle branch block; LV, left ventricular; LVAD, left ventricular assist device; LVEF, left ventricular ejection fraction; MCS, mechanical circulatory support; MI, myocardial infarction; MRA, mineralocorticoid receptor antagonist; PYP, pyrophosphate; QoL, quality of life; RCT, randomized controlled trial; RV, right ventricular; SGLT2-I, sodium–glucose co-transporter 2 inhibitor; T2DM, type 2 diabetes mellitus.
[a]Class of recommendation.
[b]Level of evidence.

Table 6 Revised recommendations

Recommendations in 2021 version	Class[a]	Level[b]	Recommendations in 2026 version	Class[a]	Level[b]
Prevention of heart failure—*Section 4*					
Treatment of hypertension is recommended to prevent or delay the onset of HF, and to prevent HF hospitalizations.	I	A	Strict blood pressure control (systolic blood pressure target <130 mmHg) is recommended in patients with hypertension or stage B HF to reduce the risk of HF.	I	A
Diagnosis of chronic heart failure—*Section 5*					
CMR is recommended for the assessment of myocardial structure and function in those with poor echocardiographic acoustic windows.	I	C	Contrast-enhanced CMR is recommended in patients with suspected cardiomyopathy, or where the underlying aetiology of HF is uncertain if further characterization is likely to add value to patient care.	I	C
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.	I	C			
CMR with LGE should be considered in DCM to distinguish between ischaemic and non-ischaemic myocardial damage.	IIa	C			
Invasive coronary angiography is recommended in patients with angina despite pharmacological therapy or symptomatic ventricular arrhythmias.	I	B	Invasive coronary angiography is recommended in patients with HF, angina, and high probability of obstructive CAD who are potential candidates for revascularization.	I	C
Invasive coronary angiography may be considered in patients with HFrEF with an intermediate to high pre-test probability of CAD and the presence of ischaemia in non-invasive stress tests.	IIb	B	Invasive coronary angiography should be considered in patients with HFrEF and high pre-test likelihood of obstructive CAD, taking into account the risk-to-benefit ratio of the procedures and potential revascularization strategies.	IIa	C
Management of chronic heart failure—*Section 6*					
An MRA is recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.	I	A	An MRA (sMRA for HFrEF and sMRA/nsMRA for HFpEF) is recommended in patients with symptomatic HF independent of LVEF to reduce the risk of HFH or CV death.	I	A
An MRA may be considered for patients with HFmrEF to reduce the risk of HF hospitalization and death.	IIb	C			

Continued

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	A cardiac glycoside (digoxin or digitoxin) should be considered in patients with symptomatic HFrEF with LVEF ≤40%, despite optimal FMT, to reduce the risk of HFH.	IIa	B1
Vericiguat may be considered in patients in NYHA classes 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 and HF hospitalization. [*In patients with HFrEF according to the 2021 classification.*]	IIb	B	Vericiguat may be considered in patients with symptomatic HFrEF and LVEF <45% despite treatment with optimal FMT to reduce the risk of HFH and CV death.	IIb	B1
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	CRT, rather than RV pacing, should be considered in 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 the risk of HFH and death.	IIa	B1
Decompensated heart failure—*Section 7*					
Combination of a loop diuretic with thiazide-type diuretic should be considered in patients with resistant oedema who do not respond to an increase in loop diuretic doses.	IIa	B	The addition of short-term intravenous acetazolamide or oral hydrochlorothiazide should be considered in patients with fluid overload previously treated with loop diuretics, to reduce congestion.	IIa	B1
IABP is not routinely recommended in post-MI cardiogenic shock.	III	B	IABP is not recommended in unselected patients with cardiogenic shock, due to the lack of effect.	III	B1
Short-term MCS should be considered in patients with cardiogenic shock as a BTR, BTD, BTB. Further indications include treatment of the cause of cardiogenic shock or long-term MCS or transplantation	IIa	C	Temporary MCS should be considered in selected patients with HF-related haemodynamic instability as a BTR, BTD, BTB, BTC, or BTT.	IIa	C
Advanced heart failure—*Section 8*					
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	Continuous inotropes should be considered in patients with advanced HFrEF, low cardiac output, and evidence of hypoperfusion or end-organ dysfunction, as BTD, BTT, or as bridge to durable MCS, to increase cardiac output and improve symptoms.	IIa	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	Durable MCS (LVAD) is recommended in selected patients with advanced HFrEF, despite FMT and GDIT, as BTT, BTC, BTR, or as destination therapy to improve symptoms and reduce the risk of death.	I	C
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			
Cardiovascular comorbidities—*Section 9*					
Beta-blockers should be considered for short- and long-term rate control in patients with HF and AF.	IIa	B	Beta-blockers are recommended in stable patients with HFrEF and AF as first-line therapy for short- and long-term rate control.	I	C

Continued

In cases of a clear association between paroxysmal or persistent AF and worsening of HF symptoms, which persist despite MT, catheter ablation should be considered for the prevention or treatment of AF.	IIa	B	Catheter ablation for AF should be considered in selected patients with symptomatic AF and HFrEF to improve QoL and reduce the risk of HFH or death.	IIa	C
Coronary revascularization should be considered to relieve persistent symptoms of angina (or an angina-equivalent) in patients with HFrEF, CCS, and coronary anatomy suitable for revascularization, despite OMT including antianginal drugs.	IIa	C	Coronary revascularization is recommended in patients with HF, obstructive CAD, and persistent angina, despite FMT for HF and antianginal drugs, to relieve symptoms.	I	C
Aortic valve intervention, TAVI or SAVR, is recommended in patients with HF and severe high-gradient aortic stenosis to reduce mortality and improve symptoms.	I	B	Aortic valve intervention, SAVR or TAVI, is recommended in patients with severe aortic stenosis and HF to improve symptoms and reduce the risk of death.	I	B1
Percutaneous edge-to-edge mitral valve repair should be considered in carefully selected patients with secondary mitral regurgitation, not eligible for surgery and not needing coronary revascularization, who are symptomatic despite OMT and who fulfil criteria for achieving a reduction in HF hospitalizations.	IIa	B	Mitral transcatheter edge-to-edge repair is recommended in haemodynamically stable, symptomatic patients with HFrEF and persistent severe secondary mitral regurgitation despite optimized FMT and CRT if indicated, who fulfil specific clinical and echocardiographic criteria, in order to reduce the risk of HFH and improve QoL.	I	B1
Multidisciplinary management—*Section 11*					
Monitoring of pulmonary artery pressure using a wireless haemodynamic monitoring system may be considered in symptomatic patients with HF in order to improve clinical outcomes.	IIb	B	Remote haemodynamic monitoring of PA pressure should be considered in symptomatic patients with HF, NYHA class III and an HFH in the past 12 months in order to reduce the risk of HFH.	IIa	B1
Specific conditions—*Section 12*					
Tafamidis is recommended in patients with genetic testing proven hTTR-CA and NYHA class I or II symptoms to reduce symptoms, CV hospitalization and mortality.	I	B	Treatment with a TTR silencer (vutrisiran) or stabilizer (tafamidis or acoramidis) for patients with variant or wild-type transthyretin cardiac amyloidosis and NYHA class I–III is recommended to reduce progression of symptoms and the risk of CV hospitalization and all-cause death.	I	A
Tafamidis is recommended in patients with wtTTR-CA and NYHA class I or II symptoms to reduce symptoms, CV hospitalization and mortality.	I	B			

ACE-I angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; ARNI, angiotensin receptor–neprilysin inhibitor; AV, atrioventricular; BTC, bridge to candidacy; BTD, bridge to decision; BTR, bridge to recovery; BTT, bridge to transplantation; CAD, coronary artery disease; CCS, chronic coronary syndrome; CMR, cardiac magnetic resonance; CRT, cardiac resynchronization therapy; CV, cardiovascular; DCM, dilated cardiomyopathy; FMT, foundational medical therapy; HF, heart failure; HFH, heart failure hospitalization; HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; hTTR-CA, hereditary transthyretin cardiac amyloidosis; IABP, intra-aortic balloon pump; LGE, late gadolinium enhancement; LV, left ventricular; LVAD, left ventricular assist device; LVEF, left ventricular ejection fraction; MCS, mechanical circulatory support; MI, myocardial infarction; MRA, mineralocorticoid receptor antagonist; MT, medical therapy; nsMRA, non-steroidal mineralocorticoid receptor antagonist; NYHA, New York Heart Association; OMT, optimal medical therapy; PA, pulmonary artery; QoL, quality of life; RV, right ventricular; SAVR, surgical aortic valve replacement; sMRA, steroidal mineralocorticoid receptor antagonist; TAVI, transcatheter aortic valve implantation; TTR, transthyretin; wtTTR-CA, wild-type transthyretin cardiac amyloidosis.
[a]Class of recommendation.
[b]Level of evidence.

3. Definition, epidemiology, and classifications

3.1. Definition of heart failure

Heart failure is a clinical syndrome comprising signs and/or symptoms caused by structural and/or functional abnormalities of the heart that result in elevated intracardiac pressures and/or inadequate cardiac output at rest and/or during exercise.[11] In addition to the subjective symptoms of HF, clinically assessed objective evidence of cardiogenic pulmonary and/or systemic congestion and diagnostic supportive tests are needed to reach the diagnosis (see *Section 5*).[11]

People who are in asymptomatic stages are not included under the above definition as having HF. They are defined as being at risk for HF (stage A) or having pre-HF (stage B) (see *Section 3.3*).

Identification of the aetiology of the underlying cardiac dysfunction is not included in the definition of HF, although determining aetiology is clinically important as the specific pathology can determine subsequent treatment and prognosis. Specific investigations needed to identify underlying aetiologies are described in *Section 5*.

3.2. Epidemiology of heart failure

The prevalence of HF is estimated to be 1%–3% in the general adult population, with significant geographical, age- and sex-related

variations.[12,13] Both the incidence and prevalence of HF are increasing with age and risk-factor burden, with wide variation depending on the population and setting studied and the diagnostic criteria used.[14] In addition, several factors, such as level of education, income, neighbourhood deprivation, climate, and air pollution, influence the risk of HF, contributing to varying epidemiology worldwide.[13]

In European countries, current prevalance-estimates range from 12–58 cases per 1000 people.[15]

As a result of the growing cohort of older people in Western populations, the crude incidence of HF has been increasing and is currently 2–13 per 1000 person-years in Europe (ranging from <1 per 1000 person-years for people aged 45–54 years to >12 per 1000 person-years for people aged >74 years).[16,17] However, age-adjusted HF incidence rates have been declining over the past three decades, probably because of better risk-factor control and treatment of CV conditions.[15,17,18] Among younger adults, incidence rates of HF appear to be either increasing or stagnating. There are several possible explanations for this, including (i) a greater burden of CV risk factors, (ii) increasing numbers of patients with congenital heart disease reaching adulthood, and (iii) a change in surveillance patterns.[16,19,20] Furthermore, the mortality of HF has improved, which has led to a higher prevalence of HF.[13]

3.2.1. Epidemiology of heart failure phenotypes

In population-based samples, nearly half of all HF cases have HF with preserved ejection fraction (HFpEF), and this proportion may be increasing due to better treatment of coronary artery disease (CAD) and the rising burden of hypertension, obesity, and other HFpEF risk factors.[21] Patients with HFpEF are older and are more often female. The Swedish HF registry reported an average age at HFpEF onset of 77 years with 55% female.[22] In patients with heart failure with reduced ejection fraction (HFrEF), 71% were male and the mean age at onset was 72 years.[22] Several subtypes of HFpEF have been suggested, with up to 50% of patients having a predominantly metabolic/obesity subtype [younger, higher body mass index (BMI)] in some regions, and up to 50% with a predominantly ageing, vascular subtype [older, stiff arteries, high prevalence of chronic kidney disease (CKD)] in other regions.[23,24]

Heart failure with reduced ejection fraction is often subdivided into ischaemic vs non-ischaemic aetiologies, with approximately half of all cases being considered ischaemic.

3.2.2. Natural history and prognosis

Although the mortality rates after HF onset have improved considerably over the past three decades, the 5-year overall survival rates are still <60%.[25,26] For younger patients, data from Denmark suggest survival has improved with contemporary management, with a current 5-year mortality rate of 15% for patients <65 years and 39% for patients aged 65–79 years.[25] In patients ≥80 years, improvements in mortality have also been observed, although these improvements are not as pronounced as those observed in younger patients, partly due to a greater burden of comorbidity and a greater proportion of non-CV mortality in the elderly.[17,25,27] Mortality may be lower in HFpEF than HFrEF, but overall differences are small as patients with HFpEF are considerably older, and the risk of hospitalization is similar.[28,29] Patients diagnosed with HF in an outpatient setting have better prognosis than patients diagnosed during a HFH, and patients with repeated HFH have a particularly high risk of mortality.[30,31]

The overall burden of HF as well as HFH can be expected to rise over the next few decades due to greater survival, an ageing population, and greater prevalence of risk factors and obesity in the younger population.

3.3. Classifications

3.3.1. Classification based on left ventricular ejection fraction

Traditionally, HF has been divided into distinct phenotypes based on the measurement of LVEF. In the *2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure*, three different HF phenotypes were identified: HFrEF (LVEF ≤40%); HF with mildly reduced ejection fraction (HFmrEF, LVEF 41%–49%); and HFpEF (LVEF ≥50%).[3] The rationale behind this classification relates to the inclusion criteria of the trials of therapies that improved outcomes in patients with HF and LVEF ≤40%. The HFmrEF phenotype was introduced to focus on patients usually not included in HFrEF trials. The nomenclature was changed from 'mid-range' to 'mildly reduced' to highlight that patients with HFmrEF are similar to patients with HFrEF in terms of both clinical characteristics, outcomes, and response to treatments.[32,33] Patients with HFmrEF have similar underlying aetiology of HF to patients with HFrEF, and the pathophysiology of HFmrEF is more similar to HFrEF (reduced contractility and systolic dysfunction) than HFpEF (increased stiffness and diastolic dysfunction).[34] In addition, the efficacy of medical treatment of HFmrEF is more similar to HFrEF than HFpEF.[35–45] Finally, it is important to consider LVEF trajectories, as many patients with LVEF 41%–49% may experience a deterioration in LVEF.[46] The Task Force for the *2026 ESC Guidelines for the management of heart failure* has eliminated the phenotype of HFmrEF and reclassified HF based on a pathophysiological classification of HF, including two distinct phenotypes:

(i) HFrEF: characterized by LVEF <50% and symptoms and/or signs of HF.
(ii) HFpEF: characterized by LVEF ≥50% and symptoms and/or signs of HF and objective evidence of cardiac structural and/or functional abnormalities consistent with the presence of left ventricular (LV) diastolic dysfunction/raised LV filling pressures, supported by raised natriuretic peptides.

Using a single LVEF value as cut-point for distinguishing HFpEF and HFrEF is somewhat arbitrary and has to be evaluated in the clinical situation, as there is variability in measurement depending both on the modality and the interpreter. Furthermore, LVEF may be falsely high in certain situations, e.g. mitral regurgitation (MR). Natriuretic peptides may be used as supportive evidence for the diagnosis of HF. Importantly, drug and device therapies can lead to positive LV reverse remodelling in patients with HFrEF and, thus, improvement of LVEF. Patients with HFrEF and improved LVEF have a more favourable prognosis. However, it is important to ensure that these patients are still managed with optimal medical therapy except for selected patients. The current definition of improved LVEF requires an increase of at least 10% in LVEF (absolute) and must be at least above 40% (often normal).[47]

3.3.2. Classification based on heart failure stages

An additional classification based on HF stages has been proposed previously.[4] The Task Force has included this classification as we focus more on prevention of HF and early diagnosis (*Figure 2*).

3.3.3. Other classifications of heart failure

Heart failure can also be classified according to clinical presentation: *de novo* (patients without a previous diagnosis of HF) vs pre-existing (patients with a diagnosis of HF), and chronic HF vs decompensated HF (DHF). Chronic HF may deteriorate to DHF. Details on the definitions and subtypes of DHF are provided in *Section 7*.

Finally, an additional classification in isolated left-sided HF vs isolated right-sided HF vs combined left- and right-sided HF can be used. The main aetiology of chronic right-sided HF is LV dysfunction-induced pulmonary hypertension [World Health Organization (WHO) group 2] leading to combined left- and right-sided HF. However, there are a number of causes of isolated right-sided HF, e.g. right ventricular (RV) myocardial infarction (MI); arrhythmogenic RV cardiomyopathy (ARVC); pulmonary hypertension WHO groups 1, 3, 4, and 5; and tricuspid or pulmonary valve regurgitation. Diagnosis and management of chronic right-sided HF is covered comprehensively in a recent Heart Failure Association (HFA) position paper.[48]

3.3.4. Classifications of treatments in heart failure

The term guideline-directed medical therapy (GDMT) was introduced in the *2013 ACCF/AHA Guideline for the management of heart failure* and is the cornerstone of pharmacological treatment for patients with HF.[49] The term was meant to represent optimal medical therapy primarily with a Class I recommendation, which at that time included treatment with angiotensin-

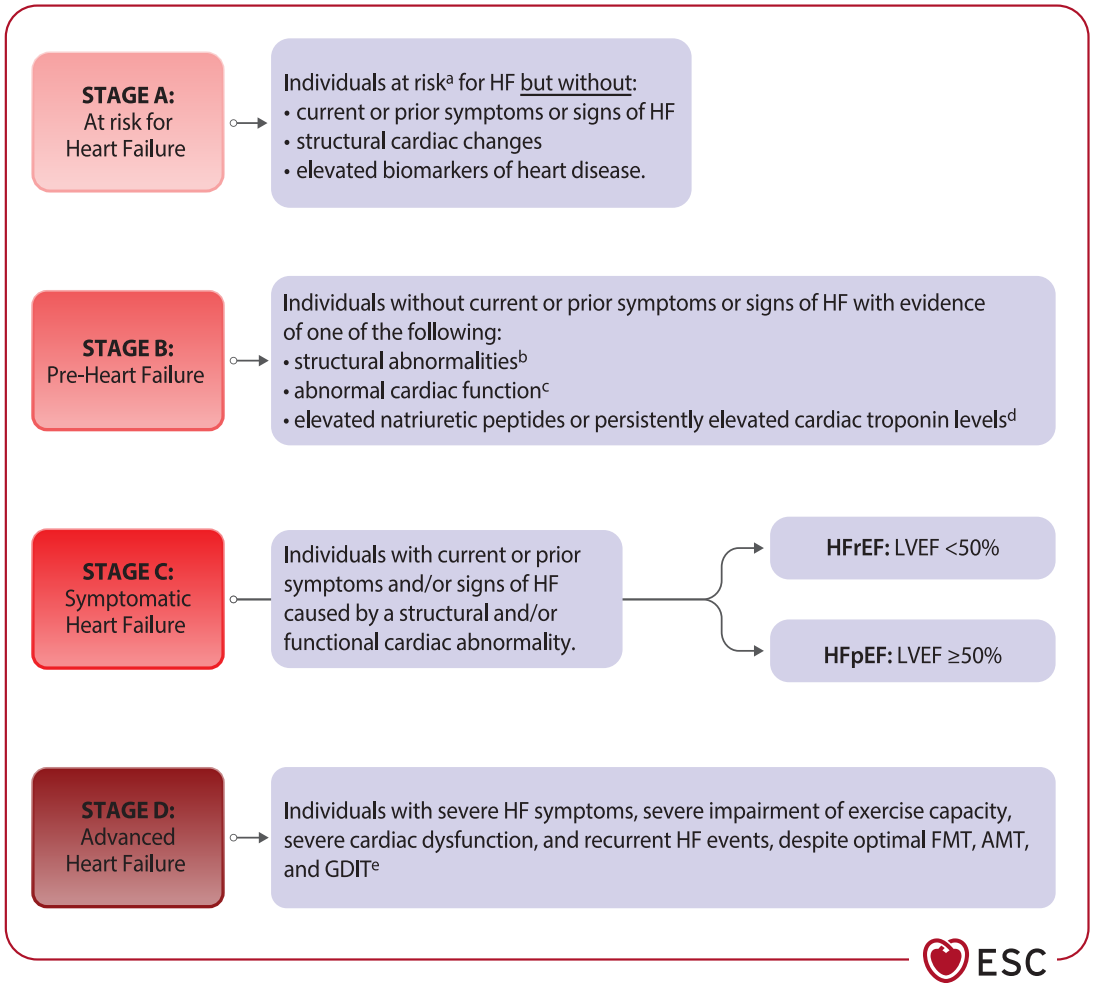

Figure 2 Heart failure stages and classifications. AMT, additional medical therapy; FMT, foundational medical therapy; GDIT, guideline-directed interventional therapy; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; LVEF, left ventricular ejection fraction. [a]See section 4.1. Not all will develop HF, but risk factor intervention may be warranted. [b]For example, left ventricular hypertrophy, cardiac chamber enlargement, ventricular wall motion abnormality, myocardial tissue abnormality (e.g. evidence of myocardial oedema, scar/fibrosis abnormality by T2-weighted cardiac magnetic resonance imaging or late gadolinium enhancement imaging), valvular heart disease. [c]For example, reduced left or right ventricular systolic function, evidence of increased filling pressures (by invasive or non-invasive measures), abnormal diastolic function. [d]Especially in the setting of exposure to cardiotoxins. [e]For details see *Table 14*.

converting enzyme inhibitors (ACE-Is)/angiotensin II receptor blockers (ARBs), beta-blockers, and mineralocorticoid receptor antagonists (MRAs) for HFrEF. Since 2013, there have been further advances in the management of patients with HF. Class I recommendations have now been presented for the use of angiotensin receptor–neprilysin inhibitors (ARNIs) and sodium–glucose co-transporter 2 inhibitors (SGLT2-Is) in HFrEF. Furthermore, there are now data to support Class I recommendations for the use of SGLT2-Is and MRAs in HFpEF. Although these foundational therapies are crucial to improving the prognosis in HF, many other pharmacotherapies have guideline recommendations, e.g. ivabradine, vericiguat, cardiac glycosides, and, more recently, glucagon-like peptide-1 receptor agonists (GLP-1 RAs). All of these therapies could be viewed as GDMT but are currently not included in the definition of GDMT. Furthermore, the use of the term GDMT ignores the crucial role of devices that work in synergy with medical therapy and new procedural therapies with effect on patient-reported outcomes, morbidity and mortality. The current Task Force has decided to introduce new classifications to describe medical, device, and procedural therapies in HF (*Figure 3*). These classifications are designed to be dynamic, so the terms can remain contemporary over time as new therapies may be easily incorporated into the terms.

Foundational medical therapy (FMT) constitutes the foundation of any HF management. Foundational medical therapy is defined as medical therapy with a guideline Class I recommendation for the treatment of the general HF population, with convincing evidence of an improvement in morbidity and/or mortality. In this guideline, FMT will include beta-blocker, ACE-I/ARNI/ARB, MRA, and SGLT2-I for HFrEF, and MRA and SGLT2-I for HFpEF. The term 'optimal FMT' may be used for FMT at the highest tolerated doses according to the guideline-recommended target doses (see *Section 6.1*). Medical therapies with a Class I recommendation only for specific subsets of patients with HF are *not* included in the definition of FMT.

Additional medical therapy (AMT) is defined as all other medical therapies that receive a Class IIa/IIb recommendation OR a Class I recommendation with proven effect only on symptoms and/or quality of life (QoL) OR a Class I recommendation in specific subsets of patients/HF phenotypes.

Guideline-directed medical therapy therefore covers both FMT and AMT.

Guideline-directed interventional therapy (GDIT) includes all cardiac implantable electronic devices (CIED) and interventional therapies that have a recommendation in the guidelines.

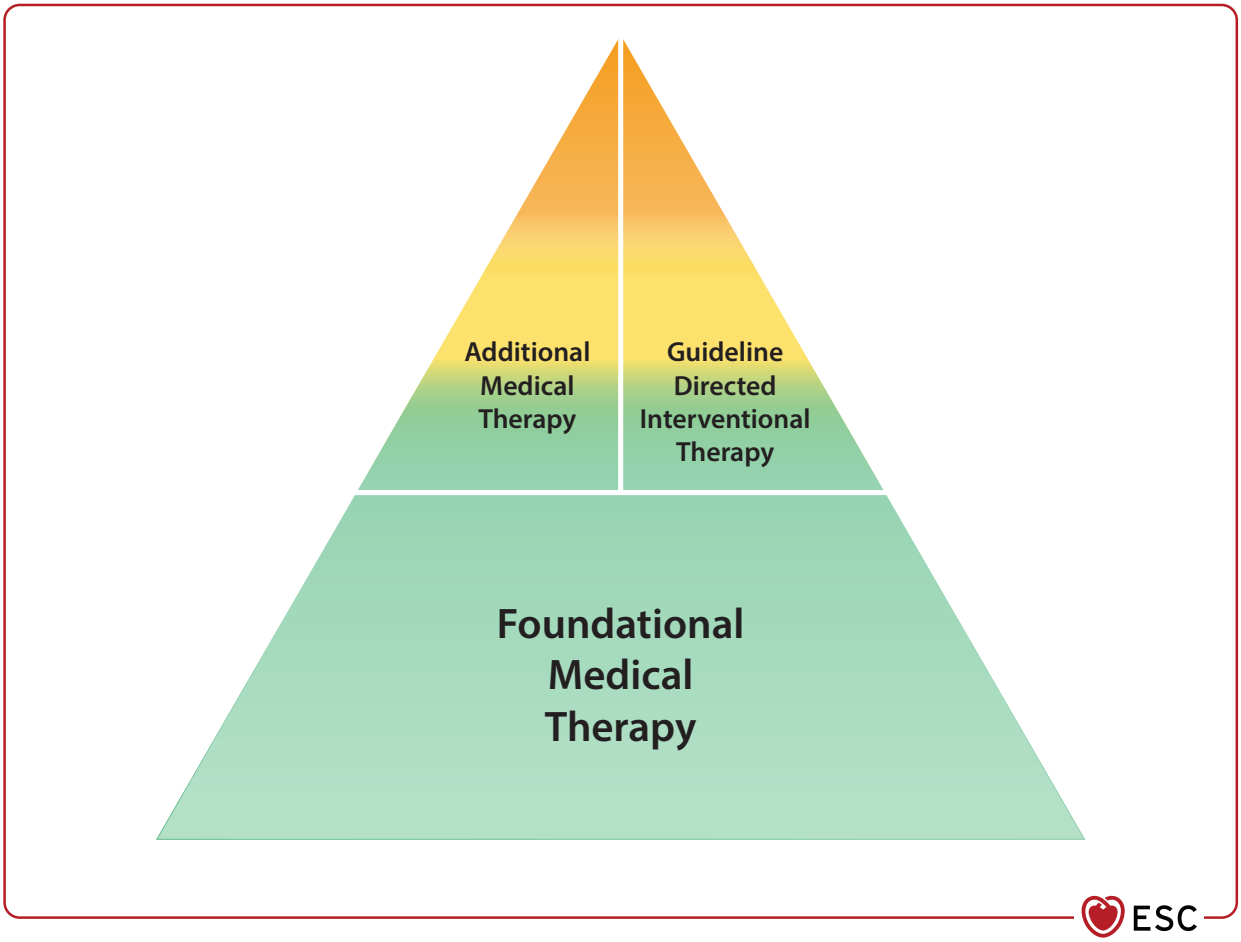

Figure 3 New nomenclature for heart failure therapies. Guideline-directed medical therapy (GDMT) includes foundational medical therapy (FMT) and additional medical therapy (AMT). Guideline directed interventional therapy is abbreviated as GDIT.

4. Prevention of heart failure

4.1. Patients at risk of heart failure (stage A heart failure)

4.1.1. Cardiometabolic risk factors

Diabetes, hypertension, obesity, and smoking account for approximately 50% of all HF events on a population-based level, ranging from 30%–40% among the oldest individuals (over 75 years) to 75%–80% among individuals aged <55 years, and are similar for HFpEF and HFrEF.[50–52] These risk factors often cluster within the same individuals and tend to be stable over the life course unless intervened upon.[53–56] Unhealthy lifestyle changes have led to a rising incidence and prevalence of obesity, hypertension, and type 2 diabetes over the past decades in many regions across Europe, particularly among young to middle-aged adults.[57–59] Concomitantly, increases have been observed in the incidence rates of HF among young adults, underscoring the need for earlier and better prevention strategies on a population-based level.[16,19,20] As the risk of HF is related to both risk-factor burden (intensity) and risk-factor duration (exposure time), early risk-factor management should be considered for younger people with longer anticipated exposure time. Personalized HF risk estimations (see *Section 4.1.2*) may aid clinicians and patients in discussions, management, and treatment decisions.

Specific recommendations on the management of obesity, hypertension, and diabetes are outlined in the ESC guidelines on prevention of CV disease (CVD), hypertension, and diabetes, respectively.[60–62] For hypertension, most evidence supports targeting a blood pressure <130 mmHg to reduce HF risk, although there are likely additional benefits of achieving lower treatment targets if tolerated.[63–69] For diabetes, glucose-lowering drugs without proven HF safety should be avoided,[70] and among those at particular risk of HF [especially in the presence of atherosclerotic CVD (ASCVD)], SGLT2-Is and GLP-1 RAs have been shown to lower risk of HFH and CV death.[71–73] For obesity, declines in fat mass and waist circumference, but not lean mass, lowers HF risk and should be targeted.[74] High cholesterol levels increase the risk of HF mainly through CAD, and the use of statins has shown to modestly lower HF events in people at high risk of ASCVD and HF.[75,76]

4.1.2. Risk scores for individuals without heart failure

To assist in more individualized HF risk estimation, the use of risk scores may be considered. In addition to risk scores to predict HFH and mortality among ambulatory patients with established HF[77–80] several risk scores for primary HF prevention have been developed[81–83]. The American Heart Association (AHA) PREVENT-HF risk score[81] and the ESC SCORE2-HF[82] were both derived to estimate risk in people without pre-existing HF over a 10-and 30-year horizon. The ESC risk scores have been calibrated for low-, moderate-, high-, and very high-risk countries to fit the European population. The ESC SMART2-HF risk score[83] was derived to estimate 10-year risk of HF in people with pre-existing ASCVD. These risk scores are described in Supplementary data online, *Section S1* and *Figure S1*.

4.1.3. Lifestyle-related factors

4.1.3.1. Diet and physical activity

Epidemiological studies have shown that diets high in sugars, saturated fats, refined grains, and processed food are associated with increased HF risk (especially HFpEF).[84–90] In contrast, adherence to a diet rich in vegetables, nuts, whole grains, fish, and unsaturated fats have been associated with lowered HF risk.[84,87] However, a secondary analysis of the PREDIMED trial comparing a Mediterranean diet (with olive oil vs nuts) to a low-fat diet in individuals at high risk of CVD did not show a significant difference in HF incidence between the groups over a median follow-up of 4.8 years.[89] Similarly, sedentary behaviour and physical inactivity are strong risk factors for especially HFpEF development[60,91], but no randomized controlled trials (RCTs) have investigated the role of physical activity for the prevention of HF.[91–93] Recommendations on exercise type and intensity to promote general CV health are outlined in the *2020 ESC Guidelines on sports cardiology and exercise in patients with cardiovascular disease*.[94]

4.1.3.2. Smoking, alcohol, and substance abuse

Smoking cessation has been shown to reduce HF risk over time in epidemiological studies and should be encouraged in all individuals.[95–97] Similarly, heavy alcohol use is associated with increased risk of HF and is discouraged, whereas light-to-moderate intake has shown more mixed data with regard to HF risk.[98] Any form of substance abuse, recreational or continuous, with drugs such as cocaine, amphetamine, and anabolic steroids is associated with increased risk of cardiomyopathy and HF.[99–101] If use is suspected, this should be addressed with the patient and advised against.

Recommendation Table 1 — Recommendations for prevention of heart failure (see *Evidence Tables 1–15*)

Recommendations	Class[a]	Level[b]
Strict blood pressure control (systolic blood pressure target <130 mmHg) is recommended in patients with hypertension or stage B HF to reduce the risk of HF.[63–69,102]	I	A
An SGLT2-I is recommended in patients with T2DM at risk of HF (multiple ASCVD risk factors or established ASCVD) to reduce the risk of HF and CV death.[103]	I	A
An SGLT2-I is recommended in patients with T2DM and CKD[c] to reduce the risk of HF or CV death.[104]	I	A
Finerenone is recommended in patients with T2DM and CKD[d] to reduce the risk of HF.[105–108]	I	A

Continued

Counselling on healthy lifestyle choices including maintaining a healthy weight, consuming a well-balanced diet, avoiding sedentary behaviour, abstaining from smoking and heavy alcohol consumption as well as counselling against the use of drugs such as cocaine, amphetamines, and anabolic steroids is recommended for all patients with stage A or B HF to reduce the risk of HF progression.[74,84,85,87,91,95–100,109–112]	I	C
Treatment with a statin should be considered in people at high risk of, or with established ASCVD, to reduce the risk of HF.[75]	IIa	A
A GLP-1 RA should be considered in patients with T2DM and at least one other additional CV risk factor to reduce the risk of HF or CV death.[71,113,114]	IIa	A

ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; CV, cardiovascular; eGFR, estimated glomerular filtration rate; GLP-1 RA, glucagon-like peptide-1 receptor agonist; HF, heart failure; SGLT2-I, sodium–glucose co-transporter 2 inhibitor; T2DM, type 2 diabetes mellitus.
[a]Class of recommendation.
[b]Level of evidence.
[c]CKD was defined as follows: an eGFR 25–75 mL/min/1.73 m^2 and a urinary albumin-to-creatinine ratio ≥200–5000 mg/g in DAPA-CKD; an eGFR 20–45 mL/min/1.73 m^2 or an eGFR 45–90 mL/min/1.73 m^2 with a urinary albumin-to-creatinine ratio ≥200 mg/g in EMPA-KIDNEY; and eGFR 30–<90 mL/min/1.73 m^2 with a urinary albumin-to-creatinine ratio >300 to ≤5000 mg/g in CREDENCE.[115–117]
[d]CKD was defined as follows: an eGFR 25–60 mL/min/1.73 m^2, a urinary albumin-to-creatinine ratio 30–300 mg/g, and diabetic retinopathy, or an eGFR 25–75 mL/min/1.73 m^2 and a urinary albumin-to-creatinine ratio 300–5000 mg/g, in FIDELIO-DKD[106]; and an eGFR 25–90 mL/min/1.73 m^2 and a urinary albumin-to-creatinine ratio 30 to <300 mg/g, or an eGFR >60 mL/min/1.73 m^2 and a urinary albumin-to-creatinine ratio 300–5000 mg/g, in FIGARO-DKD[107].

4.1.4. Specific populations at risk

4.1.4.1. Arrhythmias

Atrial fibrillation (AF) and other supraventricular tachyarrhythmias, as well as frequent ventricular ectopy and conduction disease, can all lead to HF. Prevention of HF in these conditions mainly relates to treatment of the underlying condition, which is covered in the *2024 ESC Guidelines for the management of atrial fibrillation*[118] and the *2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death*.[119]

Investigation of LV systolic dysfunction and for underlying causes driving the arrhythmia should be considered based on clinical presentation (e.g. genetic, infiltrative, or inflammatory cardiomyopathy). In some patients, AF may be a marker of especially subclinical HFpEF, and evaluation and treatment of common cardiometabolic and lifestyle-related risk factors is warranted in such patients.

4.1.4.2. Myocardial infarction

Patients with MI are at high risk of HF even in absence of wall motion abnormalities or structural dysfunction. Treatment of cardiometabolic risk factors should be optimized. In post-MI patients with preserved LVEF (>50%), no difference in the risk of HF was shown for beta-blocker therapy vs placebo in the REDUCE-AMI trial, arguing against routine use of beta-blockers in this setting.[120] A meta-analysis of BETAMI–DANBLOCK and the REBOOT-CNIC trials showed no difference in major CV outcomes.[121]

4.1.4.3. Chronic kidney disease

Chronic kidney disease is a strong risk marker for future HF risk, and efforts should be undertaken to optimize the control of concomitant risk factors (diabetes, hypertension, ASCVD) to prevent or delay HF onset.[76] There is strong evidence that both SGLT2-Is and finerenone lower HF risk in patients with type 2 diabetes mellitus (T2DM) and CKD.[104–108] Recommendations on specific preventive treatments for patients with CKD and CVD are outlined in the *2026 ESC Guidelines on cardiovascular disease and chronic kidney disease*.[122]

4.1.4.4. Cancer survivors

Cancer survivors, especially those with prior radiation or exposure to cardiotoxic agents (anthracycline, cyclophosphamide, immune checkpoint inhibitors, trastuzumab) are at higher risk of asymptomatic LV systolic dysfunction and HF. The prevention of HF in these patients, as well as surveillance and risk modification strategies among those undergoing active cancer treatment, are outlined in the *2022 ESC Guidelines on cardio-oncology*.[6]

4.1.4.5. Familial and genetic predisposition but no overt clinical disease

Because modifiable risk factors are likely to be significant contributors to disease onset in many genetically predisposed individuals, optimal risk-factor control is recommended in individuals with familial or genetic predisposition to HF, but without clinical disease.[123] In carriers of dilated cardiomyopathy (DCM), non-dilated LV cardiomyopathy, or ARVC-related variants, regular follow-up and cardiac screening is suggested, according to the specific recommendations provided in the *2023 ESC Guidelines for the management of cardiomyopathies*.[124]

4.1.4.6. Pulmonary disorders and sleep-disordered breathing

Poor sleep quality, sleep-disordered breathing (SDB), sleep apnoea, and chronic obstructive pulmonary disease (COPD) are all associated with a higher incidence of HF.[125–127] Recommendations for screening and treatment of these conditions are outlined in the *2021 ESC Guidelines on cardiovascular disease prevention in clinical practice*.[61]

4.1.4.7. Endocrine disorders

Thyroid disorders, acromegaly, and pheochromocytoma are all associated with increased risk of HF.[61,128] Prevention of HF is primarily related to correction of the underlying hormonal dysfunction and should otherwise follow the general principles outlined in this section.

4.1.4.8. Congenital heart disease

Advances in surgical repair and life expectancy for patients with congenital heart disease have led to an increasing burden of HF in this population.[129,130] Patients with congenital heart disease have an eight-fold overall increased relative risk of developing HF and are on average 20–25 years younger at the time of HF onset, compared with age- and sex-matched controls.[131] The risk is greatest in complex lesions such as conotruncal defects

(e.g. tetralogy of Fallot, transposition of the great arteries, truncus arteriosus, double-outlet right or left ventricle, with up to 42-fold risk), and severe non-conotruncal defects (e.g. atrioventricular septal defects, single ventricle and hypoplastic left heart syndrome, with up to 21-fold increased risk).[131] Conventional HF risk factors (e.g. CAD, hypertension, diabetes, and obesity) are common in patients with congenital heart disease and contribute significantly to HF risk.[132–134] Careful attention to risk-factor modification is warranted as they are likely to contribute to the risk of developing HF.

4.2. Patients with stage B heart failure

4.2.1. Asymptomatic left ventricular dysfunction

Based on normal reference values of LVEF in adult population-based samples, LV systolic dysfunction should be considered present if patients are asymptomatic and have an LVEF <50% in the absence of alternative explanations (e.g. athlete's heart) for both men and women and regardless of age. Treatment with an ACE-I (or ARB if intolerant) if LVEF ≤40% and a beta-blocker if LVEF <50% are recommended to reduce the risk of HF and mortality. The evidence behind these recommendations are derived from the SOLVD-Prevention trial,[135,136] which randomized patients with asymptomatic LV systolic dysfunction (LVEF ≤35%) to enalapril or placebo, and the TRACE[137] and SAVE[138] trials, which randomized patients post-MI with LVEF ≤35%–40% to trandolapril or placebo (TRACE) and captopril vs placebo (SAVE). These studies were conducted in the 1990s and contemporary management of multiple comorbidities (MI, diabetes, CKD) has since changed. One RCT, CAPRICORN, published in 2001, investigated beta-blockers post-MI in patients with LV systolic dysfunction, where patients were randomized to carvedilol or placebo.[139] It should be noted that this trial allowed patients to receive intravenous (i.v.) diuretics for acute HF, but excluded those with continuous need for i.v. diuretics, meaning not all had truly asymptomatic LV systolic dysfunction. The hazard ratio (HR) for all-cause mortality was 0.77 [95% confidence interval (CI) 0.60–0.98] in the group receiving carvedilol vs placebo. Additional observational data from SOLVD and SAVE suggested similar improved outcomes with a beta-blocker.[140–142] Further, the REVERT trial, which randomized asymptomatic patients with LVEF <40% to metoprolol extended release or placebo, showed that metoprolol reversed LV remodelling.[142] The role of these drugs for asymptomatic individuals with mildly reduced LVEF (41%–49%) is not well studied, but their use is reasonable also in this range of LVEF given the shared pathophysiology with more depressed LV systolic function. A meta-analysis of BETAMI–DANBLOCK and REBOOT-CNIC showed a significant reduction in the combined endpoint of mortality, MI and HF with beta-blockers vs placebo in post-MI patients with stage B HF and mildly reduced LVEF.[121] Careful follow-up to assess for progressive decline in LVEF is otherwise warranted for patients without treatment. Based on the results of the EPHESUS trial, eplerenone is recommended in patients after MI with LVEF ≤40% and diabetes to reduce the risk of HFH or death.[143]

4.2.2. Valvular heart disease

Prevention of HF in patients with valvular disease should follow the recommendations outlined in the *2025 ESC/EACTS Guidelines for the management of valvular heart disease*.[9]

Recommendation Table 2 — Recommendations for stage B heart failure and left ventricular dysfunction (see *Evidence Table 16*)

Recommendations	Class[a]	Level[b]
An ACE-I or ARB (if intolerant to ACE-I) is recommended in patients with stage B HF and LVEF ≤40% to reduce the risk of HFH and death.[135–138,144]	I	A
A beta-blocker is recommended in patients with stage B HF and LVEF <50% to reduce the risk of HFH or death.[35,139,140]	I	B1
Eplerenone is recommended in patients with LVEF ≤40% after myocardial infarction with signs of HF or diabetes to reduce the risk of HFH and death.[143]	I	B1

ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; HF, heart failure; HFH, heart failure hospitalization; LVEF, left ventricular ejection fraction.
[a]Class of recommendation.
[b]Level of evidence.

4.3. Risk prediction in patients with established heart failure

Several risk scores have been developed to predict HFH and mortality among ambulatory patients with established HF, including e.g. the MAGGIC risk score,[77] the Seattle Heart Failure Model,[78] and the more recent ESC initiated LIFE-HF[79] (HFrEF) and LIFE-Preserved (HFpEF).[80] It should be noted that LIFE-HF included patients with LVEF ≤40% and LIFE-Preserved patients with LVEF ≥50%. The ESC scores therefore need to be validated for HFrEF patients in the upper range of LVEF (>40%–49%) and, ideally, in external samples across the entire LVEF spectrum before widespread implementation (see Supplementary data online, *Section S1* and *Figure S1*). Although pharmacological treatments are indicated in patients with established HF regardless of estimated risks (as outlined in *Section 6*), these risk scores may be helpful in identifying high-risk patients that may benefit from closer follow-up and to facilitate discussions around patient goals of care.

5. Diagnosis of chronic heart failure

5.1. Key steps in the diagnosis of chronic heart failure

The failing heart causes a clinical syndrome with a wide array of signs and symptoms, which vary in sensitivity and specificity (*Table 7*), and none of which are entirely characteristic. The severity of HF symptoms can be classified according to the New York Heart Association (NYHA) functional class (*Table 8*).

Specialist assessment relies on clinical evaluation, the examination of individual risk factors, and previous medical history as well as 12-lead ECG and chest X-ray evaluation. Clinical suspicion should be followed by testing of natriuretic peptides and echocardiography (*Figure 4*). In the very elderly patients, suspicion should be raised even with an atypical presentation. A recent HFA consensus paper provides a diagnostic framework for general practice and non–cardiology-based physicians.[145]

Table 7 Symptoms and signs of heart failure

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

HF, heart failure.
[a]Elderly patients may present with more atypical symptoms of HF.
[b]Breathlessness on bending forward/flexing the body.

Table 8 New York Heart Association functional classification based on severity of symptoms and physical activity

NYHA class	Severity of symptoms and physical activity
Class I	No limitation of physical activity. Ordinary physical activity does not cause undue breathlessness, fatigue, or palpitations.
Class II	Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in undue breathlessness, fatigue, or palpitations.
Class III	Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity results in undue breathlessness, fatigue, or palpitations.
Class IV	Unable to carry on any physical activity without discomfort. Symptoms at rest can be present. If any physical activity is undertaken, discomfort is increased.

NYHA, New York Heart Association.

5.1.1. Natriuretic peptides

Adverse clinical events often occur soon after a new presentation of HF in the community; therefore, timely diagnosis and initiation of treatment are essential. Natriuretic peptide testing is recommended to support the diagnosis of HF and improves efficiency by avoiding unnecessary echocardiography and/or specialist assessment.[146–150] N-terminal pro-B-type natriuretic peptide (NT-proBNP) is the most widely used natriuretic peptide in the management of HF in Europe and has two key advantages: better stability at room temperature, enabling reliable testing in both hospital and community settings; and unaltered results despite treatment with ARNIs, which affect B-type natriuretic peptide (BNP) degradation.[149,150]

However, testing for NT-proBNP is not universally available, and some regions employ BNP or mid-regional pro-atrial natriuretic peptide (MR-proANP) testing.

The *2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure* recommended a single natriuretic peptide threshold to 'rule out' HF (<125 pg/mL for NT-proBNP, <35 pg/mL; for BNP, <40 pg/mL; for MR-proANP). Single natriuretic peptide rule-out thresholds have the advantage of simplicity; however, natriuretic peptide levels are strongly related to age and lack specificity in older people.[151] More than 75% of a healthy population >80 years were found to exceed the 125 pg/mL NT-proBNP threshold.[152–156] The HFA-ESC consensus statement on NT-proBNP testing recommends introducing age-related thresholds determined from the 95th percentile of the Generation Scotland cohort to improve specificity and reduce unnecessary demand on echocardiography and HF services.[157] The suggested age-adjusted NT-proBNP levels, above which HF is 'likely' in the outpatient setting, were ≥125 pg/mL for those aged <50 years, ≥250 pg/mL between 50 and 75 years, and ≥500 pg/mL over 75 years.[151,157] Currently there are insufficient data for determining age-specific BNP cut-offs. For the diagnosis of HFpEF, natriuretic peptide interpretation may be challenging as a variety of conditions associated with HFpEF affect natriuretic peptide levels (*Table 9*).[158] Especially obesity is associated with lower cut-off values for natriuretic peptides, and caution is advised when interpreting natriuretic peptide levels in obese patients.[158–160] Reduced kidney function has been shown to be associated with higher NT-proBNP levels, although NT-proBNP measurements should not be disregarded in the setting of kidney dysfunction.[161,162] Furthermore, many other factors can elevate natriuretic peptide levels (*Table 9*). Clinicians must consider these factors in conjunction with clinical assessment and investigation findings when interpreting natriuretic peptide measurements; however, the higher the natriuretic peptide level the greater the likelihood of HF as the diagnosis.

Natriuretic peptides also provide important prognostic information, enabling rapid triage of high-risk patients. Primary care data from England demonstrate that patients with HF and NT-proBNP levels exceeding 2000 pg/mL exhibit a two-fold increased risk of early HFH. Accordingly, expedited specialist assessment of this high-risk cohort is warranted.[163]

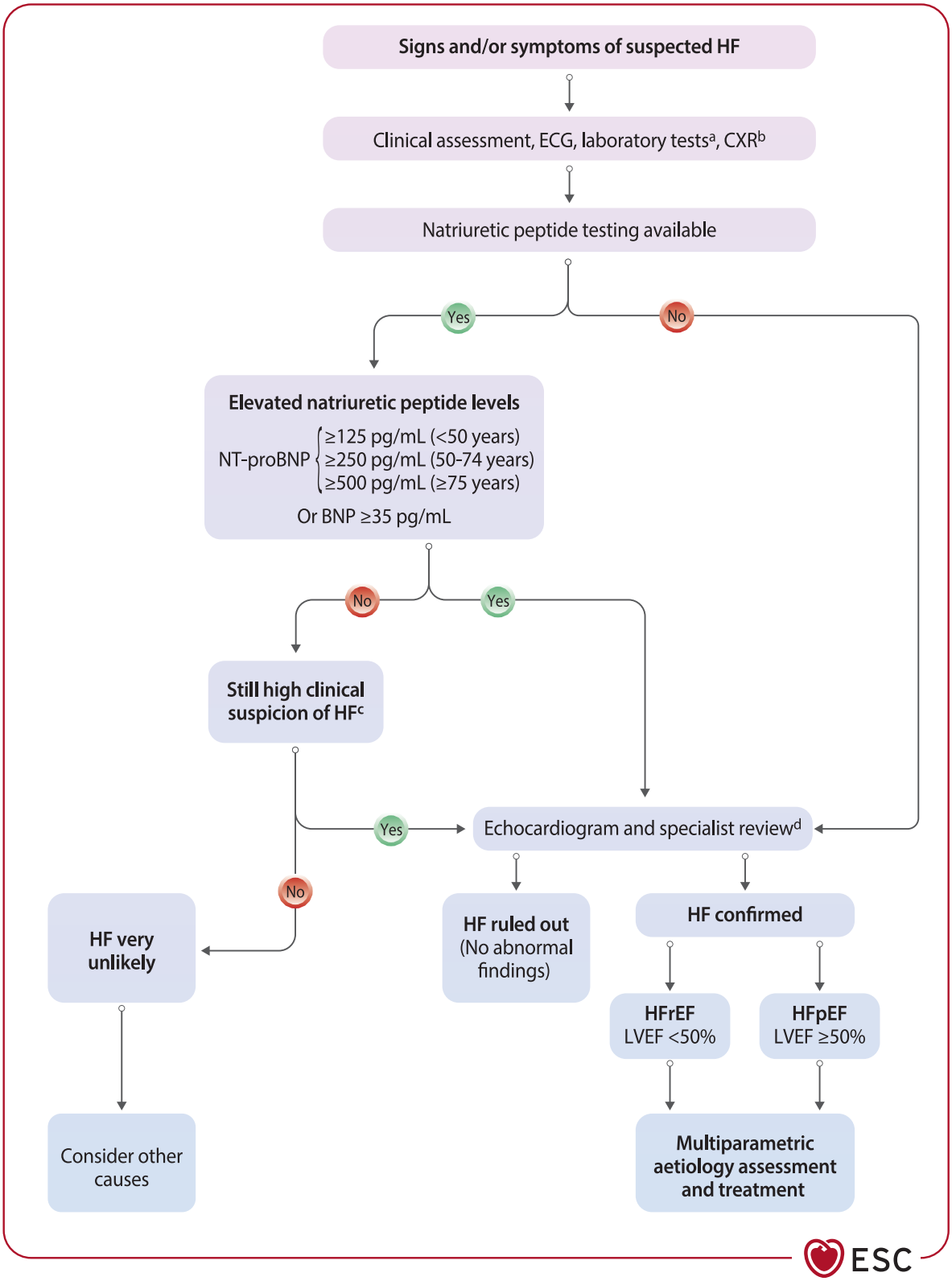

Figure 4 Diagnostic algorithm for chronic heart failure presenting in the outpatient or community setting. BNP, B-type natriuretic peptide; CXR, chest X-ray; ECG, electrocardiogram; HbA1c, glycated haemoglobin; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro-B-type natriuretic peptide; POCUS, point-of-care ultrasound; TSAT, transferrin saturation; UACR, urine albumin-to-creatinine ratio. [a]Full blood count, kidney function, electrolytes, UACR, liver function, thyroid function, HbA1c, lipids, and iron status (TSAT and ferritin). [b]Examination by POCUS may aid in diagnosis although echocardiography is recommended. [c]Natriuretic peptides may be false low in certain settings (*Table 9*). [d]Preferable performed within 2 weeks if NT-proBNP >2000 pg/mL.

Table 9 Causes for increase or decrease in natriuretic peptide levels

Causes for increased natriuretic peptide levels
Acute coronary syndrome
Advanced age[a]
Atrial fibrillation
Cardiac contusion
COPD
Critical illness
Female sex
Kidney dysfunction
LV hypertrophy
Myocarditis
Obstructive sleep apnoea
Paraneoplastic syndrome
Pulmonary embolism
Pulmonary hypertension
RV pacing
Severe anaemia
Severe endocrine dysfunction
Severe infections (including pneumonia and sepsis)
Severe liver disease
Severe metabolic acidosis and diabetic ketoacidosis
Subarachnoid haemorrhage
Systemic hypertension
Valvular heart disease
Causes for decreased natriuretic peptide levels
African ancestry
ARNI[b]/ACE-I/ARB
Beta-blockers
Constrictive pericarditis
MRA
Obesity
SGLT2-I

ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; ARNI, angiotensin receptor–neprilysin inhibitor; BNP, B-type natriuretic peptide; COPD, chronic obstructive pulmonary disease; LV, left ventricular; MRA, mineralocorticoid receptor antagonist; RV, right ventricular; SGLT2-I, sodium–glucose co-transporter 2 inhibitor.
[a]See *Figure 4*.
[b]ARNI may raise BNP levels.

5.1.2. Other laboratory tests

Basic investigations, such as serum urea and electrolytes, creatinine, full blood count, glycated haemoglobin, lipids, iron status [transferrin saturation (TSAT) and ferritin], liver and thyroid function tests, are recommended to assess for and evaluate comorbidities, to provide prognostic information, and to guide potential therapy.

Urine albumin-to-creatinine ratio (UACR) has been added to the initial baseline investigations, because the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines advise that both estimated glomerular filtration rate (eGFR) and UACR (graded A1, <30 mg/g; A2, 30–300 mg/g; A3, >300 mg/g) are required in the assessment of kidney function.[164] UACR is independent of glomerular filtration rate (GFR), and severe albuminuria (grade A3) may be present despite GFR ≥90 mL/min/1.73 m^2. UACR has strong independent prognostic value for patients with HF.[165,166] Albuminuria is a potentially treatable and reversible disorder, amenable to medications also used in HF, including ACE-Is/ARNIs/ARBs, MRAs, and SGLT2-Is.[167]

Recommendation Table 3 — Recommendations for diagnostic investigations in all patients with suspected heart failure (see *Evidence Tables 17–19*)

Recommendations	Class[a]	Level[b]
In patients with suspected HF, the following laboratory tests are recommended when screening for comorbidities: full blood count, kidney function (eGFR and UACR), electrolytes, liver function, thyroid function, HbA1c, lipids, and iron status (TSAT and ferritin).[168]	I	C
Natriuretic peptide measurement is recommended in patients with suspected HF (interpreted in relation to patient age, obesity, and other factors known to affect natriuretic peptide level[c]).[146–148,151–153,169]	I	C
A 12-lead ECG is recommended in patients with suspected HF.	I	C
Chest radiography (X-ray) is recommended in patients with suspected HF.	I	C
Transthoracic echocardiogram is recommended in patients with suspected HF to confirm the diagnosis, differentiate between HF phenotypes and aid in identifying the underlying aetiology of HF.	I	C

ECG, electrocardiogram; eGFR, estimated glomerular filtration rate; HbA1c, glycated haemoglobin; HF, heart failure; NT-proBNP, N-terminal pro-B-type natriuretic peptide; TSAT, transferrin saturation; UACR, urine albumin-to-creatinine ratio.
[a]Class of recommendation.
[b]Level of evidence.
[c]See *Figure 4* for age-adjusted cut-offs for NT-proBNP levels, and *Table 9* for factors affecting natriuretic peptide levels.

5.2. Heart failure phenotypes based on left ventricular ejection fraction

Echocardiography provides evaluations of both systolic and diastolic function and valvular function and enables the distinction between HF (stage C) phenotypes based on LVEF.

5.2.1. Heart failure with reduced ejection fraction

The diagnosis of HFrEF requires the following criteria:

(i) Presence of current or prior symptoms and/or signs of HF (*Table 7*)
(ii) LVEF <50%.

Elevated natriuretic peptides strongly support the diagnosis of HFrEF in the presence of symptoms, and may aid in the

diagnostic pathway, especially if echocardiography is not readily available. However, many factors may cause false positive or false negative results, which should be considered when evaluating natriuretic peptide (*Table 9*). LVEF is a continuous measure and may differ between methods used as well as sex. For this reason, a precise value is only given as guidance.

Aetiology assessment is important, as it may result in finding potential treatable and/or reversible causes. The major aetiologies of HFrEF are illustrated in *Figure 5*.

5.2.2. Heart failure with preserved ejection fraction

The diagnosis of HFpEF is more challenging and should start with the assessment of pre-test probability.[170] Several clinical factors may contribute to or be associated with HFpEF, as illustrated in *Figure 6*. The more factors present the higher the likelihood of HFpEF.

The following criteria must all be present for the diagnosis of HFpEF:

(i) Presence of current or prior symptoms and/or signs of HF (*Table 7*)
(ii) LVEF ≥50% (requires that LVEF has not previously been <50%)
(iii) Objective evidence of cardiac structural and/or functional abnormalities consistent with the presence of LV diastolic dysfunction/raised LV filling pressures (*Table 10*), supported by raised natriuretic peptides (*Figure 4*).

Testing for elevated levels of natriuretic peptides may in most patients support the diagnosis of HFpEF. However, diagnostic thresholds for HFpEF should be critically evaluated based on patient characteristics, especially in the presence of obesity and other factors that may cause reduced natriuretic peptide levels (*Table 9*).[158]

A pragmatic approach to the diagnosis of HFpEF is advised to facilitate access to diagnosis for the large population of elderly patients potentially affected. More complicated scoring systems[171,172] have shown conflicting results in the community setting, but a meta-analysis indicates acceptable specificity and sensitivity for detection of HFpEF.[173–175] If employed, diagnostic scoring systems should be interpreted with caution and used primarily to raise clinical suspicion of HFpEF rather than to establish a definitive diagnosis. In cases of diagnostic uncertainty, further investigations—such as cardiopulmonary exercise testing (CPET) [including measurement of peak oxygen consumption (VO_2) to confirm reduced exercise capacity and elucidate the underlying cause of dyspnoea], exercise stress echocardiography, or invasive haemodynamic assessment—may be considered.[176]

The gold standard, confirmatory test for the diagnosis of HFpEF is invasive haemodynamic exercise testing. An invasively measured pulmonary capillary wedge pressure of ≥15 mmHg (at rest), or ≥25 mmHg (with exercise), or an LV end-diastolic pressure ≥16 mmHg (at rest) is generally considered diagnostic. In recognition that invasive haemodynamic exercise testing is expensive and is not available in many centres worldwide, its main use should be limited to research settings or to patients with diagnostic uncertainty despite non-invasive testing. In most patients, the diagnosis of HFpEF can be made based on clinical history and echocardiographic signs (*Table 10*). Thus, invasive testing is indicated in only a minority of patients where the diagnosis is uncertain and where establishing the diagnosis or an alternative cause of signs or symptoms is likely to affect patient management. Therefore, current guidelines do not mandate invasive haemodynamic testing in every patient with suspected HFpEF to make the diagnosis.

Table 10 Simplified echocardiographic criteria for supporting objective evidence of heart failure with preserved ejection fraction

Criteria	Echocardiographic threshold
LV hypertrophy	LV mass index ≥95 g/m^2 (female) ≥115 g/m^2 (male) OR Relative wall thickness >0.42
LA dilatation (volume indexed by BSA)	>34 mL/m^2 (sinus rhythm) >40 mL/m^2 (AF)
Increased likelihood of elevated LV filling pressure	E/e′ >9 at rest[a]
Raised estimated systolic PA pressure	>35 mmHg OR TR velocity at rest >2.8 m/s

The probability for an HFpEF diagnosis increases with the number of parameters in the pathological range.
AF, atrial fibrillation; BSA, body surface area; HFpEF, heart failure with preserved ejection fraction; LA, left atrial; LV, left ventricular; PA, pulmonary artery; TR, tricuspid regurgitation.
[a]E/e′ ≥15 is more specific, but less sensitive, for the diagnosis of HFpEF.

5.3. Aetiology and subtypes of heart failure

Assessment of aetiology is fundamental for the management of HF, as treatment should, if possible, address the underlying cause. Some treatments may be aetiology dependent, and some causes of HF are potentially reversible. Disease-modifying therapies are increasingly available, and early identification and treatment can improve survival. Targeted therapies for specific cardiomyopathies are under investigation, and precise aetiological assessment will become increasingly important in the future. Aetiology assessment also determines prognosis,[177] is relevant to the patient, and imperative for care planning.

Common causes of HF include ischaemic heart disease, hypertension, and valvular heart disease, although a multitude of other causes and contributing factors exist (*Figures 5 and 6*) and often more than one possible cause may be present.

Determining the aetiology often involves a multiparametric evaluation beginning with obtaining a medical history from the patient, continuing through patient examination and clinical tests (*Figure 7*). Often non-invasive testing accompanied by medical history will be sufficient to determine aetiology. Characteristic findings indicating the underlying

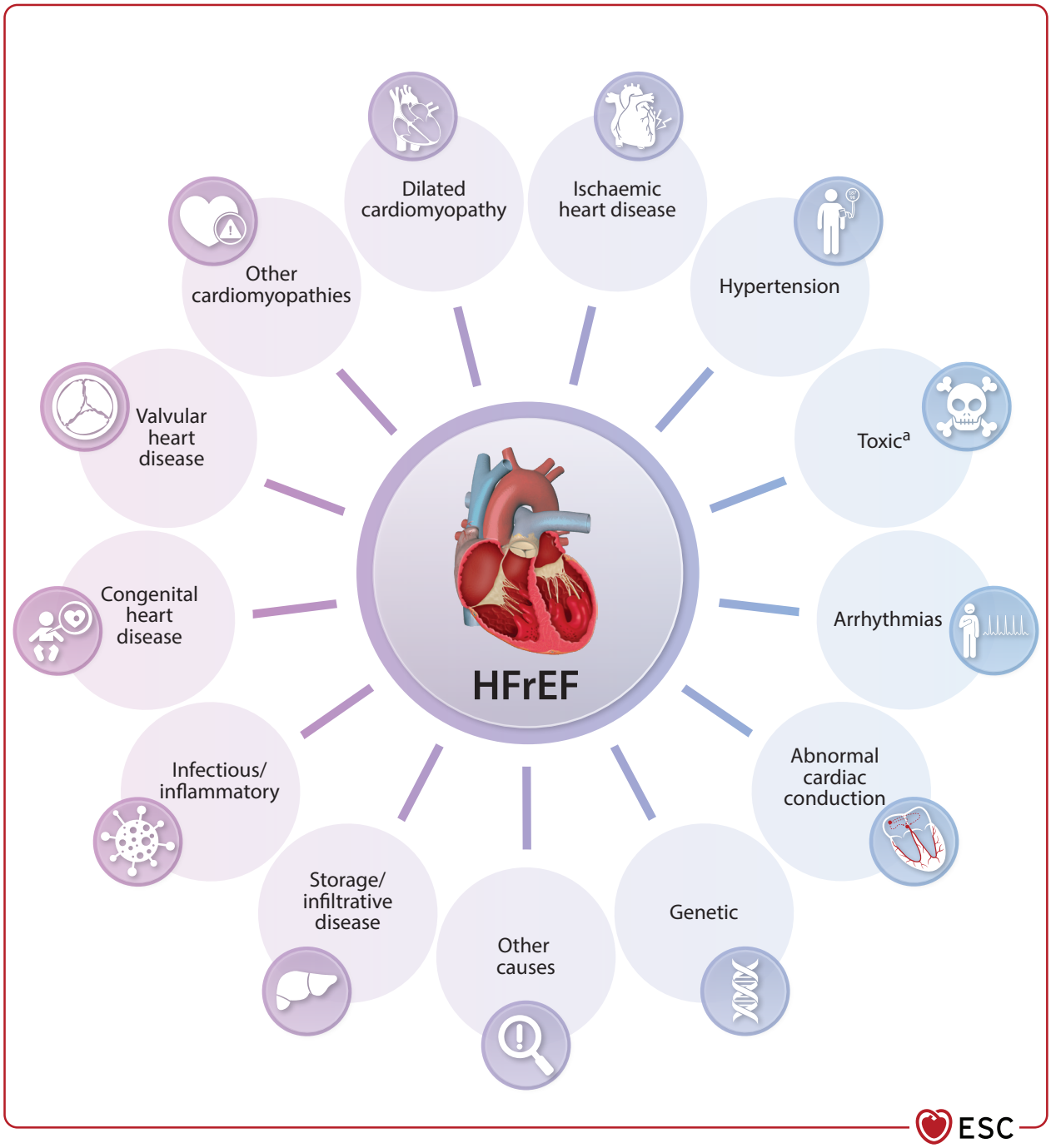

Figure 5 Major contributing causes of heart failure with reduced ejection fraction. HFrEF, heart failure with reduced ejection fraction. [a]Toxic may include both drug-related and chemotherapy-related causes.

aetiology are noted in many patients at the time of echocardiography. Patients with ischaemic aetiology may have regions of akinesis/dyskinesis and thinning/aneurysm formation in the myocardial areas affected by coronary disease. Valvular disease is detected, often also with characteristic valvular findings dependent on cause (e.g. rheumatic or ischaemic), and the long-term sequelae of untreated hypertension may be observed (LV hypertrophy, aortic dilatation with or without central aortic regurgitation). Findings consistent with other cardiomyopathies, cardiac amyloidosis (CA), or ventricular dyssynchrony in left bundle branch block (LBBB) may also be noted.

When considering further investigation for CAD, non-invasive assessment is often sufficient, and before proceeding to invasive assessment the risks and benefits should be considered.[178–180]

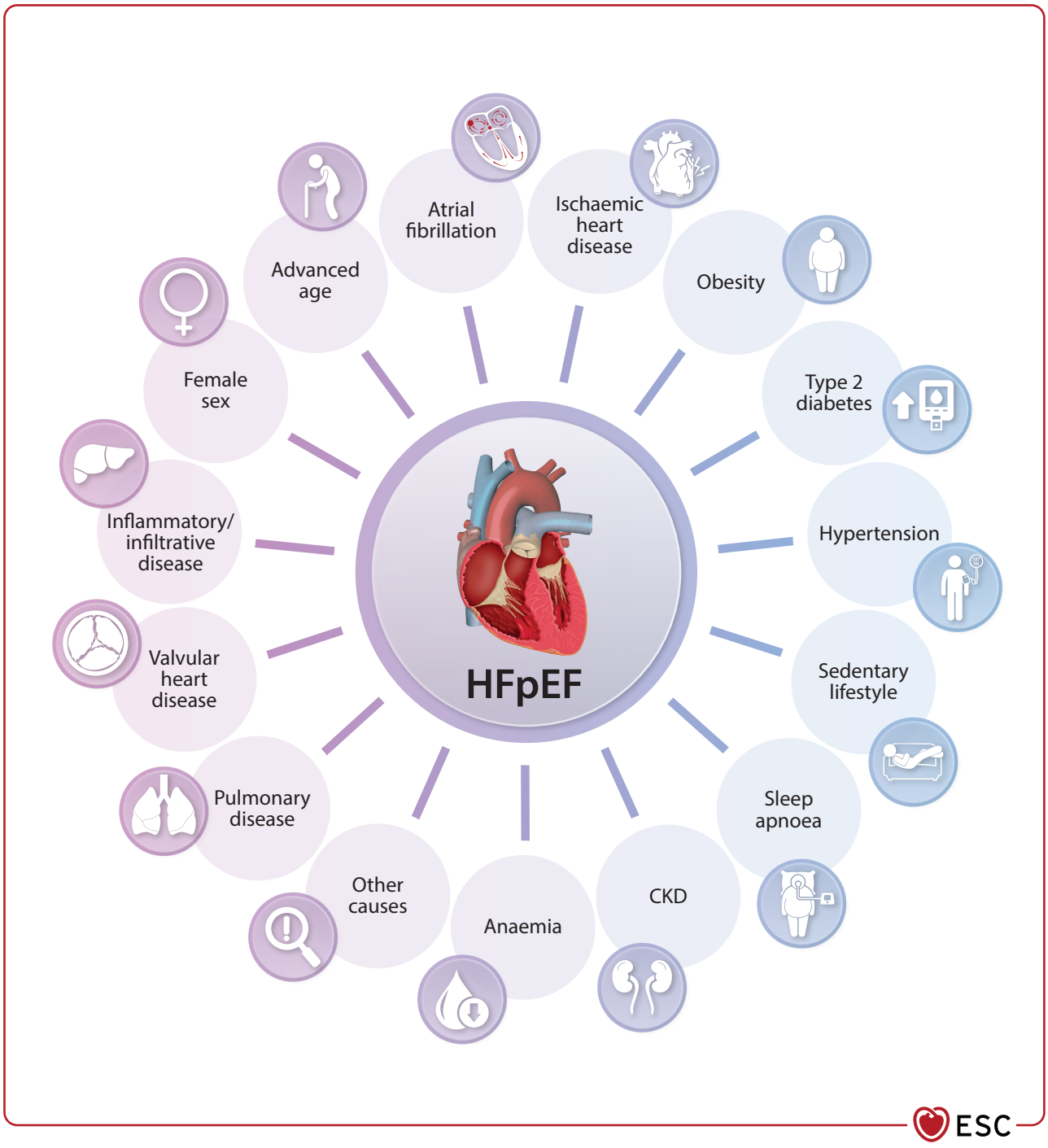

Figure 6 Major risk factors of heart failure with preserved ejection fraction. CKD, chronic kidney disease; HFpEF, heart failure with preserved ejection fraction.

If an underlying cardiomyopathy is suspected or the aetiology is unclear, further imaging with cardiac magnetic resonance (CMR) imaging is recommended. We refer to the *2023 ESC Guidelines for the management of cardiomyopathies* regarding specific recommendations and approaches for investigations into specific cardiomyopathies.[124] An approach with laboratory and imaging tests chosen according to the five subtypes [hypertrophic cardiomyopathy (HCM), DCM, restrictive cardiomyopathy, ARVC, and non-dilated LV cardiomyopathy] has been recommended.[124]

In patients with unexplained dyspnoea, CPET may be used to identify the cause of unexplained dyspnoea and/or exercise intolerance.

When a specific aetiology is suspected, further investigations may be required, such as 18F-fluorodeoxyglucose-positron emission tomography (18F-FDG-PET) for suspected

cardiac sarcoidosis (see Supplementary data online, *Table S2*).[181,182] Genetic testing may be appropriate when a genetic cause is suspected and the results may provide management and prognostic guidance, result in cascade family screening or reproductive management. For more specific guidance on genetic testing in specific cardiomyopathies, we refer to the *2023 ESC Guidelines for the management of cardiomyopathies*.[48,124]

5.3.1. Cardiac imaging in heart failure: a multimodality approach

Multimodal cardiac imaging plays a pivotal role in the diagnosis, management, and prognostic assessment of HF, enabling precise subtyping to aid in disease-specific therapy selection and is supported by a growing body of evidence (*Figure 7*).

Echocardiography is considered the first-line imaging modality in HF and remains the cornerstone of assessment. Echocardiography has widespread availability, is non-invasive, and provides the ability for real-time dynamic evaluation of cardiac structures, dimensions, volumes, filling patterns, haemodynamics, and function. Tissue Doppler imaging and speckle-tracking echocardiography have allowed clinicians to quantify myocardial global longitudinal strain, offering more sensitive measures of early systolic dysfunction even before LVEF declines, which is of particular value in patients undergoing chemotherapy, or specific strain patterns that may be suggestive of amyloidosis or HCM.[183–185] In patients with HFpEF, diastolic stress testing is emerging as an important tool to unmask diastolic dysfunction that may not be apparent at rest. Depending on echocardiography findings, additional imaging modalities or

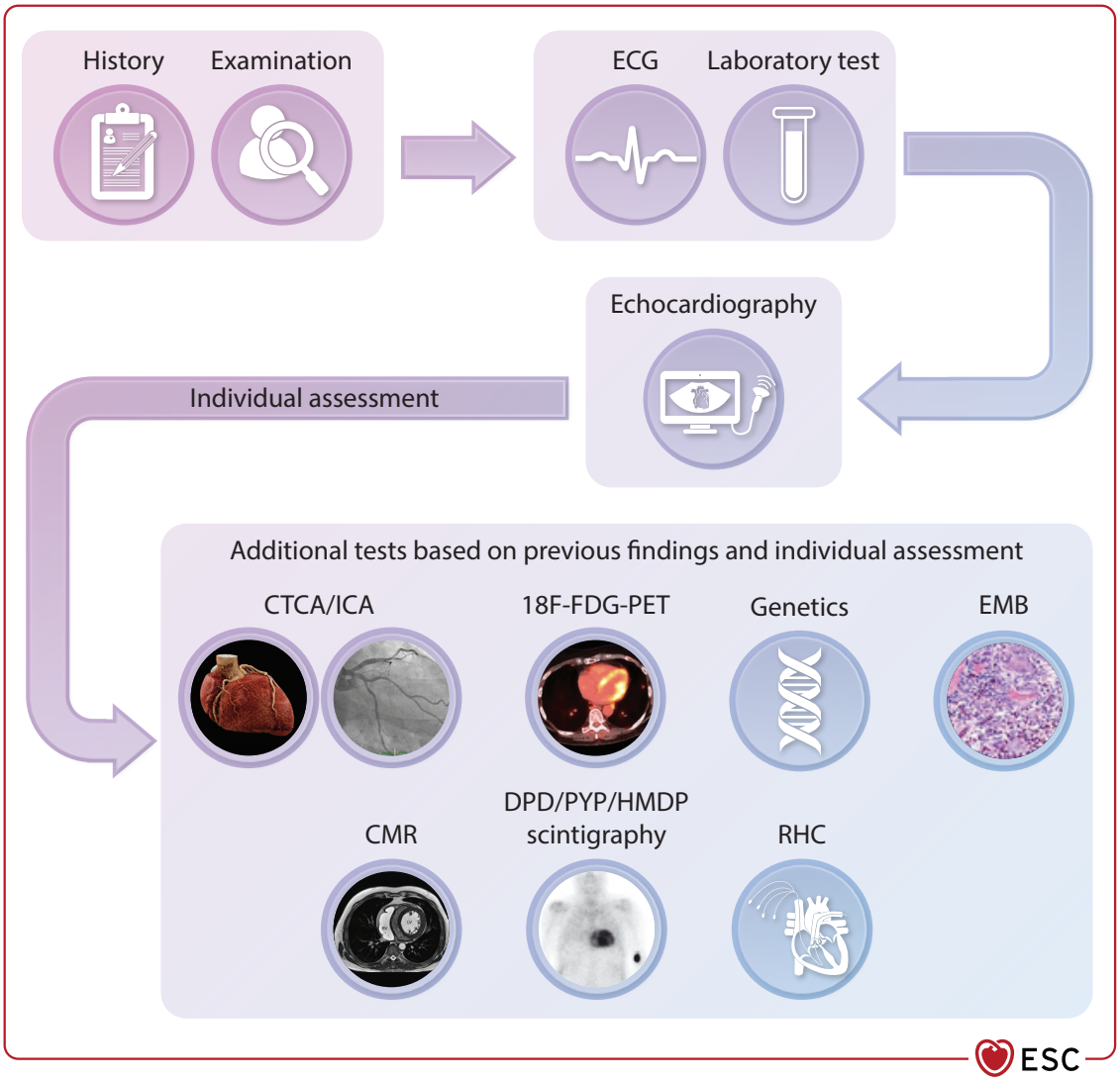

Figure 7 Multiparametric approach to aetiology assessment in heart failure. 18F-FDG-PET, 18F-fluorodeoxyglucose-positron emission tomography; CMR, cardiac magnetic resonance; CTCA, computed tomography coronary angiography; DPD, 3,3-diphosphono-1,2-propanodicarboxylic acid; ECG, electrocardiogram; EMB, endomyocardial biopsy; HMPD, hydroxymethylene diphosphonate; ICA, invasive coronary angiography; PYP, pyrophosphate; RHC, right heart catheterization.

testing may be needed (see Supplementary data online, *Table S2*).

Advances in multimodal imaging, including CMR, stress testing, and computed tomography (CT), have significantly enhanced our capacity to comprehensively assess HF, offering complementary information that is crucial in complex cases.[183–185] CMR is considered the gold standard for assessing LV volumes and mass, owing to its high spatial resolution and reproducibility. Late gadolinium enhancement (LGE) provides detailed insights into fibrosis and scarring and is useful in distinguishing ischaemic from non-ischaemic aetiology as well as certain cardiomyopathies.[124] CMR myocardial tissue characterization with parametric mapping [T1, T2, T2* (longitudinal, transverse, and observed transverse relaxation times), LGE and extracellular volume (ECV) expansion] enables classification of cardiomyopathies[124,186–193] and of cardiac amyloid.[194] An overview of typical CMR findings in cardiomyopathies can be found in the *2023 ESC Guidelines for the management of cardiomyopathies*.[124] Description of other specific imaging modalities is provided in the Sections on specific comorbidities.

5.3.2. Investigations for coronary artery disease

Coronary artery disease is highly prevalent in HF and the most common cause of HFrEF.[13,33,195] Even though assessment of aetiology is essential in HF, investigations for CAD should be tailored to the individual patient's risks and benefits (*Figure 8*). For frail patients, a typical medical history of angina accompanied by echocardiography showing coronary territory scarring or regional wall motion abnormalities may suffice. In patients with potential for revascularization, further examinations may be needed, considering individual risks and benefits.

Computed tomography coronary angiography (CTCA) has a high negative predictive value and should be considered in patients with HF when the likelihood of CAD is low to moderate.[196] If patients are possible candidates for revascularization, invasive coronary angiography (ICA) is indicated in patients with HFrEF with a high likelihood of CAD and in patients with angina, regardless of LVEF.

Computed tomography coronary angiography and ICA should be used with caution in patients with eGFR <30 mL/min/1.73 m^2 and/or contraindication for contrast medium administration. Evidence supporting the efficacy of viability testing to identify suitable patients for revascularization is lacking.[178,179]

5.3.3. Heart failure caused by arrhythmia or conduction disease

Arrhythmia-associated HF is a broad term that encompasses HF caused by tachyarrhythmias, including AF, atrial flutter, other supraventricular tachycardias, ventricular tachycardia, and premature ventricular contraction (PVC).[197,198] The identification

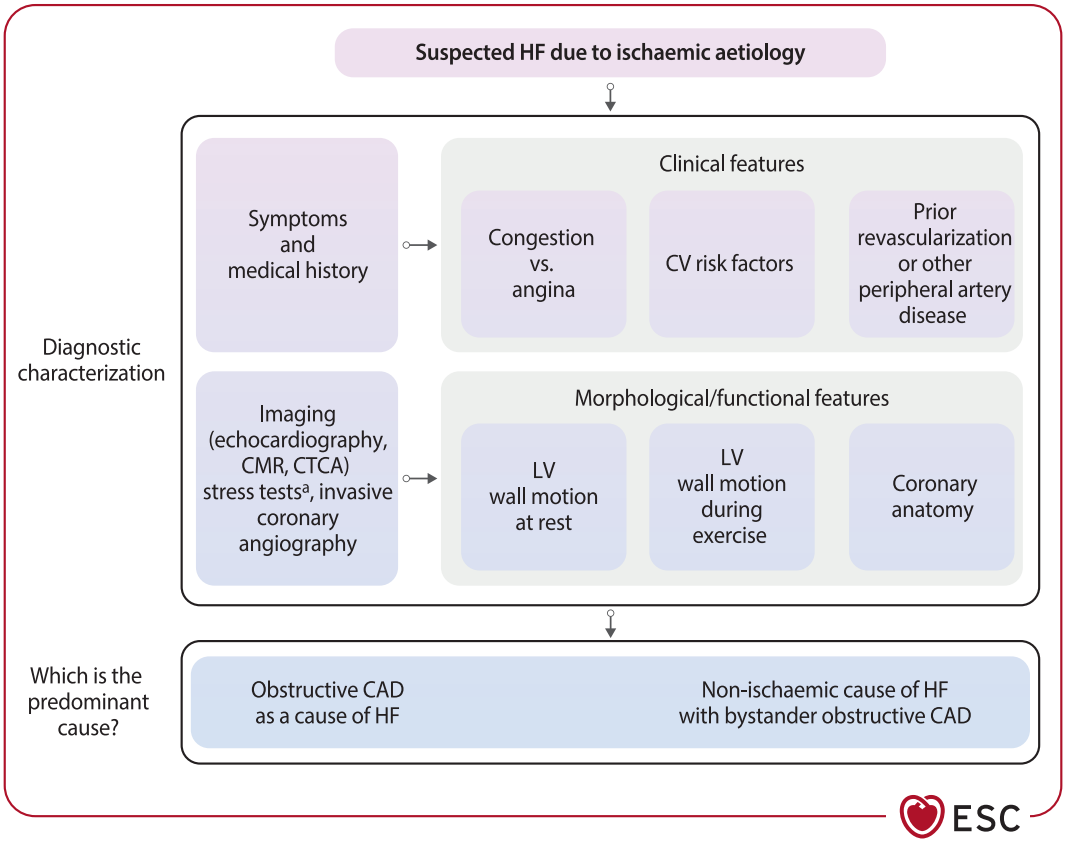

Figure 8 Diagnosis of heart failure due to ischaemic aetiology. CAD, coronary artery disease; CMR, cardiac magnetic resonance; CTCA, computed tomography coronary angiography; CV, cardiovascular; HF, heart failure; LV, left ventricular. [a]Stress tests include stress echocardiography, stress CMR, or nuclear imaging. Electrocardiographic exercise test has not been shown to properly assess coronary stress.

of arrhythmia-associated HF is important in patients with HFrEF, in whom a rhythm strategy for AF may potentially be beneficial. The diagnostic work-up may include an ECG and ambulatory ECG to characterize the electrical subtype, and CMR imaging to characterize the morphological/functional subtype. Arrhythmias may be the sole cause of HFrEF or merely a bystander in the context of other causes of HF.

Heart failure associated with abnormal cardiac conduction is defined as LV dysfunction due to abnormal electrical conduction and should be suspected in patients with LV dysfunction and a QRS duration ≥130 ms, without evidence of other causes for HF.[199] It should also be considered in patients with implanted pacemakers or implantable cardioverter-defibrillators (ICDs) delivering RV pacing (see *Section 6.2.2.2*).[200–203]

The diagnosis is a diagnosis of elimination, and it may only be reached retrospectively, if LV function improves following cardiac resynchronization therapy (CRT) implantation.[204]

In terms of likelihood of response, there is a spectrum. At one end, abnormal cardiac conduction may be the sole culprit, whereas at the other, it may be a bystander in the context of HF due to other causes (*Figure 9*). CMR may be useful in identifying myocardial scar and morphological abnormalities pointing to other aetiologies of HF. Abnormal cardiac conduction, as the sole cause of HFrEF, is most likely in patients with HFrEF, LBBB, wide QRS duration, with no myocardial scarring on CMR and in patients with RV pacing-induced HF.[199]

Recommendation Table 4 — Recommendations for specialized diagnostic investigations in patients with established heart failure to detect reversible/treatable causes of heart failure (see *Evidence Tables 20–28*)

Recommendations	Class[a]	Level[b]
Investigations for underlying aetiology in patients with HFpEF or HFrEF		
Contrast-enhanced CMR is recommended in patients with suspected cardiomyopathy, or where the underlying aetiology of HF is uncertain if further characterization is likely to add value to patient care.[205–215]	I	C
Initial diagnostic testing with serum and urine immunofixation, serum free light chains assay, and DPD/PYP/HMDP bone scintigraphy is recommended in patients with HF and a suspicion of cardiac amyloidosis.[216–222]	I	B
Genetic testing is recommended in patients fulfilling diagnostic criteria for cardiomyopathy in cases where it enables diagnosis, prognostication, therapeutic stratification, or reproductive management of the patient, or where it enables cascade genetic evaluation of their relatives who would otherwise be enrolled into long-term surveillance.[223–227]	I	C
Invasive coronary angiography is recommended in patients with HF, angina, and high probability[c] of obstructive CAD who are potential candidates for revascularization[d].	I	C
18F-FDG-PET scanning should be considered for the diagnostic work-up in patients with cardiomyopathy in whom cardiac sarcoidosis is suspected.[181,182]	IIa	C
Endomyocardial biopsy should be considered to aid in diagnosis and management in patients with rapidly progressive HF despite standard therapy or when the results of other clinical investigations suggest myocardial inflammation, infiltration, or storage that cannot be identified by other means.[228]	IIa	C
Right heart catheterization[e] should be considered in patients where HF is thought to be due to constrictive pericarditis or congenital heart disease.[229]	IIa	C
Right heart catheterization[f] may be considered in selected patients with suspected HFpEF or structural heart disease to confirm the diagnosis, or when clinical examination and non-invasive testing are insufficient to understand the haemodynamic state.[230,231]	IIb	C
Investigations for patients with HFrEF		
Invasive coronary angiography should be considered in patients with HFrEF and high pre-test likelihood[c] of obstructive CAD, taking into account the risk-to-benefit ratio of the procedures and potential revascularization strategies.[178–180]	IIa	C
CTCA should be considered in patients with HFrEF and low-moderate pre-test likelihood[c] of obstructive CAD.[196,232–234]	IIa	C
Review of the proportion of RV pacing should be considered in all patients with CIED and *de novo* or worsening HFrEF.[202,235–239]	IIa	C
Electrical cardioversion as a diagnostic tool may be considered in patients with persistent AF where there is uncertainty about the value of sinus rhythm restoration on symptoms or to assess improvement in left ventricular function.[240]	IIb	C

18F-FDG-PET, 18F-fluorodeoxyglucose-positron emission tomography; AF, atrial fibrillation; CAD, coronary artery disease; CIED, cardiac implantable electronic device; CMR, cardiac magnetic resonance; CTCA, computed tomography coronary angiography; DPD, 3,3-diphosphono-1,2-propanodicarboxylic acid; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; HMDP, hydroxymethylene diphosphonate; PYP, pyrophosphate; RV, right ventricular.

[a]Class of recommendation.

[b]Level of evidence.

[c]Based on cardiovascular risk factors and clinical history.

[d]Exclude frailty, multiple severe comorbidities, limited life expectancy.

[e]Right and left heart catheterization needed for the differential diagnosis of constrictive pericarditis and restrictive cardiomyopathy.

[f]Potentially including exercise right heart catheterization.

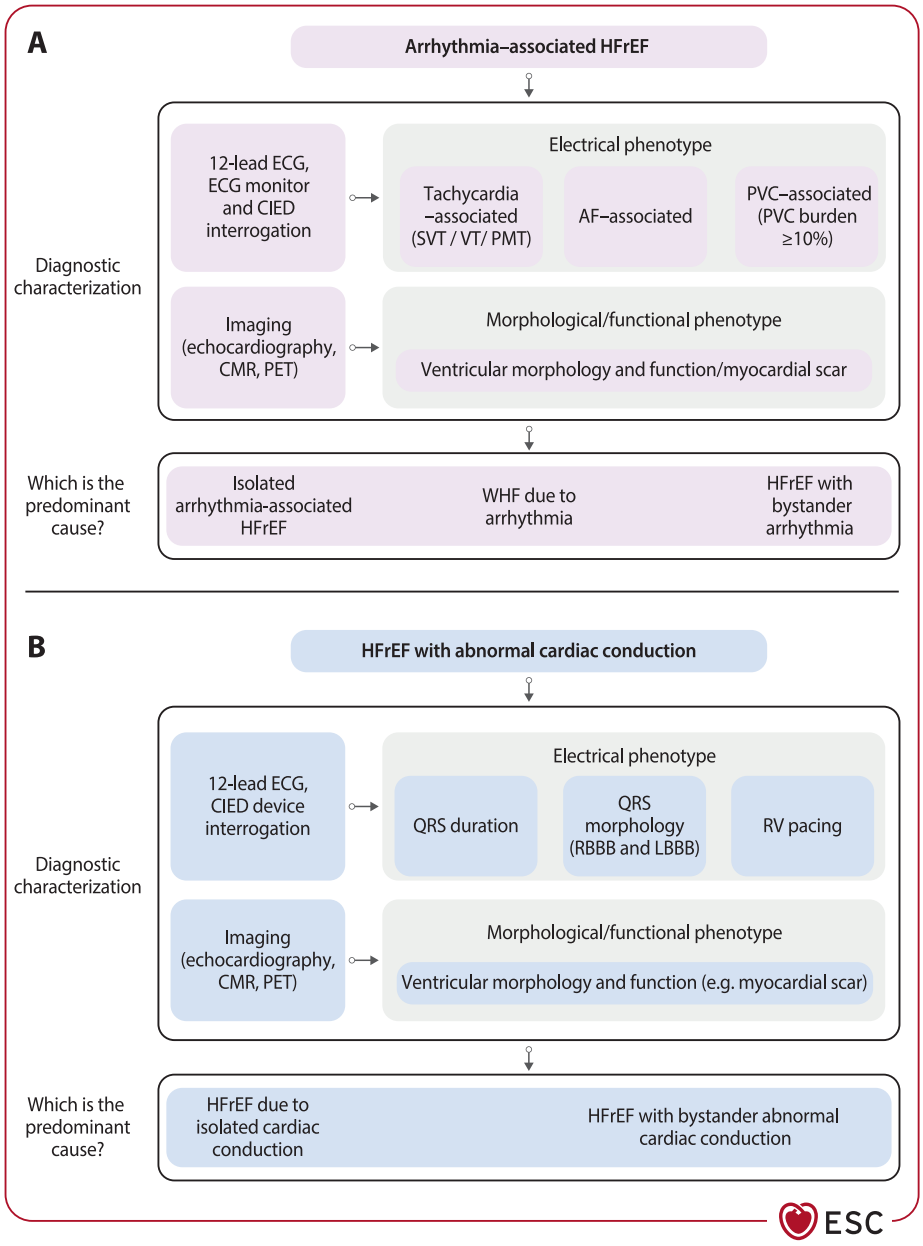

Figure 9 Diagnosing arrhythmia-associated heart failure and heart failure with abnormal cardiac conduction. AF, atrial fibrillation; CIED, cardiac implantable electronic device; CMR, cardiac magnetic resonance; ECG, electrocardiogram; HFrEF, heart failure with reduced ejection fraction; LBBB, left bundle branch block; PET, positron emission tomography; PMT, pacemaker tachycardia; PVC, premature ventricular contraction; RBBB, right bundle branch block; RV, right ventricular; SVT, supraventricular tachycardia; VT, ventricular tachycardia; WHF, worsening heart failure.

6. Management of chronic heart failure

6.1. Guideline-directed medical therapy for heart failure

The Task Force have decided to introduce the terms FMT and AMT, as described in *Section 3* (*Figure 3*). Together FMT and AMT cover GDMT. For HFrEF, FMT currently includes beta-blockers, ACE-Is/ARNIs/ARBs, MRAs, and SGLT2-Is, whereas for HFpEF it includes SGLT2-Is and MRAs.

Importantly, AMT and GDIT based on the underlying cause of HF, phenotypical characteristics, and comorbidities are discussed in other sections.

6.1.1. Goals of pharmacotherapy for patients with heart failure

Pharmacotherapy remains the cornerstone of treatment for stage C HF and should be implemented at doses used in RCTs in patients with HF before considering device therapy, and alongside non-pharmacological interventions (*Figure 1* and *Table 11*).

There are three major goals of treatment for patients with HF: (i) reduction in mortality; (ii) prevention of recurrent

hospitalizations due to worsening HF (WHF); and (iii) improvements in clinical status, functional capacity and QoL. The recommendations for each treatment depending on LVEF are summarized below. Overall, there are no sex differences in recommendations for HF pharmacotherapy.

In this section, we address the management of predominantly left-sided HF. Management of right-sided HF is covered comprehensively in a recent HFA consensus paper.[48]

6.1.2. Foundational medical therapy in all patients with heart failure, independent of left ventricular ejection fraction

Mineralocorticoid receptor antagonists and SGLT2-Is are recommended for all symptomatic patients with HF, regardless of LVEF, as these drugs reduce mortality and the risk of HFH. The recommended doses of these drugs are given in *Table 11*. Other agents can be used in selected patients.

6.1.2.1. Sodium–glucose co-transporter 2 inhibitors

The SGLT2-Is dapagliflozin and empagliflozin have been shown to reduce the composite endpoint of HFH or CV mortality in symptomatic ambulatory patients with HF.[241–245] Although there were consistent reductions in the primary endpoint across the LVEF ranges studied, the individual endpoint of CV mortality was only reduced in HFrEF.[44,241,246] Thus, it is recognized that in HFpEF the reduction in the primary endpoint is driven by a reduction in HFH. The guideline Task Force has decided to base recommendations on the primary endpoints. SGLT2-Is also improve QoL.[247,248] Common side effects include genital and urinary infections. A mild initial decline in eGFR is expected, but long-term kidney function is improved.[249–253]

Practical guidance in the use and initiation of SGLT2-Is are provided in Supplementary material online, *Table S9*.

The use of SGLT2-Is in DHF is discussed in *Section 7*.

6.1.2.2. Mineralocorticoid receptor antagonists

Mineralocorticoid receptor antagonists have been shown to reduce the composite endpoint of HFH or death in patients with HF.[43,254–257] The guideline Task Force decided to base recommendations on the primary endpoints. Although there were consistent reductions in the primary endpoint across the LVEF ranges studied, the individual endpoint of mortality was only reduced in HFrEF.[43,254,256] There were differences in the mortality endpoints used in HFrEF and HFpEF trials, with all-cause mortality used in HFrEF trials and CV mortality used in HFpEF trials. Furthermore, different RCTs have included patients with different LVEF ranges not entirely consistent with the distinction between HFrEF and HFpEF. Whereas spironolactone was studied across LVEF ranges, eplerenone was only studied in HFrEF (LVEF up to 35%) and finerenone in patients with LVEF >40%. Although finerenone reduced the composite endpoint of HFH and CV mortality in the FINEARTS-HF trial, spironolactone did not in the overall results of the TOPCAT trial.[255,257] However, a meta-analysis demonstrated a significant effect of the MRAs used in FINEARTS-HF and TOPCAT on the primary endpoint of HFH and CV mortality in patients with LVEF >40%.[43]

Mineralocorticoid receptor antagonists are chemically and structurally different; they block the receptors that bind aldosterone with different affinity and distribution in the heart and kidneys and also block other steroid hormones with different degrees of affinity (e.g. corticosterone blockade) (see Supplementary data online, *Table S3*).[258] Eplerenone and the non-steroidal MRA finerenone are more mineralocorticoid receptor-specific and therefore induce less gynaecomastia. Caution should be exercised when MRAs are started in patients with impaired kidney function (MRAs have not been tested in patients with eGFR <25 mL/min/1.73 m^2) and in those with potassium levels ≥5.0 mmol/L.[259] In patients taking MRAs whose serum potassium is >5.5 mEq/L, there might be an indication for dose reduction of the MRA or temporary discontinuation of the MRA to avoid life-threatening hyperkalaemia. The first step would be to recheck potassium levels. If the MRA dose is reduced or temporarily discontinued, the drug should be restarted if hyperkalaemia resolves. Practical guidance in the use and uptitration of MRAs are provided in Supplementary material online, *Table S8*.

6.1.3. Additional medical therapy in all patients with heart failure, independent of left ventricular ejection fraction

6.1.3.1. Loop diuretics

Loop diuretics are recommended to reduce signs and/or symptoms of congestion in patients with HF and volume overload. Their effects on morbidity and mortality have not been studied in adequately powered RCTs. However, the major disease-modifying treatment trials for HF were always conducted with a high background use of loop diuretic therapy. One meta-analysis has shown that in patients with HF, diuretics appear to reduce the risk of death and WHF compared with a placebo, and compared with an active control, diuretics improved exercise capacity.[260]

Several observational studies have linked loop diuretic use to higher mortality, even after adjustment or propensity matching.[261] However, several biases remain as sicker patients are generally prescribed higher doses of loop diuretics. Clearly, patients benefit from maintenance therapy with a loop diuretic to prevent or control congestion. However, the use of loop diuretics may result in electrolyte disturbances, further neurohormonal activation, accelerated kidney function decline, and symptomatic hypotension. The latter may be especially relevant as it could result in treatment with lower doses of FMT. It is generally advised to use the lowest possible dose of diuretics to maintain euvolaemia. Importantly, the individual diuretic dose may change significantly over time.[262] Therefore, dynamic and individualized dosing of loop diuretic is recommended.[263,264] The use of a multiparameter-based evaluation to assess congestion, using clinical assessment at rest and during dynamic manoeuvres, as well as biomarkers (eGFR, electrolytes, natriuretic peptides), supplemented with imaging assessment according to local expertise, is probably the best contemporary strategy to optimize diuretic dosing.[265] Optimal FMT and GDIT often results in less need for diuretic treatment.[266,267] The chronic use of thiazide diuretics in stable patients should be avoided, as this often induces severe electrolyte disturbances that could go undetected in the ambulatory setting.

Treatment of DHF and approach to diuretic treatment in this setting is covered in *Section 7*.

6.1.3.2. Potassium binders

Hyperkalaemia is common in HF, often as a result of comorbidities (e.g., diabetes, CKD), concomitant use of renin–angiotensin–aldosterone system inhibitors (ACE-Is/ARNIs/ARBs and MRAs),

and because of HF itself. Hyperkalaemia may increase the risk for arrhythmias and death.[268] Hyperkalaemia, and the fear of inducing it, often results in under-utilization, dose reductions, or discontinuation of ACE-Is/ARNIs/ARBs and MRAs compromising their cardio-kidney benefit in HF. The gastrointestinal potassium binders patiromer and sodium zirconium cyclosilicate remove potassium by exchanging cations, leading to increased faecal excretion. Both agents have shown favourable results to treat and/or prevent hyperkalaemia in patients receiving ACE-Is/ARNIs/ARBs and MRAs, therefore facilitating the continuation or uptitration of ACE-Is/ARNIs/ARBs and MRAs.[269–272] Whether potassium binders improve clinical outcomes is still unclear. In the REALIZE-K trial, there was a signal towards more HF deterioration with sodium zirconium cyclosilicate as compared with placebo, although the trial was not powered to detect clinical outcomes.[272] Potential adverse effects for the potassium binders include gastrointestinal symptoms (nausea, constipation, diarrhoea), hypomagnesaemia (for patiromer), and oedema (for sodium zirconium cyclosilicate).

No specific recommendations for the use of potassium binders are included in the guideline at current time, due to insufficient evidence for clinical benefit.

6.1.4. Foundational medical therapy for heart failure with reduced ejection fraction

Modulation of the renin–angiotensin–aldosterone system, sympathetic nervous systems, and sodium–glucose co-transporter (SGLT2) inhibition has been shown to improve survival, reduce the risk of HFH, and reduce symptoms in patients with HFrEF. Treatment with optimal FMT, including ACE-Is/ARNIs/ARBs, beta-blockers, MRAs, and SGLT2-Is, is recommended as the foundation of treatment for all patients with HFrEF. There is no evidence favouring any particular sequencing during initiation and uptitration. Therefore, the consensus is that FMT can be commenced together with individual variations based on clinical assessment as soon as the diagnosis of HFrEF is established. Drugs should be uptitrated and continued at the doses used in the RCTs (or to the highest tolerated doses). Misinterpretation of changes in kidney function is a leading cause of insufficient dosing or inappropriate discontinuation of FMT and should be avoided (Section 6.1.6).[273]

Additional medical therapy may be used in selected patients with HFrEF (see Section 6.1.5).

No large prospective RCT has been performed exclusively in patients with LVEF 41%–49%. Patients with LVEF 41%–49% appear to respond to FMT, similar to patients with LVEF <40%.[36,38–41] Many patients with LVEF 41%–49% may already be on ACE-Is or ARBs and beta-blockers for other CV indications such as CAD, hypertension, or post-MI LV systolic dysfunction.

Sodium–glucose co-transporter 2 inhibitors and MRAs are recommended for all ranges of LVEF, as covered in *Section 6.1.2*. The recommended doses of FMT and AMT are provided in *Table 11*. Practical guidance in the use and uptitration of FMT are provided in Supplementary material online, *Tables S4–S9*.

6.1.4.1. Angiotensin-converting enzyme inhibitors and angiotensin receptor–neprilysin inhibitor

Angiotensin-converting enzyme inhibitors were the first class of drugs shown to reduce mortality and morbidity and to improve symptoms in patients with HFrEF.[137,138,274–277] They are recommended in all patients with HFrEF unless contraindicated or not tolerated and should be uptitrated to the highest recommended doses. If these doses are not tolerated, intermediate doses should be tried. In the higher end of LVEF, evidence is limited. The PEP-CHF trial (perindopril) was conducted in patients with an LVEF >40%, but it did not report outcomes according to LVEF.[39] The PEACE trial reported a subgroup analysis showing a reduction in mortality with trandolapril in patients with LVEF from 40% to 50%.[38]

An ARNI is composed of an ARB and an inhibitor of neprilysin, an enzyme that degrades natriuretic peptides, bradykinin, adrenomedullin, and other vasoactive peptides. In the PARADIGM-HF trial, the ARNI, sacubitril–valsartan, was compared with enalapril in symptomatic patients with HFrEF who already tolerated an adequate dose of either an ACE-I or an ARB.[278] ARNI significantly reduced the composite endpoint of CV death or HFH by 20% as compared with enalapril.[278] Additional benefits included improvement in QoL, reduction in decline of eGFR, a reduction in loop diuretic dose, and lower risk of hyperkalaemia.[279,280] If patients continue to have chronic symptomatic HFrEF and they tolerate an ACE-I or an ARB, it is recommended that they be switched to an ARNI to reduce morbidity and mortality. Pre- and post-discharge initiation of ARNIs in HFrEF patients have shown similar efficacy and safety, and larger NT-proBNP reductions compared with ACE-I treatment in ACE-I/ARB naïve patients.[281–283] As such, the use of an ARNI may be efficacious as *de novo* treatment in patients with symptomatic chronic HFrEF to simplify management and maintain eGFR and QoL.

Use of an ARNI is more frequently associated with symptomatic hypotension, and a washout period of at least 36 h after ACE-I therapy is required to minimize the risk of angio-oedema. Treatment with ACE-Is or ARNIs is indicated, but should be given with caution, to patients with low blood pressures (systolic blood pressure <100 mmHg), kidney insufficiency (eGFR <30 mL/min/1.73 m^2), or elevated serum potassium (>5.2 mEq/L). Abrupt withdrawal of ACE-Is or ARNIs can lead to clinical deterioration and should be avoided, and in those patients for whom treatment with an ARNIs is not possible, continued use of an ACE-I remains strongly advised.

6.1.4.2. Angiotensin II type 1 receptor blockers

Angiotensin II receptor blockers are recommended for HFrEF patients who cannot tolerate ACE-Is or ARNIs due to side effects. Unlike ACE-Is, ARBs do not inhibit kininases and are associated with a much lower incidence of cough and angio-oedema. In the CHARM-Alternative study, candesartan reduced CV death and HFH in patients who were not receiving an ACE-I due to previous intolerance.[284] In the HEAAL study, high-dose losartan reduced HFH compared with low-dose losartan in ACE-I intolerant patients.[285] Valsartan, in addition to usual therapy, including ACE-Is, reduced HFH in the Val-HeFT trial.[286] However, no ARB has reduced all-cause mortality in any trial, and combination with an ACE-I increases adverse effects. Also, in patients with higher LVEF, evidence is limited. The CHARM-Preserved trial did not show a reduction in its primary endpoint of CV death or HFH, but a retrospective analysis showed that candesartan reduced the number of patients hospitalized for HF among those with LVEF 40%–49%.[40,41]

6.1.4.3. Beta-blockers

Beta-blockers have been shown to reduce morbidity and mortality in patients with HFrEF in addition to treatment with an ACE-I and diuretics.[36,287–292] Bisoprolol, sustained-release metoprolol (succinate), and carvedilol have been shown to reduce the risk of death in patients with HFrEF, whereas nebivolol only reduced the combined endpoint of all-cause mortality and CV hospitalization. An individual patient meta-analysis of RCTs of beta-blockers suggested similar reductions in CV and all-cause mortality for patients in sinus rhythm with HFrEF who had LVEF <40% and LVEF 40%–50%.[36] Beta-blockers should be initiated early in clinically stable patients, at low doses and gradually uptitrated to the highest tolerated dose. In patients admitted with DHF, beta-blockers should be cautiously initiated in hospital, once the patient is haemodynamically stabilized. Every effort should be made to achieve the target doses of the beta-blockers shown to be effective in major clinical trials (*Table 11*). Even if symptoms do not improve, long-term treatment should be maintained to reduce the risk of major CV events.

The effect of beta-blockers in patients with HFrEF and AF remains uncertain. A retrospective subgroup individual-patient data meta-analysis of all major beta-blocker trials in HFrEF showed no benefit on hospital admissions and mortality in the subgroup of patients with HFrEF with AF.[36,293] However, to date no RCT has ever been conducted investigating the effect of beta-blockers specifically in patients with AF and HFrEF, despite beta-blockers being potentially useful for rate control of AF.

6.1.5. Additional medical therapy for heart failure with reduced ejection fraction

6.1.5.1. I_f-channel inhibitor (ivabradine)

Ivabradine should be considered in patients with symptomatic HFrEF who at rest are in sinus rhythm with heart rate ≥70 b.p.m., LVEF ≤35%, and recent HFH, despite stable FMT including optimized beta-blocker therapy.[294] Ivabradine slows heart rate by inhibition of the I_f current. In the SHIFT trial, the primary composite endpoint of CV death or HFH was reduced, mainly driven by a reduction in HFH.[294] Importantly, only 25% of patients studied in the trial were on optimal doses of beta-blockers.[294] As beta-blockers have well-proven morbidity and mortality benefits, they should be initiated and uptitrated to target doses first, before assessing the resting heart rate for consideration of adding ivabradine.

6.1.5.2. Vericiguat

The oral soluble guanylate cyclase stimulator vericiguat may be considered in patients with symptomatic HFrEF and LVEF <45% despite optimal FMT.

The VICTORIA study assessed the efficacy and safety of vericiguat in patients with LVEF <45% and with recent episodes of WHF, who were already on the highest tolerated FMT. The incidence of the primary endpoint of CV death or HFH was lower among those who received vericiguat than among those who received placebo.[295] There was no reduction in either all-cause or CV death. The much higher event rate in VICTORIA compared with other RCTs in patients with HFrEF was associated with a shorter median follow-up to acquire the total number of events needed, which may explain why HFH were reduced, but CV mortality was not significantly reduced.[296] There was also heterogeneity in a subgroup analysis, with less benefit in patients with the highest NT-proBNP levels. The VICTOR study evaluated vericiguat in ambulatory patients with HFrEF (LVEF ≤40%) who did not have a recent WHF event and who were on contemporary FMT. VICTOR was neutral for the primary composite endpoint of time to CV death or HFH (HR 0.93; 95% CI 0.83–1.04; $P = .22$).[297] Over a median follow-up of ~18.5 months, CV death was numerically lower with vericiguat (9.6% vs 11.3%; HR 0.83; 95% CI 0.71–0.97), whereas HFH was similar between groups (11.4% vs 11.9%; HR 0.95; 95% CI 0.82–1.10). The trial therefore did not confirm a primary composite benefit in a stable, well-treated ambulatory HFrEF population, although pooled analyses combining VICTOR and VICTORIA suggest benefit across the broader HFrEF spectrum. Also, there was a reduction in all-cause mortality, a secondary endpoint in the trials.[298,299]

6.1.5.3. Hydralazine and isosorbide dinitrate

There is no clear evidence to recommend the use of hydralazine and isosorbide dinitrate in all patients with HFrEF. In a small RCT conducted in self-identified black patients the addition of the combination of hydralazine and isosorbide dinitrate to conventional therapy at that time (an ACE-I, a beta-blocker, and an MRA) reduced mortality and HFH, and improved QoL in patients with symptomatic HFrEF.[300] It is unclear if a benefit of hydralazine and isosorbide dinitrate exists for non-black patients with HFrEF. Additionally, a combination of hydralazine and isosorbide dinitrate may be considered in symptomatic patients with HFrEF who cannot tolerate any of an ACE-I, an ARNI, or an ARB (or if they are contraindicated) to potentially reduce HFH and mortality. This recommendation is based on the results of the Veterans Administration Cooperative Study, which included only male patients with symptomatic HFrEF who were treated with only digoxin and diuretics.[301]

6.1.5.4. Cardiac glycosides

Cardiac glycosides, digoxin or digitoxin, should be considered in patients with HFrEF to reduce the risk of HFH.[302–304] In the DIG trial, the overall effect on mortality with digoxin was neutral but there was a reduction in HFH.[303] Moreover, the effects of digoxin in patients with HFrEF and AF have not been studied in RCTs, but digoxin may be useful for the treatment of AF with rapid ventricular rate when other therapies cannot be used.[305–307] A serum digoxin concentration <1.2 ng/mL should be used as a target during ongoing therapy.[308] The DIGIT-HF trial examined whether low-dose digitoxin added to contemporary FMT improves outcomes in patients with chronic symptomatic HFrEF (LVEF ≤40% and NYHA class III/IV or LVEF ≤30% and NYHA class II).[304] The trial included most patients in NYHA class III and, contrary to the DIG trial, also included patients with AF. They were randomized to digitoxin [starting 0.07 mg daily, then titrated to target serum concentrations (10.5–23.6 nmol/L)] vs placebo. Over a median follow-up of 36 months, the primary composite endpoint—death from any cause or HFH—occurred in 39.5% of the digitoxin group vs 44.1% of the placebo group (HR 0.82; 95% CI 0.69–0.98; $P = .03$). There was no significant reduction in all-cause mortality alone (27.2% vs 29.5%; HR 0.86; 95% CI 0.69–1.07) or in HFH alone (28.1% vs 30.4%;

HR 0.85; 95% CI 0.69–1.05).[304] Taken together, available evidence suggests that cardiac glycosides (digoxin or digitoxin), when added to FMT, can reduce the risk of HFH in patients with chronic symptomatic HFrEF. Both agents share a narrow therapeutic window and require careful monitoring but differ in their metabolic elimination: digoxin is primarily eliminated through the kidneys, whereas digitoxin undergoes hepatic elimination.

6.1.5.5. Cardiac myosin activator

Omecamtiv mecarbil, a cardiac myosin activator, reduced the risk of HF events modestly in the GALACTIC-HF trial, but without a significant mortality benefit. The drug is not currently approved for clinical use in HF.[309]

6.1.6. The importance of uptitrating foundational medical therapy and maintaining adherence in heart failure with reduced ejection fraction

Foundational medical therapy is essential in HFrEF and must be initiated and uptitrated to target (*Table 11*) or highest tolerated doses.[306,307] A practical guidance for the use of medical therapies is available in Supplementary data online, *Tables S4–S9*.

Randomized controlled trials of medical therapy in HF initiated therapy at low doses, with protocol-driven uptitration, irrespective of symptomatic improvement, unless limited by intolerance. The target doses used in these trials established the efficacy and safety of these therapies and therefore form the basis of guideline recommendations. When target doses are not achievable or tolerated, the maximal tolerated dose is recommended.

Registry and real-life data have shown significant underimplementation of FMT in HFrEF, both with regard to number of drugs and doses used. Importantly, misinterpretation of changes in kidney function, leading to inappropriate discontinuation or down-regulation of doses of FMT, is a leading cause of insufficient FMT and should be avoided, both in decompensated and chronic HF.[273,310]

Many classes of FMT can safely be initiated in patients with lower eGFR (Supplementary data online, *Tables S4–S9* and *2026 ESC Guidelines on cardiovascular disease and chronic kidney disease*).[122,259] No statistically significant interaction has been found between the presence of CKD and the treatment effect of the components of FMT on the primary endpoint of their respective trials.[259] Therefore, in terms of relative risk reduction, these agents are equally effective in patients with CKD. Because patients with CKD are at the highest baseline risk for CV death or HFH, the absolute risk reduction effect is even more pronounced in patients with HF and CKD. Therefore, it is crucial that FMT is initiated, uptitrated, and maintained in patients with CKD.[259]

In trials that have evaluated dose responses for outcomes, composite event rates were lower with target doses compared with lower doses.[274,311]

Maintenance of FMT in patients with HFrEF is crucial for reducing the risk of HFH and improving survival and QoL. Even if symptoms and/or LVEF improve, it is recommended that optimal FMT is continued as lifelong treatment. Only in very selected cases of HFrEF with complete normalization of LV volumes and LVEF, including natriuretic peptides and in the context of a clear treatable reversible cause of HF, gradual discontinuation may be considered.

Non-adherence to FMT can be multifactorial. Patient-related factors such as side-effects, drug interactions, economic difficulties, psychosocial issues, or poor health literacy may be contributing factors. However, healthcare-related inappropriate discontinuation of FMT should not be neglected. In general, incurrent illness or infections without haemodynamic compromise should not lead to down-titration or discontinuation of FMT. Asymptomatic or tolerable hypotension should not lead to down-titration or discontinuation of FMT but may require re-evaluation of diuretic use. It is recommended that patients with HFrEF and CKD maintain FMT, as several trials have shown beneficial effects on kidney endpoints as well as CV endpoints.[312] However, temporary discontinuation of MRAs/ARNIs/ACE-Is/ARBs and SGLT2-Is may be needed in cases with acute kidney injury and eGFR <15 mL/min/1.73 m^2. Severe hyperkalaemia (potassium >5.5 or >6 mmol/L) should lead to temporary down-titration or discontinuation of MRAs and/or ARNIs/ACE-Is/ARBs (see Supplementary data online, *Tables S4, S5* and *S9*). Temporary discontinuation of beta-blockers and ARNIs/ACE-Is/ARBs is advised in patients with severe haemodynamic instability. If FMT has been temporarily discontinued for less than 14 days, it should, in most cases, be safe to initiate FMT directly at the previously tolerated doses in stable patients. Euvolaemia is important prior to initiating beta-blockers.

6.1.7. Pharmacological therapy for heart failure with preserved ejection fraction

Foundational medical therapy for HFpEF includes SGLT2-Is and MRAs, as covered in *Section 6.1.2*.

Heart failure with preserved ejection fraction differs from HFrEF as patients tend to be older, and more often female with a high burden of comorbidities including AF, CKD, obesity, diabetes, and non-CV comorbidities.[313,314]

There are numerous potential causes of HFpEF and, as the pathophysiology of various HFpEF syndromes differ, they also require distinct individualized therapies. Furthermore, it is important to exclude other conditions that might mimic the HFpEF syndrome (e.g. HCM, amyloidosis) or realize that certain diseases have similar symptoms but may coexist with HFpEF (pulmonary disease, anaemia, obesity, and deconditioning). There are Class I recommendations for SGLT2-Is and MRAs to be used in all symptomatic patients with HF, and diuretics to be used to treat signs and symptoms of congestion. Other pharmacological agents, such as ACE-Is, ARBs, and beta-blockers, may be used particularly for comorbidities, as there is uncertainty of the effect on morbidity and mortality. Recently, in RCTs, treatment with the GLP-1 RA semaglutide or the dual glucose-dependent insulinotropic polypeptide (GIP)/GLP-1 RA tirzepatide improved QoL in addition to weight reduction in patients with HFpEF and obesity, independently of diabetes status (see *Section 10*).[315–317]

6.1.7.1. Angiotensin receptor–neprilysin inhibitors

In the PARAGON-HF trial, sacubitril–valsartan compared with valsartan did not achieve a significant reduction in the primary composite endpoint of CV death or total HFH in patients with symptomatic HF and LVEF ≥45%.[42] There was a reduction in

total HFH (rate ratio 0.85; 95% CI 0.72–1.00; $P = .056$) that also did not meet statistical significance. A meta-analysis of the PARADIGM-HF and PARAGON-HF trials showed a benefit of sacubitril–valsartan compared with valsartan in patients with an LVEF below 60-65%.[318,319] ARNIs therefore may be considered in HFpEF, especially in those with lower LVEF ranges.

Although renin–angiotensin system inhibition strategies with ACE-Is and/or ARBs have been successful in the treatment of HFrEF, clinical trials have not shown a clear benefit in HFpEF patients. In a meta-analysis of four trials evaluating ARBs in patients with HFpEF, there was no signal for benefit on CV death (HR 1.02), all-cause death (HR 1.01; 95% CI 0.92–1.11), or HFH (HR 0.92; 95% CI 0.83–1.02).[320] Candesartan was associated with a reduction in recurrent HFH until LVEF was over 60%.[40] Although no strong recommendation is given to start these agents in patients with HFpEF, many have coexisting indications for ACE-I/ARB therapy (hypertension/diabetes/CKD).

6.1.8. Pharmacological treatment in heart failure with improved ejection fraction

In patients with HFrEF, FMT and GDIT can result in improvement in symptoms, functional capacity, NT-proBNP levels and LVEF (i.e. reverse remodelling). However, in most patients, LV function and structural abnormalities do not fully normalize, and symptoms and biomarker abnormalities may persist or reoccur. Many patients deemed to have recovered from HFrEF with resolution of symptoms and improvement of LVEF and natriuretic peptide levels will relapse after withdrawal of FMT. TRED-HF was a small open-label trial in which phased withdrawal of FMT was conducted in patients with HFrEF and DCM whose LVEF had improved (but not necessarily normalized—from LVEF <40% to LVEF at least 50%) after treatment with FMT , their LV volume had normalized, and the NT-proBNP concentrations were reduced to <250 ng/L. Withdrawal of FMT resulted in relapse of HFrEF in 40% of the patients within 6 months, warranting reinitiation of therapy.[321,322] In contrast, the CATHEDRAL-HF trial—a single-centre, open-label pilot study—randomized 60 patients with similar characteristics to those in the TRED-HF trial to either phased withdrawal of FMT (excluding carvedilol) or continued FMT. Phased withdrawal did not result in a higher rate of HFrEF relapse.[323,324] Taken together, there is no solid evidence at this time to suggest that resolution of symptoms and improvement in cardiac function and biomarkers after treatment reflects actual recovery but, rather, remission, which requires FMT to be maintained.

Some causes of HF might be reversible (e.g. Takotsubo syndrome, arrhythmia-associated HF, myocarditis, HF caused by abnormal cardiac conduction). In these patients, where a completely reversible cause of HF is suspected and where complete normalization of LV function and volume has occurred after treatment of the reversible cause, including normalization of natriuretic peptides, a gradual trial of FMT withdrawal might be considered. However, this may be considered with caution and only in exceptional cases upon the request of the patient. The open-label, single-centre STOP-CRT trial indicated that gradual neurohumoral blocker withdrawal (and thus a CRT-only strategy) was feasible and safe in a small number of very selected patients with normalized LVEF after CRT.[325] Such withdrawal should only be done under frequent clinical, laboratory, and imaging control to rule out relapse of HF. One should take into consideration that often coexisting comorbidities warrant continuation of FMT. However, more and larger RCTs in this domain are needed to assess the clinical effect of withdrawal of each component of FMT in patients with HFrEF and improved LVEF.

Table 11 Evidence-based doses of disease-modifying drugs in key randomized trials in patients with heart failure

Drug	Starting dose	Target dose
ACE-Is		
Captopril[a]	6.25 mg t.i.d.	50 mg t.i.d.
Enalapril	2.5 mg b.i.d.	10–20 mg b.i.d.
Lisinopril[b]	2.5–5 mg o.d.	20–35 mg o.d.
Ramipril	1.25–2.5 mg b.i.d.	5 mg b.i.d.
Trandolapril[a]	0.5 mg o.d.	4 mg o.d.
ARNIs		
Sacubitril–valsartan	49/51 mg b.i.d.[c]	97/103 mg b.i.d.
ARBs		
Candesartan	4 mg o.d.	32 mg o.d.
Losartan	(12.5) 25–50 mg o.d.	150 mg o.d.
Valsartan	40 mg b.i.d.	160 mg b.i.d.
Beta-blockers		
Bisoprolol	1.25 mg o.d.	10 mg o.d.
Carvedilol	3.125 mg b.i.d.	25 mg b.i.d.[d]
Metoprolol succinate (CR/XL)	12.5–25 mg o.d.	200 mg o.d.
Nebivolol[e]	1.25 mg o.d.	10 mg o.d.

Continued

MRAs		
Steroidal		
Eplerenone	25 mg o.d.	50 mg o.d.
Spironolactone	12.5–25 mg o.d.[f]	50 mg o.d.
Non-steroidal		
Finerenone	10–20 mg o.d.[g]	20–40 mg o.d.[g]
SGLT2-Is		
Dapagliflozin	10 mg o.d.	10 mg o.d.
Empagliflozin	10 mg o.d.	10 mg o.d.
Other agents		
Digoxin[h]	62.5 µg o.d.	250 µg o.d.
Digitoxin[h]	0.07 mg o.d.	0.1 mg o.d.
Ivabradine	5 mg b.i.d.	7.5 mg b.i.d.
Vericiguat	2.5 mg o.d.	10 mg o.d.
Hydralazine/isosorbide dinitrate	37.5 mg t.i.d./20 mg t.i.d.	75 mg t.i.d./40 mg t.i.d.

The table provides initiation and target doses of FMT and AMT. For practical guidance in use of the different drugs, see Supplementary data online, *Tables S4–S9*.
ACE-I, angiotensin-converting enzyme inhibitor; AMT, additional medical therapy; ARB, angiotensin II receptor blocker; ARNI, angiotensin receptor–neprilysin inhibitor; b.i.d., bis in die (twice daily); CR, controlled release; CV, cardiovascular; eGFR, estimated glomerular filtration rate; FMT, foundational medical therapy; MI, myocardial infarction; MRA, mineralocorticoid receptor antagonist; o.d., omne in die (once daily); SGLT2-I, sodium–glucose co-transporter 2 inhibitor; t.i.d., ter in die (three times a day); XL, extended release.
[a]Indicates an ACE-I where the dosing target is derived from post-MI trials.
[b]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 optimal dose is uncertain.
[c]Sacubitril–valsartan may have an optional lower starting dose of 24/26 mg twice daily for those with a history of symptomatic hypotension, ACE-I naïve patients and patients with eGFR 30–60 mL/min/1.73 m^2.
[d]A maximum dose of 50 mg twice daily can be administered to patients weighing over 85 kg.
[e]Indicates a treatment not shown to reduce CV or all-cause death in patients with heart failure (or shown to be non-inferior to a treatment that does).
[f]Spironolactone has an optional starting dose of 12.5 mg in patients where kidney status or hyperkalaemia warrant caution.
[g]Finerenone has a different starting and target dose according to eGFR (10–20 mg, if eGFR ≤60 mL/min/1.73 m^2; 20–40 mg, if eGFR >60 mL/min/1.73 m^2).
[h]Digoxin/digitoxin should be titrated according to plasma levels.

Recommendation Table 5 — Recommendations for pharmacological management of chronic heart failure (see *Evidence Tables 29–41*)

Recommendations	Class[a]	Level[b]
All patients with HF, independent of LVEF		
An SGLT2-I (dapagliflozin or empagliflozin) is recommended in patients with symptomatic HF independent of LVEF to reduce the risk of HFH or CV death.[241–245,326]	I	A
An MRA (sMRA for HFrEF and sMRA/nsMRA for HFpEF) is recommended in patients with symptomatic HF independent of LVEF to reduce the risk of HFH or CV death.[c43,254–257]	I	A
Dynamic individualized dosing of loop diuretics according to volume status is recommended in patients with HF and signs and/or symptoms of congestion to alleviate HF symptoms, improve exercise capacity, and reduce the risk of HFH.[d 327–329]	I	A
Uptitration of FMT at least every 1–2 weeks in patients with HF, guided by symptoms, vital signs, and laboratory findings, to achieve optimal target doses shown to be efficacious in RCTs is recommended to reduce the risk of HFH or death.[274,311]	I	C
Continuation of FMT at the highest tolerated doses is recommended in all patients with HF, including those who become asymptomatic or with LVEF improvement, in order to reduce the risk of HFH and death.[321]	I	C
HFrEF		
A beta-blocker is recommended in stable patients with symptomatic HFrEF to reduce the risk of HFH and death.[e 36,287–293,330]	I	A
An ACE-I or ARNI is recommended in patients with symptomatic HFrEF to reduce the risk of HFH and death.[e 274–278]	I	A
Switching from an ACE-I or ARB to an ARNI is recommended in patients with symptomatic HFrEF to reduce the risk of HFH and death.[e 278]	I	B1
An ARB is recommended in patients with symptomatic HFrEF to reduce the risk of HFH and CV death if they are unable to tolerate an ACE-I or ARNI.[e 284–286,331]	I	A
A cardiac glycoside (digoxin or digitoxin) should be considered in patients with symptomatic HFrEF with LVEF ≤40%, despite optimal FMT, to reduce the risk of HFH.[303,304]	IIa	B1

Continued

Ivabradine should be considered for patients with symptomatic HFrEF, LVEF ≤35%, in sinus rhythm, resting heart rate >70 b.p.m., on the highest tolerated ACE-I/ARNI, MRA, SGLT2-I, and beta-blockers to reduce the risk of HFH or CV death.[294]	IIa	B1
Ivabradine should be considered in patients with symptomatic HFrEF, LVEF ≤35%, in sinus rhythm, who are unable to tolerate a beta-blocker, on the highest tolerated ACE-I/ARNI and MRA to reduce the risk of HFH or CV death.[294]	IIa	C
Hydralazine and isosorbide dinitrate should be considered in self-identified black patients with symptomatic HFrEF with LVEF ≤40% on top of optimal FMT to reduce the risk of HFH and death.[300]	IIa	B2
Hydralazine and isosorbide dinitrate may be considered in patients with symptomatic HFrEF with LVEF ≤40% who cannot tolerate ARNI, ACE-I, or ARB to reduce the risk of HFH and death.[301]	IIb	C
Vericiguat may be considered in patients with symptomatic HFrEF and LVEF <45% despite treatment with optimal FMT to reduce the risk of HFH and CV death.[295,297,298]	IIb	B1
Gradual discontinuation of FMT under frequent clinical, laboratory, and imaging surveillance may be considered in highly selected patients who are asymptomatic with complete normalization of LV function and volume as well as natriuretic peptide levels after specific treatment of reversible causes of HF, in order to accommodate patient preference.[325]	IIb	C
HFpEF		
ACE-I/ARB/ARNI may be considered in patients with symptomatic HFpEF to reduce the risk of HFH.[39,40,42,319,332–337]	IIb	C

ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; ARNI, angiotensin receptor–neprilysin inhibitor; CV, cardiovascular; FMT, foundational medical therapy; HF, heart failure; HFH, heart failure hospitalization; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; LV, left ventricular; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist; nsMRA, non-steroidal mineralocorticoid receptor antagonist; RCT, randomized clinical trial; SGLT2-I, sodium–glucose co-transporter 2 inhibitor; sMRA, steroidal mineralocorticoid receptor antagonist.

[a]Class of recommendation.

[b]Level of evidence.

[c]The evidence for using MRAs in patients with HFrEF is based on RCTs conducted with sMRAs (spironolactone and eplerenone), whereas the evidence for patients with HFpEF originates from a meta-analysis of RCTs using both steroidal (spironolactone) and non-steroidal MRAs (finerenone).

[d]This recommendation is considered by the Task Force to have level of evidence A due to clear clinical effectiveness. Dynamic dosing of loop diuretics has been widely accepted as effective and therefore no adequately powered RCTs have ever been conducted or are likely to be conducted for ethical reasons.

[e]No large prospective RCT has been performed on the use of beta-blockers, ACE-I/ARNI/ARB exclusively in patients with LVEF 41%–49%.

6.2. Guideline-directed interventional therapies for chronic heart failure

The term GDIT includes all guideline-directed interventional therapies for HF (see *Section 3*). In this section, we provide recommendations for ICDs and CRT. Other implantable devices, for which recommendations have not been made, will be discussed at the end of this section. *Section 7* provides recommendations for interventional therapies in the setting of DHF, and *Section 8* provides recommendations for interventional therapies in the setting of advanced HF. *Section 9* covers comorbidity-specific interventional therapies.

6.2.1. Implantable cardioverter-defibrillators

The recognition that arrhythmic sudden cardiac death (SCD) accounted for ~30%–60% of all deaths in the early HF trials[338] paved the way for the use of ICDs in patients with HFrEF. Antiarrhythmic drugs, such as amiodarone and dronedarone, are effective in reducing ventricular arrhythmias, but they do not prolong survival and may shorten it.[339,340] In contrast, ICDs are effective in preventing SCD and prolonging survival in patients with HFrEF who are at high risk of SCD.[340–344]

6.2.1.1. Secondary prevention of sudden cardiac death

Unlike antiarrhythmic drugs such as amiodarone, ICDs reduce mortality in cardiac arrest survivors and those with sustained ventricular arrhythmias, regardless of LVEF or presence of HF.[345–348] Recommendations for secondary prevention ICD implantation are provided in the *2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death*.[119] Cardiomyopathy-specific recommendations for secondary prevention ICD implantation are provided in the *2023 ESC Guidelines for the management of cardiomyopathies*.[124]

6.2.1.2. Primary prevention of sudden cardiac death in heart failure

In the SCD-HeFT trial, compared to amiodarone, ICD reduced all-cause death by 23% in patients with HFrEF.[340] In MADIT-II, 1232 patients were randomized to an ICD or control, and ICD therapy reduced all-cause death by 31%.[342] Although the risk of SCD has declined over time, the residual risk of SCD is still high (annual rate of 3.3 per 100 patient-years in PARADIGM-HF), warranting primary prevention ICD implantation in patients with HFrEF deemed at high risk of SCD.[349] For details, see Supplementary data online, *Section S3.1.1.1*.[340,342,349–352]

6.2.1.3. Patient selection for implantable cardioverter-defibrillator therapy

Selection of patients with HFrEF for ICD implantation should be based on LVEF thresholds established in RCTs and underlying aetiology, as individuals with non-ischaemic HF may derive less benefit than those with ischaemic heart disease.[341,343,353,354] However, a meta-analysis of RCTs demonstrated an overall survival benefit, even in patients with non-ischaemic HF.[344] The effect of ICD treatment depends on the competing risk of non-sudden death, both CV and non-CV. Thus, in patients with many comorbidities and older age, the benefit of ICD therapy may be substantially lower.[355] Shared decision-making is essential when considering ICD implantation in patients with HF.

Both patient preferences and clinical factors should be carefully considered. Individualized patient information on the potential risks and benefits should be provided to support an informed decision.

The presence and the extent of myocardial fibrosis, genotypes, and additional factors may help arrhythmic risk stratification in patients with cardiomyopathies.[124,356,357]

6.2.1.4. Timing of implantable cardioverter-defibrillator therapy

Two studies have shown that primary prevention ICD implantation within 40 days of an MI does not improve outcomes.[358,359] A 3-month period after uptitration of FMT before considering ICD implantation is reasonable. Delaying ICD implantation carries a risk of SCD at 2%–4% by 6 months and ~7% by 1 year.[360]

6.2.1.5. Implantable cardioverter-defibrillator generator replacement

As with FMT, the commitment to GDIT is in most cases lifelong. Implantation of an ICD commits the patient to lifelong monitoring and the need for generator replacements. The lifelong risk of complications should be considered in the decision to implant. A further question is whether ICD generators should be replaced in patients who have not had appropriate ICD therapies. ICD shocks occur in more than 15% of patients after generator replacement in those who have not had an appropriate ICD shock during the lifetime of their first ICD generator.[361] Even in patients with LVEF improvement after FMT and CRT, a considerable residual risk of SCD remains.[362,363] As HFrEF and comorbidities progress, the benefit of ICD therapy may diminish. The need for ICD and the risk of SCD should be reconsidered over time and prior to every generator replacement, taking risk of SCD, remaining lifespan of the patient, risk of complications, competing risks of death due to comorbidities, frailty, and patient choice into account.[364–367]

6.2.1.6. Non-transvenous implantable cardioverter-defibrillator and wearable cardioverter-defibrillator

In a subcutaneous ICD (S-ICD), the lead is extravascular and, therefore, not prone to intravascular infection. It is particularly attractive in patients with difficult venous access or those who are at risk of infection. The S-ICD is comparable to transvenous ICDs in terms of efficacy, complication rates, and inappropriate shock rates.[368,369] Importantly, the S-ICD cannot treat bradyarrhythmia (other than post-shock pacing) and does not provide anti-tachycardia pacing.

The extravascular ICD consists of a generator implanted in a subfascial or submuscular pocket and a substernally deployed lead.[370] A notable advantage over the S-ICD is that the generator is similar in size to a transvenous ICD. Long-term data on efficacy and safety are required.

A wearable defibrillator may be considered in patients deemed at especially high risk of SCD or as a bridge to decision for ICD implantation, although no mortality benefit has been shown in RCTs[371,372] (see Supplementary data online, *Section S3.1.1.2*).

Recommendation Table 6 — Recommendations for implantable cardioverter-defibrillator implantation (see *Evidence Tables 42–48*)

Recommendations	Class[a]	Level[b]
An ICD is recommended in patients who have recovered from a ventricular arrhythmia causing haemodynamic instability (secondary prevention), 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 an MI, to reduce the risk of sudden death and all-cause death.[346]	I	A
An ICD is recommended in patients with symptomatic HFrEF (NYHA class II/III) of an ischaemic aetiology (unless they have had an MI in the prior 40 days), and an LVEF ≤35% despite ≥3 months of optimal FMT, provided they are expected to survive longer than 1 year with good functional status, to reduce the risk of sudden death and all-cause death.[340,342,373,374]	I	B1
An ICD should be considered in patients with symptomatic HFrEF (NYHA class II/III) of a non-ischaemic aetiology, and an LVEF ≤35% despite ≥3 months of optimal FMT, provided they are expected to survive longer than 1 year with good functional status, to reduce the risk of sudden death and all-cause death.[340,341,344,375]	IIa	B1
Prior to generator replacement for CIEDs, a shared decision-making process between the patient and a cardiologist experienced in CIEDs and HF should be considered to ensure that the balance between risks and benefits still favour a CIED.[376–380]	IIa	C
A wearable cardioverter-defibrillator may be considered in patients with HF who are at risk of sudden cardiac death for a limited period in order to increase survival as a bridge to decision for permanent ICD implantation or while listed for heart transplantation.[381–384]	IIb	C
ICD implantation for primary prevention is not recommended within 40 days of an MI as implantation during this period does not improve prognosis.[358,359]	III	B1
ICD implantation 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 heart transplantation.[374,385–387]	III	C

CIED, cardiac implantable electronic device; CRT, cardiac resynchronization therapy; FMT, foundational medical therapy; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; ICD, implantable cardioverter-defibrillator; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NYHA, New York Heart Association.
[a]Class of recommendation.
[b]Level of evidence.

6.2.2. Cardiac resynchronization therapy

In carefully selected patients with HFrEF, CRT improves cardiac function, QoL, and reduces hospitalizations and death. Landmark RCTs support CRT use across a range of HF severity.[388–398]

The first RCT to address the effects of CRT on morbidity and mortality was COMPANION[388] in which CRT with pacemaker (CRT-P) and CRT with defibrillator (CRT-D) reduced the composite endpoint of all-cause death and hospitalizations for any cause by 20%. A reduction in all-cause death was shown with CRT-D, but not with CRT-P. In contrast, in the CARE-HF trial,[392] which randomized participants to medical therapy with or without CRT-P, CRT-P reduced all-cause death and HFH. In the MADIT-CRT trial, in which 1820 patients in NYHA classes I and II were randomized to CRT-D or ICD, CRT-D reduced all-cause death or HF events by 34%.[397] In the REVERSE trial,[396] which also involved patients in NYHA classes I and II with primary prevention ICD indications, CRT improved LVEF and reduced HFH. Importantly, in the 5-year follow-up of REVERSE, annualized death was low at 2.9% in patients randomized to 'CRT-on'.[399] Together, these findings have provided compelling evidence for using CRT across the spectrum of severity of HFrEF. For landmark trials of CRT, see Supplementary data online, *Table S10*.[388,389,392,396–398,400–412] *Figure 10* provides an overview of factors to consider when evaluating patients for CRT.

6.2.2.1. Cardiac resynchronization therapy for heart failure caused by abnormal cardiac conduction

Heart failure associated with abnormal cardiac conduction is defined as LV dysfunction due to conduction abnormalities (*Figure 9* and *Section 5.3.3*). In patients with HF, where no other cause of HF other than abnormal cardiac conduction can be found, and there is a low likelihood of LVEF improvement, planning for CRT implantation may be considered early—even before full FMT uptitration.

6.2.2.2. Right ventricular pacing-induced heart failure

As expected from the effects of ectopic cardiac stimulation, RV pacing leads to HFrEF in some patients.[202,413] The incidence of pacemaker- or RV pacing-induced HF varies between 5.9% and 39%, depending on the definition.[202,236–239] In the recent BUDAPEST-CRT Upgrade trial, upgrading to CRT-D significantly reduced death and HFH in patients with ≥20% RV pacing burden and QRS ≥150 ms (HR 0.27; *P*<.001). The BUDAPEST-CRT Upgrade trial is the first RCT and included only 360 patients in total. Therefore, CRT-D upgrade should be considered in such patients.[202,237,238,412,414]

6.2.2.3. Timing of cardiac resynchronization therapy implantation

The timing of CRT in relation to hospitalizations has not been addressed by RCTs. In an observational study of 64 968

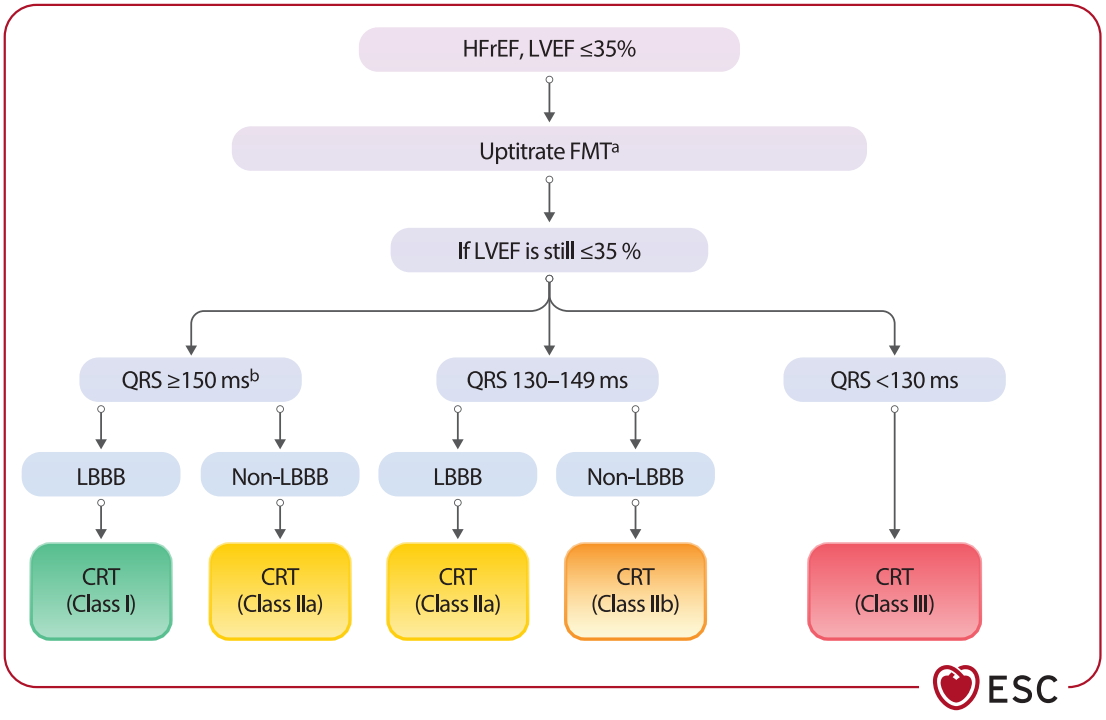

Figure 10 Indications for cardiac resynchronization therapy in heart failure. CRT, cardiac resynchronization therapy; FMT, foundational medical therapy; HFrEF, heart failure with reduced ejection fraction; ICD, Implantable cardioverter-defibrillator; LBBB, left bundle branch block; LVEF, left ventricular ejection fraction. In the decision on device implantation consider the following: patient preference, likely benefit of ICD/CRT at the patient's age, frailty and comorbidities, risk of complications, venous access issues. [a]Uptitration to the highest tolerated doses of HFrEF FMT (see *Table 11*). [b]Initiation of FMT and planning for CRT implantation may be considered simultaneously in patients with symptomatic HFrEF, an LBBB with QRS ≥150 ms, and LVEF ≤35%, to improve symptoms and reduce morbidity and mortality, although reassessment of LVEF should be conducted prior to CRT implantation. (Class IIb).

patients undergoing CRT, the combined endpoint of all-cause death and HFH was lowest in patients with no HFH prior to implantation (9.7 per 100 person-years) and those who had CRT during the first HFH (11.1 per 100 person-years) compared with patients who had a CRT implantation within a year of their first HFH (17.3 per 100 patient-years).[415] In a study of 15 619 CRT-eligible patients with HF in the Get With The Guidelines-HF registry, all-cause death was lower in those who received CRT implantation during HFH (adjusted HR 0.63; *P*<.0001) compared with patients who did not have CRT.[416] A lower rate HF rehospitalization was observed in patients with CRT implanted during the first hospitalization (adjusted HR 0.64; *P*<.0001), but not in those prescribed CRT at discharge. As HFH is a critical step in the progression of HF, it may be beneficial to implant CRT at an early stage in patients who are most likely to benefit (LVEF ≤35%, LBBB with QRS ≥150 ms), ideally before an HFH has occurred.

Recommendation Table 7 — Recommendations for cardiac resynchronization therapy implantation (see *Evidence Tables 49–58*)

Recommendations	Class[a]	Level[b]
CRT is recommended in patients with symptomatic HFrEF, LVEF ≤35%, despite optimal FMT, in SR with LBBB and QRS duration ≥150 ms in order to improve symptoms and reduce the risk of hospitalizations and death.[388–398]	I	A
An upgrade to CRT should be considered in patients with an LVEF ≤35% who have received a conventional pacemaker or an ICD and subsequently develop worsening HF despite optimal FMT and who have a significant proportion of RV pacing in order to reduce the risk of HFH or death.[412]	IIa	B1
CRT, rather than RV pacing, should be considered in 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 the risk of HFH and death.[409]	IIa	B1
CRT should be considered in patients with symptomatic HFrEF, LVEF ≤35%, despite optimal FMT, who are in SR with non-LBBB QRS morphology and QRS duration ≥150 ms in order to improve symptoms and reduce morbidity and death.[388–398]	IIa	C
CRT should be considered in patients with symptomatic HFrEF, LVEF ≤35%, despite optimal FMT, who are in SR with LBBB QRS morphology and QRS duration of 130–149 ms in order to improve symptoms and reduce morbidity and death.[390,417]	IIa	C
CRT may be considered in patients with symptomatic HFrEF, LVEF ≤35%, despite optimal FMT, who are in SR with non-LBBB QRS morphology and QRS duration of 130–149 ms in order to improve symptoms and reduce morbidity and death.[391,397]	IIb	C
Initiation of FMT and planning for CRT implantation may be considered simultaneously in patients with symptomatic HFrEF, an LBBB with QRS ≥150 ms, and LVEF ≤35%, to improve symptoms and reduce morbidity and death, although reassessment of LVEF should be conducted prior to CRT implantation.[418–423]	IIb	C
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.[410,424,425]	III	A

Continued

AV, atrioventricular; CRT, cardiac resynchronization therapy; FMT, foundational medical therapy; HF, heart failure; HFH, heart failure hospitalization; 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; RV, right ventricular; SR, sinus rhythm.
[a]Class of recommendation.
[b]Level of evidence.

6.2.3. Conduction system pacing

Conduction system pacing (CSP), including His bundle and left bundle branch area pacing, aims to engage the Purkinje network for rapid and synchronous LV activation.[426] Left bundle branch area pacing may prove to be a feasible alternative to CRT when implantation is challenging. However, no RCT with patient-centred outcomes has evaluated the efficacy or long-term safety of CSP in HFrEF. Therefore, no recommendations can currently be made. See *Evidence Table 22* and Supplementary data online, *Section S3.1.3* for further details.[427–433]

6.2.4. Cardiac implantable electronic device programming and follow-up

In the same way that FMT implies lifelong adherence to drugs, a CIED requires a lifelong commitment to device follow-up. For the clinician, skills in interpretation of device-derived electrograms, device-related problem solving, and programming are essential.[434,435]

For ICDs, routine defibrillation testing of shock efficacy does not reduce arrhythmic death and is therefore no longer recommended.[436] Programming a high-rate cut-off and long detection intervals between detection of ventricular tachycardia and anti-tachycardia pacing or shocks dramatically reduce inappropriate shocks and unnecessary ICD therapy.[436,437] At follow-up, the RV pacing burden as well as the intrinsic QRS duration are an important focus for deciding whether to upgrade from an ICD to a CRT-D device.

In patients with a CRT device, regular follow-up and optimization should be implemented, as CRT programming and FMT may require further optimization after implantation.[435] Appropriate programming of atrioventricular intervals and optimal LV lead vectors are required to optimize CRT response. In patients

with AF, the percentage of effective biventricular pacing (without fusion or pseudofusion) is an important focus. Further details on CRT follow-up and optimization are outlined in an HFA position paper.[435]

6.2.5. Other cardiac implantable electronic devices

In a small unblinded RCT, cardiac contractility modulation marginally improved peak oxygen uptake and QoL in patients with advanced HFrEF and a QRS <130 ms.[438] In a small pilot study, cardiac contractility modulation improved the Kansas City Cardiomyopathy Questionnaire (KCCQ) score by 18 points in patients with HFpEF.[439] No clinical outcome studies have emerged. Similarly, baroreceptor activation therapy led to improvements in 6-min walk distance and QoL in an unblinded RCT, but long-term clinical outcome data were neutral.[440,441]

Current evidence for these CIEDs is insufficient to support guideline recommendations. Although promising, these findings require confirmation in large, well-designed trials.[439]

6.2.6. Other implantable devices

It has been hypothesized that an interatrial shunt could improve HF symptoms and outcomes by decompressing the left atrium. In the RELIEVE-HF study, 508 patients with HF and predominantly NYHA class III symptoms and any LVEF were randomized to transcatheter shunt implantation vs a sham procedure.[442] After 2 years, no difference emerged in the primary effectiveness outcome [hierarchical composite ranking of all-cause death, cardiac transplantation or LV assist device (LVAD) implantation, HFH, outpatient WHF events, and change in QoL]. Importantly, patients with reduced LVEF had fewer adverse CV events with shunt treatment, whereas patients with HFpEF had more CV events. In the REDUCE LAP-HF II study in patients with LVEF ≥40%, the atrial shunt device was no better than the sham procedure in terms of the hierarchical composite of CV death or non-fatal ischaemic stroke at 12 months, rate of total HF events up to 24 months, and change in QoL at 12 months.[443]

7. Decompensated heart failure

7.1. Definition and epidemiology

Decompensated HF is defined as acute or gradual onset of symptoms and/or signs of HF, severe enough to require urgent medical attention and treatment initiation or intensification. DHF can lead to an unplanned hospital admission, an emergency department visit, or an unplanned ambulatory visit requiring treatment for HF. DHF may present as either worsening of pre-existing HF or as the initial manifestation of the disease (*de novo* HF). In the setting of patients with pre-existing HF, WHF is characterized by a deterioration in the symptoms and/or signs of HF and represents an event in HF progression, whereas DHF is specifically characterized by the requirement for treatment modification.[444]

Decompensated HF is associated with a high risk of death: 3%–10% during HF admission; 20%–30% at 1 year, >50% after 5 years.[445–450] Compared to DHF occurring in patients with pre-existing HF, *de novo* DHF may be associated with higher in-hospital death, but lower post-discharge death and rehospitalization rates.[451–453] Following a hospitalization for DHF, 1-year rehospitalization rates range between 35% and 44%.[447,448,453–455] In addition, up to 50% of patients with HF require intensification of treatment in the emergency service or in outpatient settings.[456–462]

7.2. Diagnosis

Decompensated HF requires prompt diagnosis to ensure early treatment.[463] If DHF is suspected, assessment of signs and symptoms of congestion and hypoperfusion must be done at the first medical contact. Non-invasive blood pressure, respiratory rate, pulse oximetry monitoring, body temperature measurement, and ECG should be performed early.[464] In haemodynamically unstable patients with suspected hypoperfusion, assessment of serum lactate levels should be performed promptly.[465]

The currently recommended, non-age-adjusted, natriuretic peptide 'rule-out' thresholds for DHF are: NT-proBNP <300 pg/mL, or BNP <100 ng/mL, or MR-proANP <120 pg/mL.[157,466–469] However, if clinical suspicion of HF remains despite values below 'rule-out' thresholds, specialist assessment and echocardiogram should be sought. Age-related thresholds for NT-proBNP, above which DHF is considered 'likely', are given in the footnote of *Figure 11*. In the older population, using the age-related NT-proBNP threshold may aid appropriate triage and help reduce unnecessary exams. NT-pro-BNP >5000 pg/mL indicates very high risk, and admission is generally recommended. For other laboratory tests and investigations for patients with suspected DHF, see Supplementary data online, *Table S11*. Initial investigations are carried out to diagnose DHF and rapidly detect any possible triggers.

Transthoracic echocardiography should be performed in patients with high levels of NT-proBNP and in those for whom there is a high clinical suspicion of DHF.

Where trained personnel are available, lung ultrasound identifies patients with pulmonary congestion and has utility in serial assessments.[470–473]

7.3. Clinical presentation

Congestion and hypoperfusion are two major clinical manifestations of DHF.[447,453] Congestion may stem from fluid overload, fluid redistribution, increased vascular permeability, and increased intracardiac pressures. Different clinical, laboratory, and imaging utilities should be used to assess congestion and its dynamic changes (see Supplementary data online, *Table S12*). Hypoperfusion is not a synonym for hypotension,[474,475] although patients with DHF and hypotension also experience inadequate perfusion. An objective marker, serum lactate, may help identify patients with peripheral hypoperfusion and monitor therapy.[465] Signs and symptoms associated with congestion and hypoperfusion are reported in *Table 12*.

Four categories of DHF can be recognized based on clinical presentation: decompensated left-sided HF, decompensated right-sided HF, acute pulmonary oedema (APO), and cardiogenic shock (CS).

Pathophysiology, timing of onset, and speed of deterioration differ between the four categories, but possible overlaps exist.

7.3.1. Decompensated left-sided heart failure

Decompensated left-sided HF, in its classical clinical presentation, is characterized by a gradual onset of signs and symptoms with accumulating congestion as the primary pathophysiological process.[476] It may occur in patients across the spectrum of LVEF and, in advanced stages, can lead to RV dysfunction and

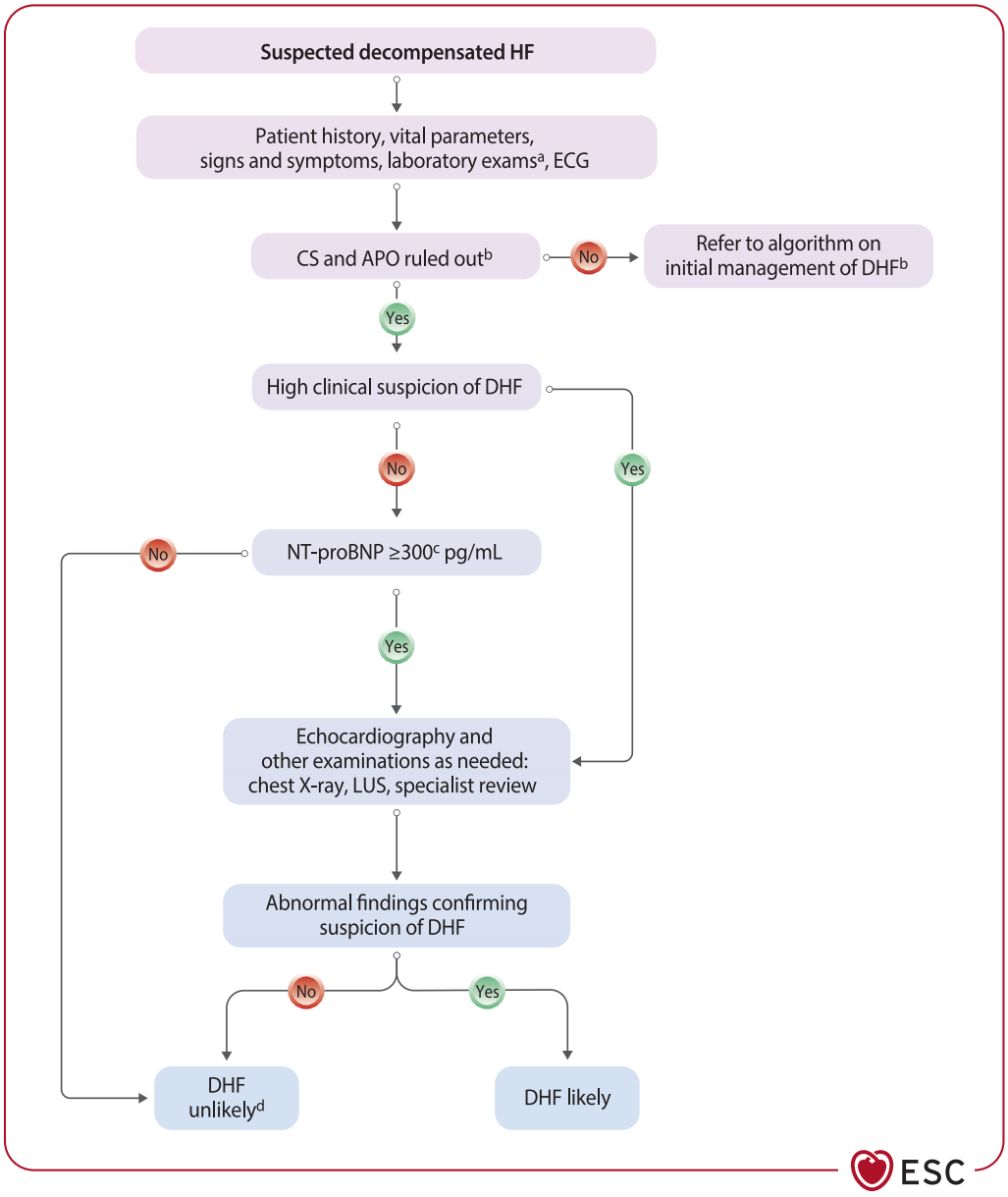

Figure 11 Diagnosing decompensated heart failure. APO, acute pulmonary oedema; BNP, B-type natriuretic peptide; CS, cardiogenic shock; DHF, decompensated heart failure; ECG, electrocardiogram; LUS, lung ultrasound; MR-proANP, mid-regional pro-atrial natriuretic peptide; NT-proBNP, N-terminal pro-B-type natriuretic peptide. [a]See Supplementary data online, Table S11 for more details on admission investigations in DHF. [b]In case of APO or CS, early treatment is recommended. [c]The currently recommended, non-age-adjusted, natriuretic peptide 'rule-out' thresholds for DHF are: NT-proBNP <300 pg/mL, or BNP <100 ng/mL, or MR-proANP <120 pg/mL. Combination with age-related 'likely' rule-in thresholds may reduce unnecessary exams: NT-proBNP >450 pg/mL (<50 years), NT-proBNP >900 pg/mL (50–74 years), NT-proBNP >1800 pg/mL (>74 years). [d]In case of DHF unlikely, look for other causes of symptoms.

decompensated right-sided heart failure. Thus, both pulmonary and peripheral congestion may be present. Hypoperfusion can occur.[447,465,476] Treatment is mainly based on decongestion by means of diuretic therapy. Site of care can be outpatient clinic or hospital.

7.3.2. Decompensated right-sided heart failure

Decompensated isolated right-sided HF is characterized by elevated RV and right atrial pressures, leading to systemic congestion and, in more advanced stages, hypoperfusion. It is often associated with tricuspid regurgitation (TR) and can also impair LV filling and reduce systemic cardiac output through ventricular interdependence. Pulmonary embolism and acute MI involving the right ventricle are possible causes of decompensated right HF that need to be excluded during initial evaluation and treated. Fluid overload, elevated central venous pressures, and multiorgan dysfunction are the most frequent elements of the clinical picture of the disease. In the most severe cases, it can manifest as a refractory shock. The RV function and its effect on other organs (kidney, liver) usually determine the clinical

Table 12 Signs, symptoms, and altered laboratory tests in congestion and hypoperfusion profiles

Left-sided congestion	Right-sided congestion	Hypoperfusion
Dyspnoea Orthopnoea Cough Tachypnoea Rales S3 Pleural effusion Elevated natriuretic peptides	Peripheral oedema Abdominal distension Hepatomegaly Jugular vein distension Hepatojugular reflux Pleural effusion Elevated serum creatinine Elevated bilirubin, ALP, GGT Slightly elevated natriuretic peptides	Cold, sweaty extremities Pale skin Dizziness Mental confusion Oliguria Narrow pulse pressure Elevated serum lactate Elevated serum creatinine Elevated aminotransferase

ALP, alkaline phosphatase; GGT, gamma glutamyl transpeptidase.

Table 13 SCAI classification for cardiogenic shock

STAGE A **'At risk'**	A patient who is not currently experiencing signs or symptoms of CS but is at risk for development of CS.
STAGE B **'Beginning/pre-shock' cardiogenic shock**	A patient who has clinical evidence of hemodynamic instability (including relative hypotension or tachycardia) without hypoperfusion.
STAGE C **'Classic' cardiogenic shock**	A patient that manifests with hypoperfusion requiring intervention (inotrope, vasopressor, or mechanical support).
STAGE D **'Deteriorating'**	A patient that is similar to stage C but deteriorating with failure to respond to initial interventions.
STAGE E **'Extremis'**	A patient with refractory shock or cardiac arrest requiring multiple simultaneous acute interventions, including CPR.

CPR, cardiopulmonary resuscitation; CS, cardiogenic shock; MI, myocardial infarction; SCAI, Society for Cardiovascular Angiography and Interventions.

trajectory, thus a close monitoring of kidney and hepatic function is needed. Onset can be gradual or rapid depending on causes, triggers, and precipitating factors. Optimal care requires a multifaceted approach, including diuretics, judicious fluid management, appropriate use of inotropes and vasopressors, and mechanical circulatory support (MCS) when indicated.

7.3.3. Acute pulmonary oedema

Acute pulmonary oedema is a life-threatening condition that needs prompt, optimally targeted rescue therapy.[477,478] Clinical criteria for the diagnosis of APO include signs and symptoms of respiratory distress [dyspnoea with orthopnoea, respiratory failure (hypoxaemia with or without hypercapnia), tachypnoea (>25 breaths/min), and increased work of breathing], caused by massive pulmonary congestion, which typically develops over a short period of time.[477] The major objectives of the treatment are relieving pulmonary congestion, treating respiratory insufficiency, and ensuring peripheral perfusion. The mechanism of development of congestion is complex, with a predominant fluid redistribution that implies pulmonary congestion without total volume overload, primarily due to blood shift into the pulmonary circulation. Such patients usually do not need high doses of diuretics, but they may need vasodilators. The cause of decompensation should be investigated in every patient, and causal treatment, if possible, is imperative.

7.3.4. Cardiogenic shock

Cardiogenic shock is defined as a state of critical end-organ hypoperfusion caused by primary cardiac dysfunction.[479–481]

The Shock Academic Research Consortium (SHARC) consensus defines CS as a cardiac disorder that results in both clinical and biochemical evidence of sustained tissue hypoperfusion.[482] Generally, CS is characterized by hypoperfusion and hypotension; however, no specific blood pressure cut-off is defined, as CS is a complex clinical condition, involving many parameters and nuances. Thus, any arbitrary blood pressure threshold will have inherent limitations. CS may also present as hypoperfusion with normotension, which has better prognosis than hypotensive CS.[483,484]

Importantly, septic and hypovolaemic shock also manifests with hypotension and end-organ hypoperfusion, and mixed forms of shock often exist simultaneously.[480,485] Clinical features of hypoperfusion are reported in *Table 12*. Biochemical manifestation of inadequate tissue perfusion is best measured by arterial lactate, where a value of >2 mmol/L is required.[479,480] Additional markers used in assessment of hypoperfusion are acute kidney injury and/or acute hepatic injury.[480]

The Society for Cardiovascular Angiography and Interventions introduced a staging scheme—SCAI classification—to address the severity of CS.[479] Based on this, there are five categories of CS: (A) at risk, (B) pre-shock, (C) classic, (D) deteriorating, and (E) extremis (*Table 13*).

7.4. General management

In-hospital management of DHF can be divided into three general phases (*Figure 12*). Importantly, each clinical category of DHF has different trajectories through these phases. For instance, CS patients usually remain in phase 1 for several days and may never reach phase 2.[474] On the other hand, patients with uncomplicated decompensated left-sided or right-sided HF or APO can experience quick transition through all phases of treatment.

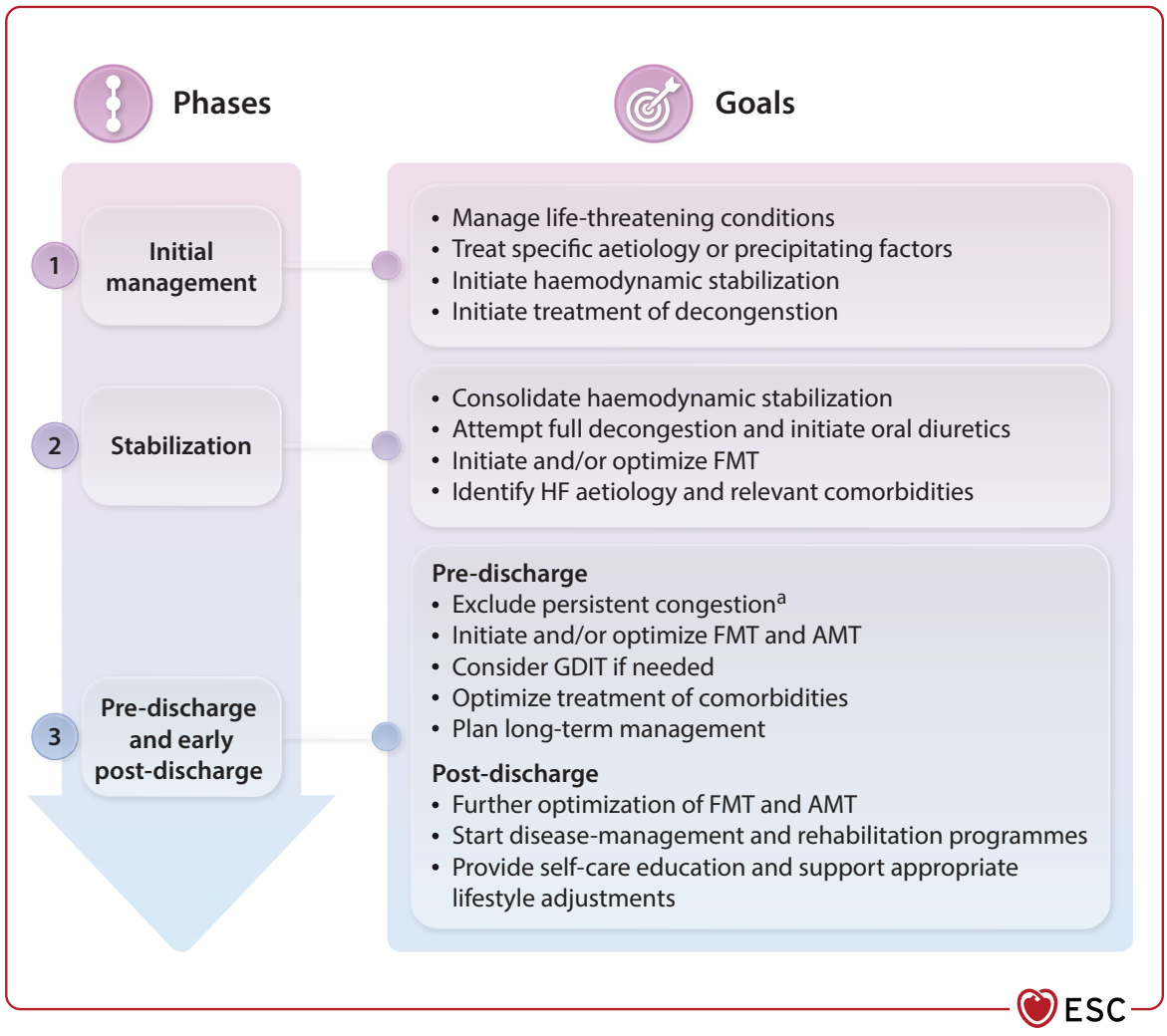

Figure 12 Phases and goals for in-hospital management of decompensated heart failure. AMT, additional medical therapy; FMT, foundational medical therapy; GDIT, guideline-directed interventional therapy; HF, heart failure. [a]See *Figure 14*.

7.4.1. Phase 1 (initial management)

The primary objectives in phase 1 are reported in *Figure 12*. In many cases, this phase starts in pre-hospital settings. Pre-hospital management should not delay the rapid transfer of the patient to the most appropriate medical setting, where further work-up is undertaken.

Patients should be triaged based on their haemodynamic and clinical status to determine the appropriate level of care and monitoring requirements. For patient risk stratification, specific scores have been proposed, but they need further validation (see Supplementary data online, *Section S4.2.1*).[486,487]

In patients with suspicion of CS and with a potential indication for temporary MCS, consultation with the Shock Team is recommended (see *Section 7.5.11*).[488] In these patients, as well as in those with other life-threatening conditions, the diagnostic work-up and appropriate rescue pharmacological and non-pharmacological treatment should be initiated promptly and simultaneously (*Figure 13*). Identification and possible treatment of acute causes is crucial.[118,119,489–491] Combination and timing of different treatments depend on clinical presentation (*Figure 13*). In patients already receiving FMT, continuation and/or rapid reintroduction as soon as possible is recommended. Discontinuation of FMT is not recommended unless there are clear signs of hypoperfusion or specific clinical indications. Monitoring during and after initial stabilization is mandatory (see Supplementary data online, *Table S12*).

7.4.2. Phase 2 (stabilization)

The primary objective of this phase is to maintain and enhance the patient's haemodynamic status and, once the patient is

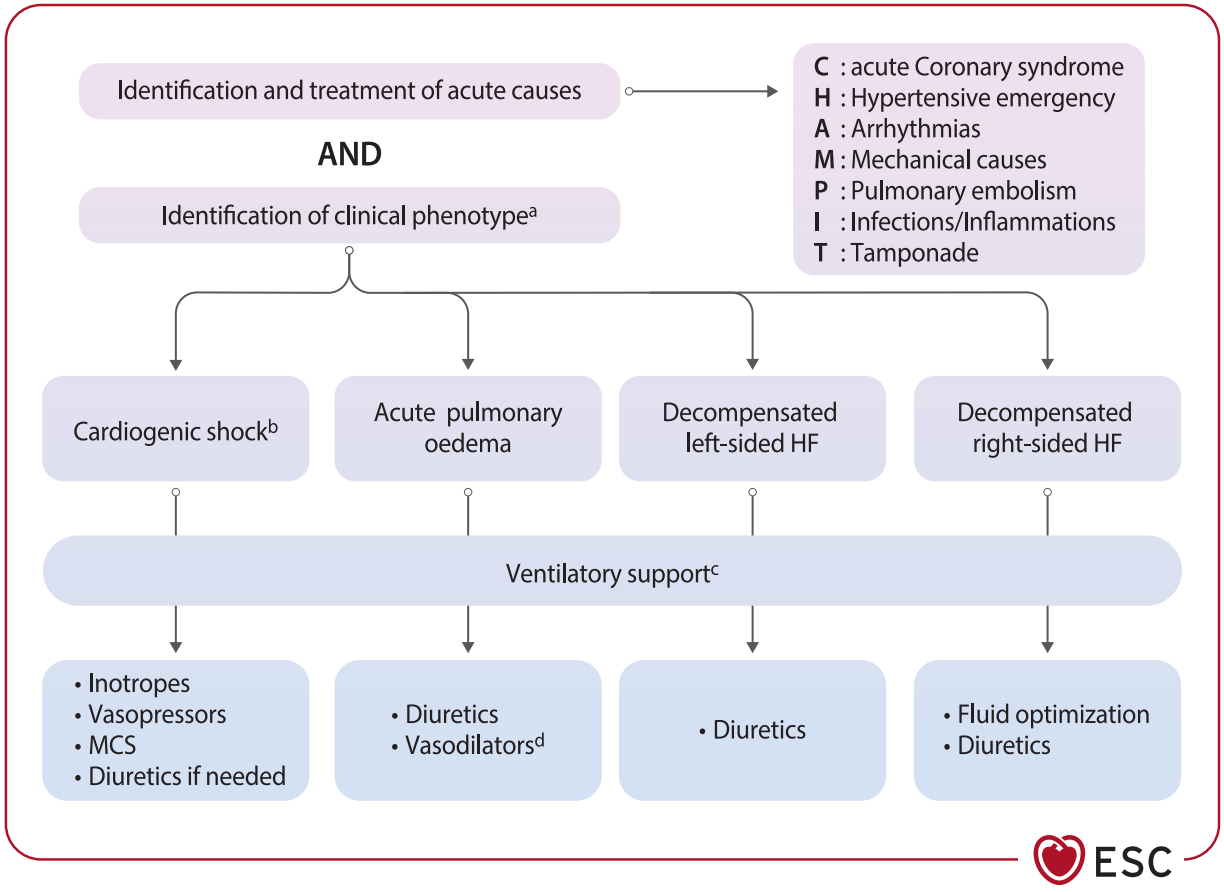

Figure 13 Initial management of decompensated heart failure. HF, heart failure; MCS, mechanical circulatory support. [a]Overlap between different clinical phenotypes can exist. [b]Consultation with the Shock Team is recommended. [c]Consider in case of hypoxaemia. [d]Consider when systolic blood pressure is >110 mmHg.

stabilized, to start/optimize long-term FMT to alter the course of the disease and improve patient outcomes. Decongestion is crucial and must be started and continued in phase 2 (*Figure 13*). Data from recent RCTs have demonstrated that initiating MRAs, SGLT2-Is, or ARNIs is feasible and safe in this phase of DHF.[281,492,493] Much debate is ongoing on the optimal FMT initiation/optimization. It is clear that the traditional sequential approach is suboptimal and time-consuming. There is growing evidence that simultaneous implementation of FMT is more effective, safe, and associated with clinical benefit, thus this approach should be preferred. As no prospective RCT has been conducted comparing the different approaches to implementing FMT, no specific recommendation can be made regarding the number of drug classes to be introduced simultaneously or sequencing of the drugs. A more conservative approach may be reserved for specific (high-risk) groups of patients, such as patients with low eGFR, hypotension, and history of hyperkalaemia.

7.4.3. Phase 3 (pre-discharge and early post-discharge)

This transition phase covers the last days of hospitalization and the first days/weeks after discharge.[494] During this period, efforts should focus on reducing the risk of subsequent DHF/WHF episodes, further optimizing FMT, and determining any indications for AMT and GDIT. The STRONG-HF trial demonstrated the safety and efficacy of an approach based on a rapid and intensive initiation and uptitration of FMT followed by close outpatient visits.[311] This study has been criticized due to several limitations, including a highly selected population (based on NT-proBNP values and changes), the suboptimal medical treatment in the control arm and the lack of SGLT2-I use (lack of evidence and recommendations at the time when the study was conducted). Nevertheless, the trial showed that a strategy of fast uptitration after HFH is safe and feasible and therefore this approach is recommended. Safety indicators, including vital signs (blood pressure and heart rate) and laboratory tests (creatinine, potassium, and NT-proBNP) are helpful to guide uptitration.[495]

Residual congestion is associated with poor outcomes and a high risk of rehospitalization. Thus, pre-discharge assessment of residual congestion using clinical, laboratory, and imaging techniques is recommended (*Figure 14*).[494] If not done earlier, the predischarge phase may also be used for iron supplementation in patients with iron deficiency (ID), based on the results of the AFFIRM-AHF trial (see *Section 10.4*).[496] Finally, patients should be enrolled in disease management and rehabilitation programmes, educated, and guided in appropriate lifestyle adjustments.

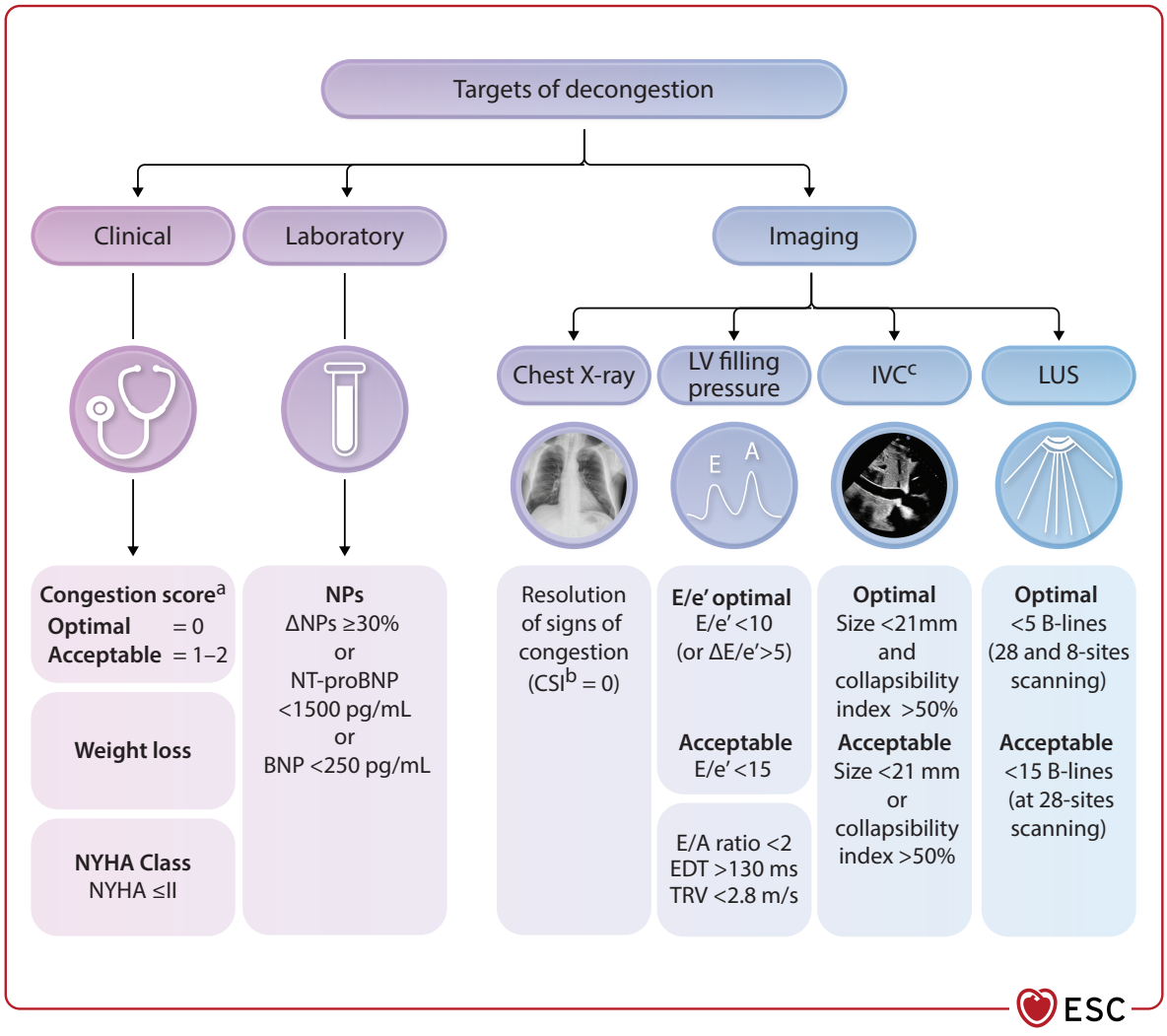

Figure 14 Tools used for assessment of decongestion during the pre-discharge phase. All these tools are intended to be optional as no evidence from randomized controlled trials exists. BNP, B-type natriuretic peptide; CSI, congestion score index; EDT, E-wave deceleration time; IVC, inferior vena cava; LUS, lung ultrasound; LV, left ventricular; NP, natriuretic peptide; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; TRV, tricuspid regurgitation velocity. [a]Congestion score = 0 denotes the absence of clinical congestion (absence of dyspnoea, orthopnoea, fatigue, rales, oedemas, jugular vein distension).[497] Congestion score = 1–2 denotes mild congestion (slight or moderate dyspnoea, orthopnoea, fatigue, rales, oedemas, jugular vein distension).[497] [b]The CSI is a six-zone evaluation of a chest X-ray, with individual scores ranging from 0 to 3. A total score of 0 indicates all zones are clear (i.e. no congestion). [c]The IVC is an optional tool to assess decongestion, although CAVA-ADHF showed no added benefit[498].

Recommendation Table 8 — Recommendations for pre-discharge and early post-discharge follow-up of patients hospitalized for decompensated heart failure (see *Evidence Tables 59–67*)

Recommendations	Class[a]	Level[b]
Careful evaluation[c] before discharge is recommended in patients hospitalized for DHF to exclude persistent signs of congestion.	I	C
An intensive strategy of rapid initiation and uptitration of FMT before discharge and during frequent follow-up visits in the first 6 weeks following an HFH is recommended to reduce the risk of HF rehospitalization or death.[311]	I	B2

DHF, decompensated heart failure; FMT, foundational medical therapy; HF, heart failure; HFH, heart failure hospitalization.
[a]Class of recommendation.
[b]Level of evidence.
[c]Clinical evaluation, natriuretic peptide levels (*Table 9*), kidney function and electrolytes, imaging (see *Figure 14*).

7.5. Treatment

7.5.1. Oxygen therapy

Oxygen therapy is recommended in patients with hypoxaemia [oxygen saturation (SpO_2) <90% or partial pressure of oxygen (PaO_2) <60 mmHg]. Studies, including RCTs, have demonstrated that indiscriminate oxygen administration in non-hypoxaemic patients may be harmful.[499–501]

7.5.2. Ventilation support

Non-invasive ventilation is recommended in patients with APO or CS and respiratory failure to improve oxygenation and reduce the need for intubation as shown by multiple trials and meta analyses.[502,503] However, the increase in intrathoracic pressure with non-invasive positive pressure ventilation decreases venous return and right and left ventricular preload. It may also decrease cardiac output and blood pressure and should therefore be used with caution in patients with reduced preload reserve and hypotension (i.e. decompensated right-sided HF). Endotracheal intubation is reserved for selected cases (see *Recommendation Table 9*).[477]

7.5.3. Diuretics (decongestion management)

Intravenous loop diuretics remain the cornerstone of decongestion in DHF. In the DOSE-AHF trial, no difference in the primary efficacy outcome of patients' symptom global assessment was shown with a high-dose regimen compared with a low-dose regimen of furosemide. There is no evidence indicating differential outcomes with i.v. bolus administration compared to continuous infusion or that one loop diuretic is superior to another.[327,504] Patients naïve to diuretics usually respond well to 40 mg of i.v. furosemide or equivalent, whereas i.v. doses of two times the patient's usual oral diuretic dose should be considered for patients who have been on loop diuretics as outpatients.[505]

Possible worsening kidney function should be evaluated in the context of diuretic response, because small and transient rises in serum creatinine during diuretic therapy are not associated with poor outcome if decongestion is achieved.[506,507]

Subsequent doses of loop diuretics during the initial days of hospitalization may be adjusted based on urinary sodium (uNa^+) assessments, diuretic response, and the patient's clinical status. A satisfactory diuretic response can be defined as a uNa^+ content ≥70 mEq/L at 2 h or by a urine output ≥100 mL/h during the first 6 h (*Figure 15*). The PUSH-AHF trial showed that a strategy based on frequent clinical assessment, and uNa^+-guided diuretic therapy led to higher natriuresis at 24 h vs standard of care.[508] In the ENACT-HF open-label study, the uNa^+-based approach also resulted in higher natriuresis and diuresis, as well as shorter hospital stay.[509] No clinical trial has thus far showed benefit of uNa^+-guided diuretic therapy on death or recurrent HFH.

Intravenous diuretics should be continued until optimal decongestion is achieved; then, a switch to oral diuretics, if needed to maintain the volume status, is recommended.

If there is an insufficient diuretic response, the loop diuretic i.v. dose can be doubled and/or a non-loop diuretic added. (*Figure 15*).

Two recent RCTs examined the role of non-loop diuretics for enhanced decongestion in DHF. In the ADVOR trial, patients were randomized to i.v. acetazolamide (500 mg) or placebo added to i.v. loop diuretics. Treatment with acetazolamide resulted in a greater incidence of successful decongestion, defined as the absence of signs of volume overload within 3 days.[510] In the CLOROTIC trial, oral hydrochlorothiazide (dose adjusted for eGFR) was compared with placebo in patients receiving i.v. furosemide.[511] The treatment with hydrochlorothiazide resulted in more pronounced weight loss at 72 h but did not impact patient-reported dyspnoea. Treatment with hydrochlorothiazide was associated with greater 24 h diuresis but also more likely worsened kidney function and hypokalaemia, warranting caution. Importantly, the study was prematurely halted due to slow recruitment. Both ADVOR and CLOROTIC did not show benefit of non-loop diuretics on hard endpoints. The pharmacotherapy of different diuretics and a practical guidance for their use in DHF is reported in Supplementary data online, *Table S13*. In patients with DHF, fluid intake should be less than urine output and fluid restriction may be appropriate in patients with hyponatraemia, based on individual assessment. Similarly, sodium intake should remain less than natriuresis.

Implementing SGLT2-I and neurohormonal blockade, including MRA, can contribute to more effective and sustainable decongestion.[512–514] Thus, it is imperative to consider early implementation and optimization of FMT in parallel to decongestion (*Figure 15*).

7.5.4. Decongestion management in the ambulatory setting

In ambulatory patients with chronic HF showing signs of worsening, both i.v. diuretic administration and intensification of oral diuretic therapy can be considered.

A practical guide for the outpatient management of WHF has been published, covering both ambulatory i.v. diuretics administered in a day-hospital setting and 'hospital-at-home' care models, including telehealth-enabled approaches.[515–517] Diuretic sessions usually consist of a 3–6 h i.v. diuretic infusion with dosing based on the patient's existing oral diuretic regimen. Close monitoring of kidney function, electrolyte levels, and treatment response, including measurements of urine output, uNa^+, signs of clinical decongestion, biomarkers, and/or ultrasound findings, is essential.[444,515,518]

The new formulations of diuretics (e.g. subcutaneous) might be particularly useful for home treatment.[519–521]

Intensification of oral diuretic therapy may include: (i) initiating a loop diuretic in previously untreated individuals; (ii) increasing the total daily dose of a loop diuretic; or (iii) temporarily adding a diuretic with a different mechanism of action. Thiazide-like diuretics—particularly oral metolazone (2.5–5 mg)—can be used in patients with advanced HF who exhibit diuretic resistance, as part of a sequential nephron blockade approach, or in those with an eGFR <30 mL/min/1.73 m^2. This strategy requires careful monitoring of eGFR and electrolytes.

Patients with WHF that progresses to advanced HF are a key population for either outpatient i.v. diuretic treatment, whether in a day hospital or 'hospital-at-home' setting, or oral thiazide-like diuretics. Indeed, these patients often experience frequent hospitalizations and spend a substantial amount of time in hospital ('frequent flyers'). Such patients require prompt evaluation for advanced HF treatments (see *Section 8*).

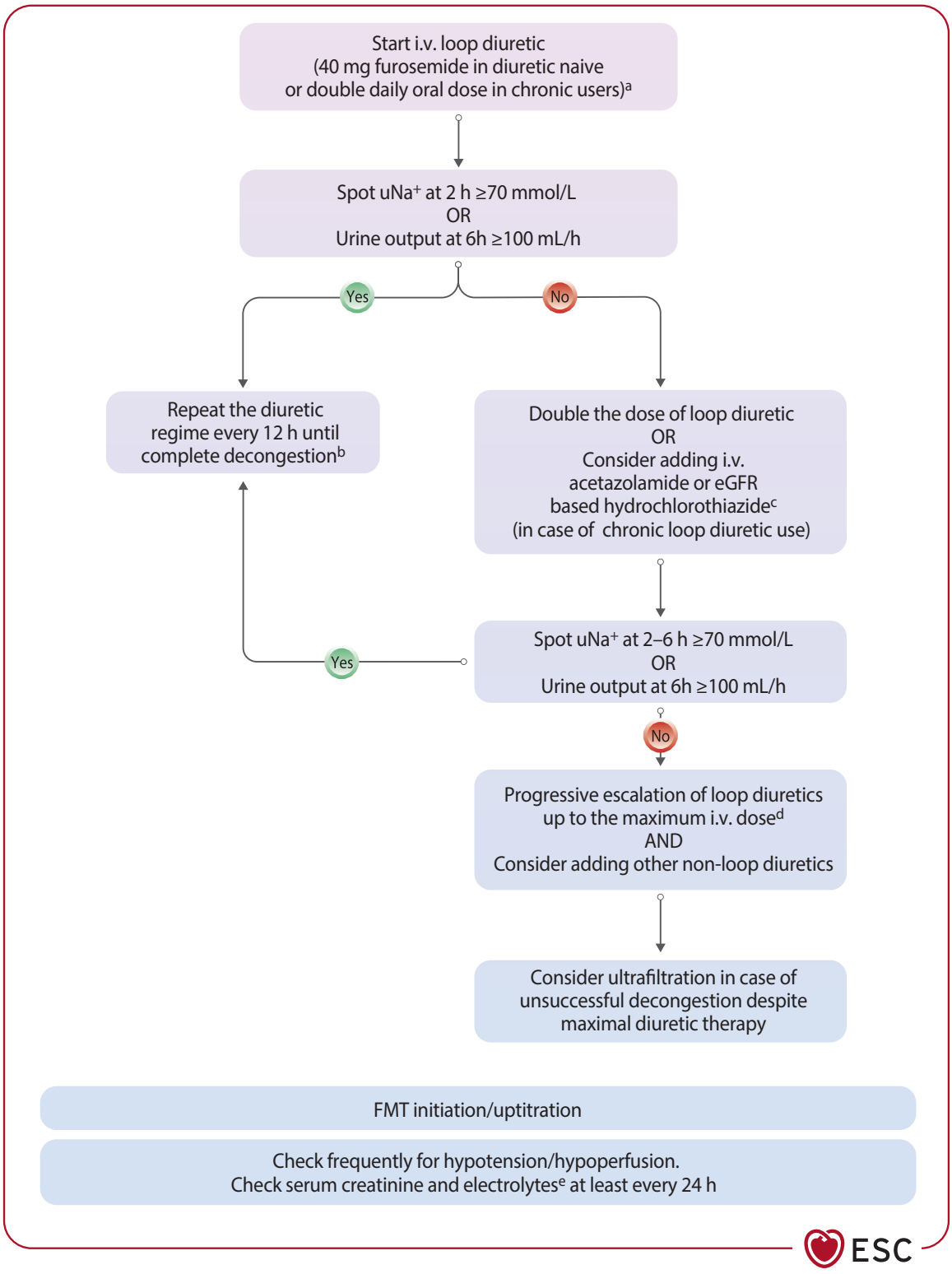

Figure 15 Management of decongestion. CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; FMT, foundational medical therapy; i.v., intravenous; K^+, potassium; MRA, mineralocorticoid receptor antagonist; uNa^+, urinary sodium. [a]Higher initial i.v. dose in case of CKD. [b]After 24 h of treatment, total diuresis should be taken into consideration. If diuresis remains <3 l and congestion persists, further diuretic escalation should be considered during the second day of treatment. [c]Acetazolamide (500 mg i.v. once daily) or hydrochlorothiazide (if eGFR >50 mL/min/1.73 m^2: 25 mg daily; eGFR 20–50 mL/min/1.73 m^2: 50 mg daily; and eGFR <20 mL/min/1.73 m^2: 100 mg daily). Acetazolamide might be preferable in more advanced CKD. [d]The highest daily dose for i.v. loop diuretics is generally considered furosemide 600 mg, although up to 1000 mg may be considered in patients with severely impaired kidney function. [e]Consider MRA and K^+ supplements in case of hypokalaemia.

7.5.5. Sodium–glucose co-transporter 2 inhibitors

Several trials and meta-analyses have confirmed the safety and clinical benefit of in-hospital initiation of an SGLT2-I.[492,522–525] The EMPULSE trial demonstrated that in-hospital initiation of 10 mg empagliflozin resulted in significantly higher chances of clinical benefit, at 90 days.[492] In the SOLOIST-WHF trial, initiation of sotagliflozin in hospital or within 3 days of discharge was safe and effective in patients with HF and diabetes.[326] Initiation of SGLT2-Is in HF has been shown to be associated with lower diuretic demand and facilitated decongestion even though the long-term 'diuretic effect' of SGLT2-Is is unknown.[514,522–524,526] Thus, early initiation of SGLT2-Is in DHF is recommended both as part of FMT (i.e. prognostic implications) and as a tool to enable optimal decongestion (*Figure 15*).

7.5.6. Ultrafiltration

Given the available data, the role of ultrafiltration in managing DHF remains uncertain, but it may be considered in selected patients who are responding insufficiently to diuretic escalation.[527,528]

7.5.7. Vasodilators

Intravenous vasodilators (i.v. nitroglycerine or nitroprusside) may be effective in patients with DHF, particularly in those with predominant vasoconstriction and volume redistribution. For example, in APO, where increased cardiac filling pressures and elevated systemic blood pressures occur in the absence of, or with minimal, systemic fluid accumulation, vasodilators can reduce pulmonary congestion (Supplementary data online, *Section S4.3* and *Table S14*).[529] Importantly, close monitoring of blood pressure is recommended during drug administration, as hypotension related to vasodilatation may be harmful.[529,530] None of the large-scale RCTs have shown a clear clinical benefit of vasodilatation on hard endpoints.[531–533] A meta-analysis of available RCTs has demonstrated that using vasodilators was associated with a lower risk of tracheal intubation in DHF with no effect on death or length of hospital stay.[534]

7.5.8. Inotropes/inodilators

Inotropic agents may be considered in patients with DHF, systolic blood pressure <90 mmHg and evidence of hypoperfusion who do not respond to standard treatment, including fluid challenge, to improve perfusion. Due to risks of arrhythmias and myocardial ischaemia, their use is not routinely recommended in patients with DHF and should be cautious.[535] A Cochrane analysis found insufficient evidence to establish mortality benefits of any inotrope in patients with CS or low cardiac output.[536] An RCT found no difference between milrinone and dobutamine.[537] For levosimendan, no relevant RCTs in CS are available. Based on the mode of action, levosimendan or phosphodiesterase-III inhibitors may be preferred over dobutamine for patients on beta-blockers. For more details on the specific inotropic agents, see Supplementary data online, *Tables S15* and *S16*.

7.5.9. Vasopressors

Vasopressors may be considered in patients with hypotension and DHF. Some studies, although with limitations, support the use of norepinephrine as first choice, compared with dopamine or epinephrine. Dopamine vs norepinephrine was associated with significantly higher rate of arrhythmic events in an RCT including patients with unspecified shock.[538] In the CS subgroup, a mortality benefit was observed with norepinephrine, although without a significant *P*-value for interaction. Comparing epinephrine and norepinephrine showed similar effects on cardiac index in a small trial of infarct-related CS.[539] However, this trial was stopped prematurely due to a higher incidence of refractory shock with epinephrine. Vasopressin has not been studied in CS so far. The target mean blood pressure is not well defined in CS. For more details, see Supplementary data online, *Table S16*.

7.5.10. Opiates

Routine use of opiates is not recommended in patients with DHF; Their use should be limited to carefully selected patients with severe anxiety or distress refractory to other treatments and must be approached with caution due to the risk of respiratory failure.

Recommendation Table 9 — Recommendations for the immediate and intermediate treatment of decompensated heart failure (see *Evidence Tables 59–67*)

Recommendations	Class[a]	Level[b]
Oxygen and ventilatory support		
Oxygen is recommended in patients with SpO_2 <90% or PaO_2 <60 mmHg to correct hypoxaemia.	I	C
Intubation is recommended in patients with DHF and persistent and progressive respiratory failure despite oxygen administration or non-invasive ventilation to correct hypoxaemia[c].	I	C
Non-invasive positive pressure ventilation should be considered in patients with respiratory distress (respiratory rate >25 breaths/min, SpO_2 <90%) and started as soon as possible in order to decrease respiratory distress and reduce the risk of endotracheal intubation.[540]	IIa	B2
Diuretics		
Intravenous loop diuretics are recommended for all patients with DHF admitted with fluid overload to improve symptoms[d].	I	A
The addition of short-term intravenous acetazolamide or oral hydrochlorothiazide should be considered in patients with fluid overload previously treated with loop diuretics, to reduce congestion.[510,511]	IIa	B1
Urinary Na^+-guided diuretic therapy may be considered during the first days of treatment of patients with DHF to improve natriuresis and diuresis.[508]	IIb	B1

Continued

SGLT2-I		
In-hospital initiation of SGLT2-I is recommended in patients with DHF after initial stabilization to improve QoL and congestion symptoms and reduce the risk of HFH.[492,522,525,541]	I	B1
Vasodilators		
Intravenous vasodilators may be considered as initial therapy in patients with DHF and systolic blood pressure >110 mmHg to improve symptoms and reduce congestion.[534]	IIb	C
Inotropic agents		
Inotropic agents may be considered in patients with systolic blood pressure <90 mmHg and evidence of hypoperfusion who do not respond to standard treatment, including fluid challenge, to improve perfusion.	IIb	C
Vasopressors		
Vasopressors, preferably norepinephrine, may be considered in patients with cardiogenic shock to increase blood pressure and vital organ perfusion.	IIb	C
Opiates		
Routine use of opiates is not recommended in patients with DHF unless severe/intractable pain or anxiety, due to risk of harm.[542]	III	C

DHF, decompensated heart failure; HFH, heart failure hospitalization; NIV, non-invasive ventilation; $PaCO_2$, partial pressure of carbon dioxide; PaO_2, partial pressure of oxygen; QoL, quality of life; SGLT2-I, sodium–glucose co-transporter 2 inhibitor; SpO_2, oxygen saturation.
[a]Class of recommendation.
[b]Level of evidence.
[c]Criteria for endotracheal intubation in DHF: cardiac or respiratory arrest, progressive worsening of altered mental status, progressive worsening of respiratory failure with hypoxaemia (PaO_2 <60 mmHg, $PaCO_2$ >50 mmHg and pH <7.35) despite NIV or intolerance to NIV, persistent haemodynamic instability, need for airway protection.[477]
[d]This recommendation is considered by the Task Force to have level of evidence A due to clear clinical benefit. Treatment of DHF with loop diuretics has been widely accepted as effective and therefore no adequately powered randomized clinical trial has ever been conducted or is likely to be conducted for ethical reasons.

7.5.11. Temporary mechanical circulatory support

Temporary MCS should be considered as an option for stabilizing haemodynamics and enhancing end-organ perfusion in highly selected patients.[434,474,543,544]

Different percutaneous devices operate through distinct mechanisms, delivering diverse haemodynamic support levels, each associated with specific potential benefits but also possible complications. In addition to single use, multiple combinations are feasible, addressing specific needs for LV unloading or combined left and right ventricular support. Decisions on the modality and type of temporary MCS should be guided by a multidisciplinary Shock Team including a cardiologist specialized in HF, a cardiothoracic surgeon, an interventional cardiologist, and an intensive care specialist, working at an experienced advanced HF centre (i.e. high-volume for temporary MCS).[488,545] A recent meta-analysis suggests that temporary MCS are beneficial in highly selected patients with ST-elevation MI complicated by CS who do not have hypoxic brain injury, although rates of severe complications remain high.[546]

7.5.11.1. Microaxial flow pumps

Microaxial percutaneous flow pumps provide support of up to 4 l/min. Newer devices with 5.5 l/min requiring surgical insertion offer complete LV support.

Until recently, the percutaneous device had been investigated in a few RCTs on infarct-related CS and in large-scale propensity-matched studies encompassing more than 100 000 patients and consistently showed no survival benefit with higher complication rates such as major bleeding and limb ischaemia.[547,548] In the DanGer Shock trial, including 360 highly selected patients with ST-elevation MI and CS, treatment with microaxial flow pump vs standard of care was associated with lower 180-day death (HR 0.74; 95% CI 0.55–0.99; $P = .04$), which persisted up to 10-year follow-up.[549,550] This trial also showed an increased incidence of bleeding and limb ischaemia compared with controls. Despite the mortality benefit observed in this trial, multiple open questions remain.[548,551]

Utilization of microaxial flow pumps should be considered in highly selected patients with CS caused by ST-elevation MI, who do not have risk of hypoxic brain injury. Routine use of microaxial flow pumps in CS is not recommended. RCTs on the efficacy of microaxial flow pumps in non-infarct-related CS have yet to be conducted.[546]

7.5.11.2. Venoarterial extracorporeal life support

Extracorporeal life support (ECLS) can deliver support of up to 6 l/min and provide full respiratory and circulatory support. In the ECLS-SHOCK trial involving patients with severe infarct-related CS, early routine ECLS use showed no significant difference in 30-day all-cause death (relative risk 0.98; 95% CI 0.80–1.19).[552] These data are in line with an individual patient data meta-analysis of ECLS RCTs in patients with infarct-related CS in which no mortality benefit was observed but more complications with ECLS were seen.[553]

Importantly, ECLS may harm the heart itself owing to the afterload increase by generation of retrograde blood flow. Active unloading with microaxial flow pumps or intra-aortic balloon pump (IABP) aims to mitigate these adverse effects. A recent RCT comparing routine LV unloading by a transseptal left atrial cannula vs ECLS alone showed no effect on death.[554] RCTs investigating the efficacy of ECLS in non-ischaemic CS have yet to be performed.

7.5.11.3. Intra-aortic balloon pump

Routine use of IABP is not recommended in unselected patients with CS. In the IABP shock trial, 40 patients with post-MI CS were randomised to IABP treatment or standard of care. Treatment with IABP did not significantly augment cardiac output or any other haemodynamic variable as compared to control.[555] In a large-scale RCT in infarct-related CS, routine use of IABP did not show a survival benefit compared with medical therapy at 30-day and longer follow-up.[556–558] Also, in advanced HF CS, IABP had no survival benefit as compared to standard of care.[559,560] The decision to use an IABP should therefore be highly individualized, based on patient-specific factors and the availability of alternative therapies.[559,561–563]

Recommendation Table 10 — Recommendations for the use of temporary mechanical circulatory support in patients with cardiogenic shock (see *Evidence Tables 68 and 69*)

Recommendations	Class[a]	Level[b]
A multidisciplinary Shock Team is recommended in potential candidates for temporary MCS to guide the device selection (modality and type) based on patient and HF characteristics.[564,565]	I	C
Cardiogenic shock caused by acute MI		
Temporary MCS with a microaxial flow pump should be considered in selected patients with cardiogenic shock caused by ST-elevation MI with left ventricular systolic dysfunction and no risk of hypoxic brain injury[c] in order to reduce the risk of death.[546,549,550]	IIa	B1
Temporary MCS is not recommended in unselected patients with cardiogenic shock caused by acute MI, due to risk of harm.[546,552,553]	III	B1
IABP is not recommended in unselected patients with cardiogenic shock, due to the lack of effect.[557,560]	III	B1
MI-related mechanical complications		
Temporary MCS[d] should be considered in patients with mechanical complications related to MI[e] as a bridge to definitive treatment.	IIa	C
Advanced HF cardiogenic shock		
Temporary MCS should be considered in selected patients with HF-related haemodynamic instability as a BTR, BTD, BTB, BTC, or BTT.	IIa	C

BTB, bridge to bridge; BTC, bridge to candidacy; BTD, bridge to decision; BTR, bridge to recovery; BTT, bridge to transplantation; HF, heart failure; IABP, intra-aortic balloon pump; MCS, mechanical circulatory support; MI, myocardial infarction; VA-ECLS, venoarterial extracorporeal life support.
[a]Class of recommendation.
[b]Level of evidence.
[c]No risk of hypoxic brain injury was defined as: (i) no out-of-hospital cardiac arrest with persistent Glasgow coma scale <8 after return of spontaneous circulation[549]; and (ii) no resuscitation or resuscitation lasting <10 min.[546]
[d]The choice of passive IABP or active percutaneous MCS should be based on the severity of cardiogenic shock as assessed by the Shock Team.
[e]In case of large ventricular septal defect, temporary MCS should be used with caution due to the potential increase of left-to-right interventricular shunt (VA-ECLS) or shunt inversion (microaxial flow pump). In case of ventricular free-wall rupture, temporary MCS should be avoided; however, VA-ECLS can be considered to allow emergent cardiac surgery in patients presenting with profound cardiogenic shock and/or cardiac arrest if no sign of irreversible brain injury is present.

7.5.12. Thromboembolism prophylaxis

Although patients with DHF are recognized as being at increased thromboembolic risk, no RCT has compared anticoagulation vs placebo in a DHF population, thus no definitive recommendation can be made.[566–570] However, in case of immobilization or other risk factors, thromboembolic prophylaxis is generally indicated.

8. Advanced heart failure

8.1. Epidemiology, definition, prognosis, and referral

Many patients with HF progress into a phase of advanced HF (stage D), characterized by persistent severe symptoms and objective measures of cardiogenic impairment despite optimal therapy. In the Framingham population, 5.1%–7.7% of patients with HF had advanced HF.[571] Prognosis in medically treated patients with advanced HF remains poor with 1-year mortality >40%.[572,573] Criteria for definition are reported in *Table 14*.[572]

Table 14 Criteria for definition of advanced heart failure

All the following criteria must be present despite FMT, AMT, and GDIT:
1. Severe and persistent symptoms of HF (NYHA class III or IV).
2. Severe cardiac dysfunction defined by at least one of the following: • LVEF ≤30% • Isolated RV failure (e.g. ARVC) • Non-operable severe valve abnormalities • Non-operable severe congenital abnormalities • Persistently high (or increasing) BNP or NT-proBNP values and severe LV diastolic dysfunction or structural abnormalities (i.e. HFpEF,[a] hypertrophic or restrictive cardiomyopathies).
3. Episodes of pulmonary or systemic congestion requiring high-dose i.v. diuretics (or diuretic combinations) or malignant arrhythmias causing ≥2 unplanned visits or hospitalizations in the last 12 months, or ≥1 episode of low output requiring inotropes or vasoactive drugs.
4. Severe impairment of exercise capacity with inability to exercise, or low 6-min walk test distance (<300 m), or pVO_2 <12–14 mL/kg/min,[b] or <50% predicted value, estimated to be of cardiac origin.

AMT, additional medical therapy; ARVC, arrhythmogenic right ventricular cardiomyopathy; BNP, B-type natriuretic peptide; FMT, foundational medical therapy; GDIT, guideline-directed interventional therapy; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; i.v., intravenous; LV, left ventricular; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; pVO_2, peak oxygen consumption; RV, right ventricular.
[a]See *Table 10*.
[b]The cut-off 12 mL/kg/min refers to patients on beta-blocker.

A severely reduced LVEF is common but not required for a diagnosis of advanced HF, as it may develop in patients with HFpEF or other structural abnormalities.

Early risk stratification and timely referral to an advanced HF centre are crucial to improve outcomes (*Figure 16*).[574,575]

Systematic assessment for advanced HF using the 'Rule of three' or 'I NEED HELP' criteria is essential for timely referral to an advanced HF centre[576–578] (*Figure 16* and *Table 15*).

Cardiopulmonary exercise testing and right heart catheterization (RHC) are key tools for risk stratification and eligibility assessment.[579–582]

Women and sociocultural minority groups are less likely to receive MCS and heart transplantation for reasons not explained by medical factors or social determinants of health and deserve extra attention for timely referral and patient communication.[583–585]

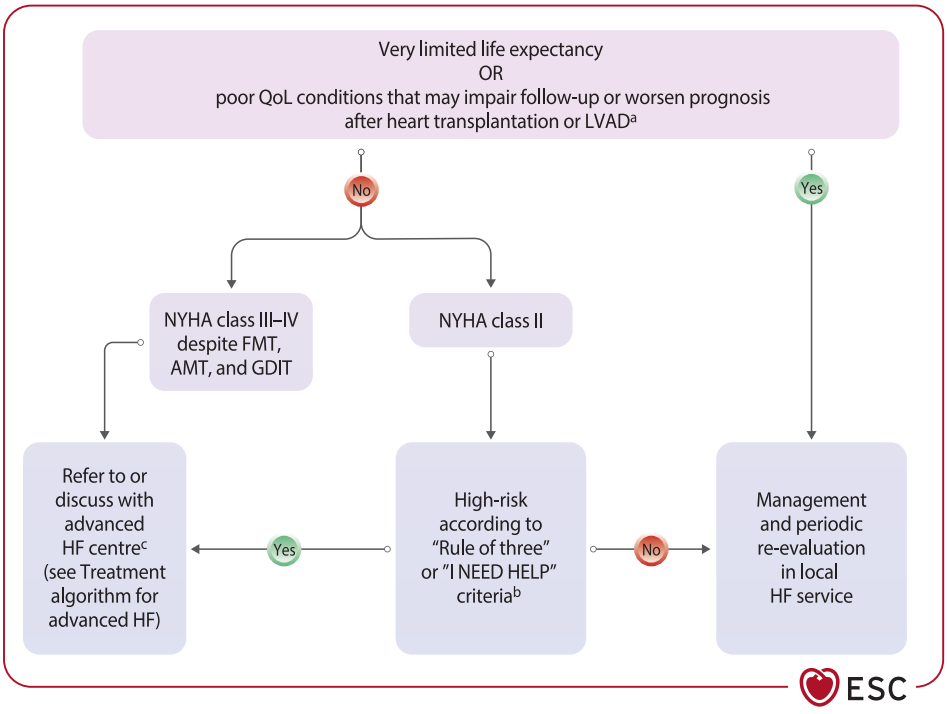

Figure 16 Triage and timely referral of patients with advanced heart failure. AMT, additional medical therapy; FMT, foundational medical therapy; GDIT, guideline-directed interventional therapy; HF, heart failure; LVAD, left ventricular assist device; NYHA, New York Heart Association; QoL, quality of life. [a]Limited life expectancy may be due to major comorbidities, such as cancer, dementia, end-stage irreversible organ dysfunction; other conditions that may impair follow-up or worsen post-treatment prognosis include frailty, irreversible cognitive dysfunction, psychiatric disorder, or psychosocial issues. [b]Refer to *Table 15* for 'Rule of three' or 'I NEED HELP' criteria. [c]A centre performing LVAD implantation and/or heart transplantation.

Table 15 Criteria for high risk of advanced heart failure

Rule of three criteria (at least 1): • HFH (≥2 or ≥1 requiring inotropes within the last year) • Diuretic resistance • Intolerance to neurohormonal drugs with onset of cardiorenal syndrome
I NEED HELP criteria (at least 1): • **I**notropes • **N**YHA class III/IV or persistently high natriuretic peptides • **E**nd-organ dysfunction (liver, kidney) • **E**F <20% or poor RV function • **D**efibrillator shocks • **H**FH >1 • **E**scalating diuretics • **L**ow blood pressure, high heart rate • **P**rognostic medication intolerance or the need to downtitrate

EF, ejection fraction; HFH, heart failure hospitalization; NYHA, New York Heart Association; RV, right ventricular.

An organizational model between centres with different levels of care complexity, based on a 'Hub and Spoke' network, is key to good patient management. A recent consensus document focuses on identifying and overcoming barriers to early referral to an advanced HF centre.[574]

Patients with contraindications to MCS or heart transplantation should receive palliative care (see *Section 11.6.2*). Advance care planning should be discussed in all patients with advanced HF regardless of treatment strategy (see *Section 11*). Frailty, malnutrition, cardiac cachexia, and sarcopenia are highly prevalent in patients with advanced HF and are associated with a greater risk of death (see Supplementary data online, *Table S17* for detailed definitions).[586–589] When evaluating frailty in patients with advanced HF, it is important to assess whether frailty is primarily due to the cardiac condition or other factors.[590]

Recommendation Table 11 — Recommendations for diagnosis and evaluation of advanced heart failure (see *Evidence Tables 70 and 71*)

Recommendations	Class[a]	Level[b]
Early consultation with an advanced HF centre[c] is recommended in patients with advanced HF or at risk of advanced HF, who are motivated and do not have absolute contraindications for heart transplantation or durable MCS[d], in order to evaluate candidacy.[e] [573,591]	I	A
Cardiopulmonary exercise testing is recommended in patients with advanced HF, as part of the evaluation for heart transplantation and durable MCS.[579,580,582]	I	C

Continued

Right heart catheterization is recommended in patients with advanced HF, as part of the evaluation for heart transplantation and durable MCS.[580–582]	I	C

HF, heart failure; LVAD, left ventricular assist device; MCS, mechanical circulatory support.
[a]Class of recommendation.
[b]Level of evidence.
[c]A centre performing LVAD implantation and/or heart transplantation.
[d]Eligibility criteria are reported in *Tables 16* and *17*.
[e]This recommendation is considered by the Task Force to have level of evidence A due to clear clinical effectiveness.

8.2. Management

The indication and timing of advanced HF treatments are guided by patient goals, comorbidities, and clinical status. Pharmacological therapy and temporary MCS may be indicated until implantation of durable MCS or heart transplantation becomes available.[543]

The SCAI classification may be useful in identifying patients for temporary MCS as a possible bridge to advanced therapies (*Table 13*). The Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) profiles[592] describe clinical parameters and characteristics consistent with a need for advanced therapies (*Figures 17* and *18*).

8.2.1. Pharmacological therapy and kidney replacement therapy

Every effort should be made to reach target doses of FMT in all patients with HF. However, patients with advanced HF are under-represented in RCTs. Most patients with advanced HF reach a stage where dose reduction or cessation of neurohormonal therapy is necessary due to progressive intolerance. Although evidence is lacking, it is reasonable to perform individualized changes in FMT, and AMT if needed, on a patient-tailored basis. For example, in a patient with hypotension and high arrhythmic burden, the ACE-I dose can be reduced so that treatment with beta-blockers can be prioritized. However, in a patient with hypoperfusion and persistently low stroke volume despite therapy, reduction or cessation of beta-blockers may be the first step to maintaining cardiac output. In these cases, amiodarone may be better tolerated than beta-blockers when arrhythmias occur. Most importantly, any of these down-titrations should prompt contact with, or referral to, an advanced HF centre if there are no absolute contraindications for MCS or heart transplantation. AMT implementation should not delay early referral to advanced HF therapies.

In patients with signs of hypoperfusion, inotropes may improve haemodynamic parameters, augmenting cardiac output and aiding peripheral perfusion. They may also reduce congestion when the response to diuretic therapy is insufficient. Inotropic therapy is often used to assess reversibility of end-organ dysfunction in the screening phase for durable MCS or heart transplantation, or to maintain cardiac output until such therapies become available (see Supplementary data online, *Table S18*). Inotropes can be used as palliative therapy for the relief of symptoms in patients without other treatment options (see Supplementary data online, *Figure S2*).[594]

However, because inotropic therapy may exacerbate or induce myocardial ischaemia and/or tachyarrhythmias, it should only be used in the lowest required dose and for as short a period as possible.[595,596]

Kidney dysfunction and loop diuretic resistance often characterize the clinical course of patients with advanced HF. Doubling the loop diuretic dose or concomitant administration of non-loop diuretics is indicated.[265] However, in patients who fail to respond to diuretic-based strategies, kidney replacement therapies should be considered. Ultrafiltration and peritoneal dialysis are the most common approaches. It may be considered in those with diuretic resistance to treat volume overload, even if data about its effects on clinical outcomes are inconclusive.[527,597]

Recommendation Table 12 — Recommendations for medical management of advanced heart failure (see *Evidence Tables 72 and 73*)

Recommendations	Class[a]	Level[b]
Down-titration or discontinuation of beta-blockers or ivabradine should be considered in selected patients with advanced HFrEF and evidence of organ hypoperfusion, despite initial treatment, to increase cardiac output and improve symptoms.	IIa	C
Continuous inotropes should be considered in patients with advanced HFrEF, low cardiac output, and evidence of hypoperfusion or end-organ dysfunction, as BTD, BTT or as bridge to durable MCS, to increase cardiac output and improve symptoms.[598,599]	IIa	C
Kidney replacement therapy should be considered in patients with refractory volume overload and end-stage kidney failure to improve symptoms.[600]	IIa	C
Ultrafiltration may be considered in patients with refractory volume overload unresponsive to escalation of diuretic therapy to reduce the risk of rehospitalization.[601]	IIb	C

BTD, bridge to decision; BTT, bridge to transplantation; HFrEF, heart failure with reduced ejection fraction; MCS, mechanical circulatory support.
[a]Class of recommendation.
[b]Level of evidence.

8.2.2. Mechanical circulatory support

Mechanical circulatory support can improve survival and symptoms of patients with advanced HF. The use of MCS should be considered for the different scenarios listed in Supplementary data online, *Table S19*. Indications for temporary and durable MCS should be based on the SCAI classification (*Table 13*, *Section 7*) and INTERMACS profiles (*Figures 17* and *18*).

8.2.2.1. Temporary mechanical circulatory support

Temporary MCS devices are indicated in selected patients to reverse critical end-organ hypoperfusion and hypoxia in the setting of CS (see *Section 7*). The aim is to support cerebral and end-organ perfusion, reverse acidosis and multiorgan failure,

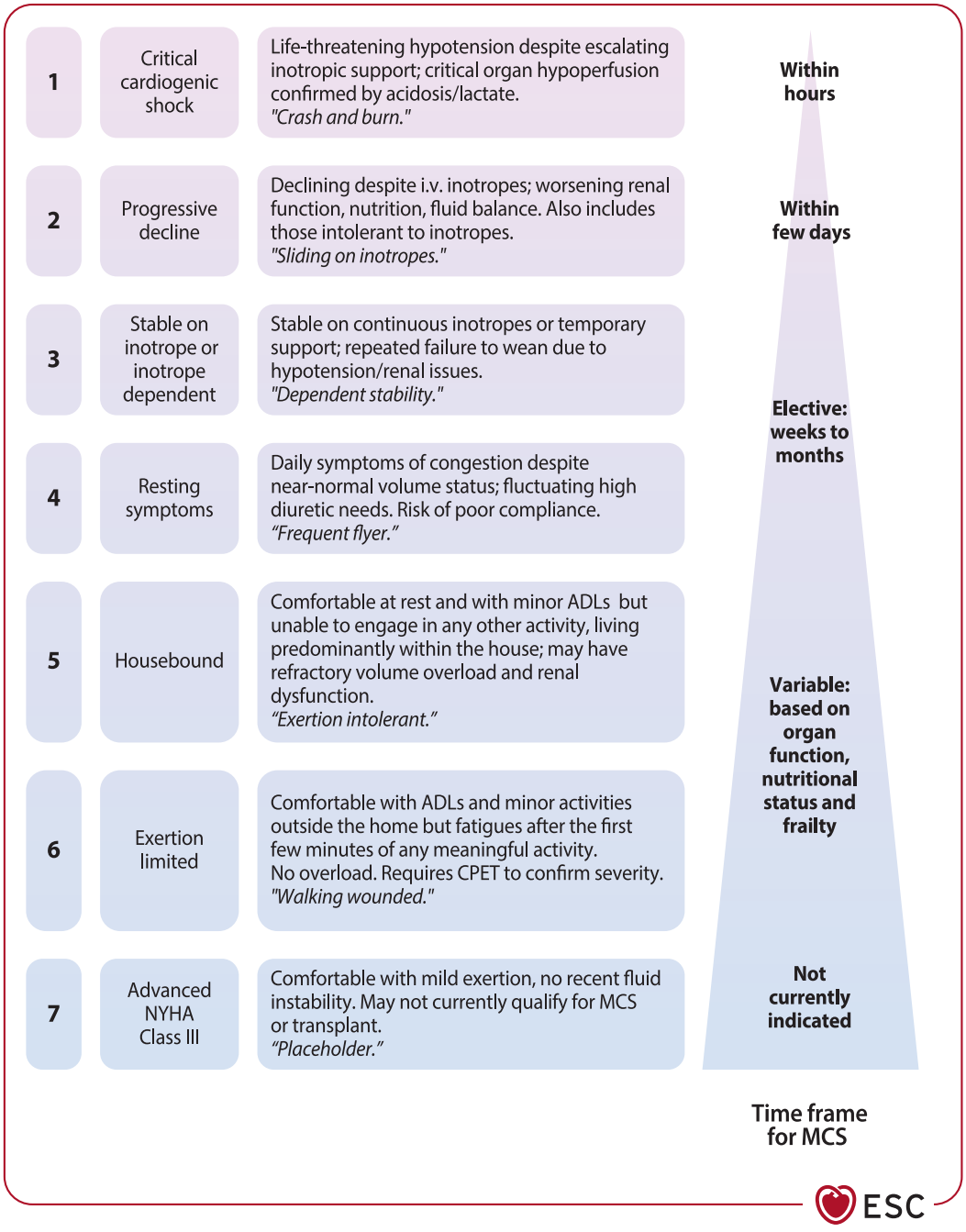

Figure 17 INTERMACS classification. ADLs, activities of daily living; CPET, cardiopulmonary exercise testing; HF, heart failure; i.v., intravenous; MCS, mechanical circulatory support; NYHA, New York Heart Association. The INTERMACS classification supports risk stratification and guides the timing of durable MCS or heart transplantation in patients with advanced HF.[593] Supplementary data online, *Table S18* provides a definition for inotrope dependence.

and provide support until the patient's trajectory clarifies, whether towards myocardial recovery, transition to durable MCS or heart transplantation, or a palliative pathway. The care of patients on temporary MCS is complex and requires specialized expertise, including predefined strategies for withdrawal of support when there is no meaningful neurological and cardiac recovery. Temporary MCS should be considered in patients with INTERMACS profiles 1 or 2 as a bridge to decision, bridge to recovery, or bridge to either durable MCS or urgent heart transplantation (*Figure 18*).

8.2.2.2. Durable mechanical circulatory support

Durable MCS is indicated to prolong life and improve QoL in selected patients when FMT, and GDIT are insufficient or when temporary MCS has not led to cardiac recovery or clinical improvement (*Table 16*).[602,603] Left ventricular assist device is by far the most common and reliable type of durable MCS; however, in cases with biventricular failure or special anatomical situations, a total artificial heart or implantable biventricular assist device is occasionally used.[582] Management of patients who are possible candidates for LVAD or heart transplantation is outlined in *Figure 18*.

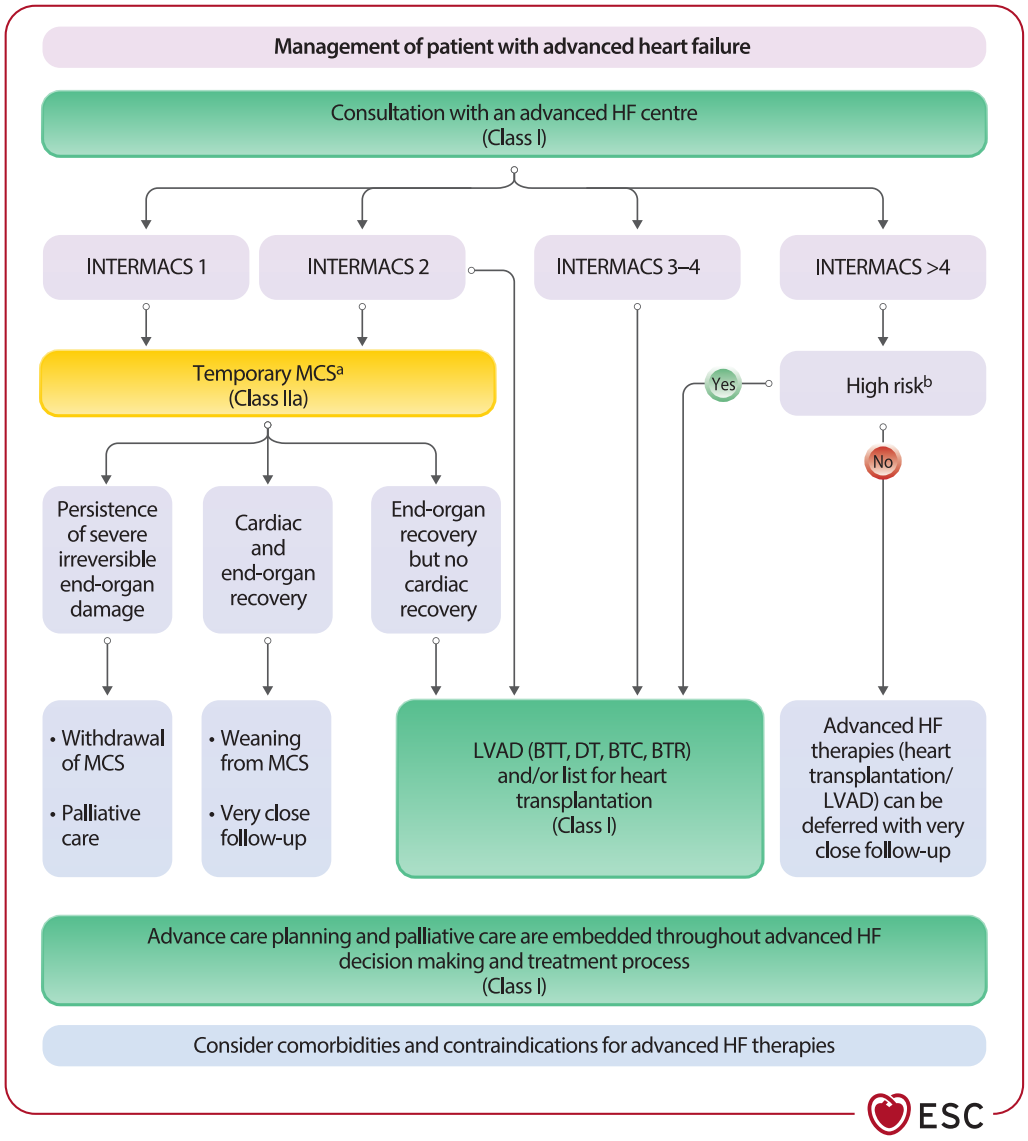

Figure 18 Treatment for advanced heart failure. ARVC, arrhythmogenic right ventricular cardiomyopathy; BTC, bridge to candidacy; BTR, bridge to recovery; BTT, bridge to transplantation; CA, cardiac amyloidosis; CMP, cardiomyopathy; DT, destination therapy; ESC, European Society of Cardiology; HCM, hypertrophic cardiomyopathy; HF, heart failure; HFA, Heart Failure Association; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; LVAD, left ventricular assist device; MCS, mechanical circulatory support. The figure depicts a guidance for advanced HF treatment based on clinical profile. Colour code for classes of recommendation: green for Class of recommendation I and yellow for Class of recommendation IIa. This algorithm can be applied to all patients with advanced HF defined according to the ESC/HFA criteria, with exception of arrhythmic storm, and refractory angina. HCM, CA, other restrictive CMP, ARVC, and adult congenital heart disease are other exceptions. [a]To be discussed with the Shock Team. [b]Recurrent hospitalization, progressive end-organ failure, refractory congestion, inability to perform cardiopulmonary exercise test or peak oxygen consumption <12–14 mL/kg/min or <50% of expected value (see *Table 16*).

Current 2-year survival rates in patients receiving the latest LVAD types are comparable to those after heart transplantation. Among patients with fully magnetically levitated continuous-flow LVADs, 2-year and 5-year survival rates were 79% and 58.4%, respectively, in the MOMENTUM 3 trial with a previous LVAD type as the control group.[604,605] These rates are considerably higher than could be expected from medical treatment in this population with >85% of patients in INTERMACS 1–3 at the time of LVAD implantation.[604,605] Comparable outcomes were described in European and North American real-world populations.[606–608]

Adverse events may negatively affect QoL in patients receiving LVAD. Although pump thrombosis has become extremely rare, driveline infections remain similar to that with older devices.[609] Right HF and arrhythmias may cause readmissions. Bleeding events can be minimized by avoiding antiplatelet therapy in addition to anticoagulation.[610] A guidance document is available to support non-LVAD specialist healthcare providers outside of the implanting centre.[609]

Although now dated, the REMATCH trial is the only RCT comparing an LVAD as destination therapy with optimal medical

Table 16 Indications and contraindications for implantation of a left ventricular assist device

Indications[a]
HF with severely reduced LVEF and one of the following:
• INTERMACS 1–2 with neurological and other end-organ recovery but no cardiac recovery on temporary MCS OR
• INTERMACS 2–4 OR
• Severe symptoms and signs (NYHA class III/IV; INTERMACS >4) despite optimal FMT and GDIT, and at least one of the following: o Unable to exercise due to HF or, if able to perform CPET, with pVO_2 <12–14 mL/kg/min and/or <50% predicted value. o End-organ dysfunction (worsening kidney and/or hepatic function, group 2 pulmonary hypertension, cardiac cachexia) due to reduced perfusion as indicated by cardiac index ≤2 L/min/m^2 despite euvolaemic or therapy-resistant hypervolaemic status. o Repeated HFH within the previous 12 months without an obvious precipitating cause.
Contraindications
Absolute:
• Severe right ventricular dysfunction despite euvolaemic status • Severe irreversible end-organ (kidney and/or liver) disease • Severe irreversible neurological disease • Severe pulmonary disease • Contraindication to long-term oral anticoagulation • Medical non-adherence and/or other psychosocial limitations • Insufficient social supports to achieve compliant care in the outpatient setting • Psychological instability that jeopardizes proper follow-up and intensive therapeutic regime after implantation
Relative:
• Obesity or malnutrition • Musculoskeletal disease that impairs rehabilitation • Malignancy (depending on type and prognosis) • Severe peripheral arterial disease • Systemic infection • Alcohol or substance abuse within the past 6 months, or active smoking • Impaired cognitive function • Frailty

CPET, cardiopulmonary exercise testing; HF, heart failure; HFH, heart failure hospitalization; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; LVEF, left ventricular ejection fraction; MCS, mechanical circulatory support; NYHA, New York Heart Association; pVO_2, peak oxygen consumption; RHC, right heart catheterization.
[a]Indication by transplantation centre includes assessment of HF severity by RHC and/or CPET.

therapy in patients with advanced HF. REMATCH showed lower all-cause death with a previous type of LVAD therapy (HeartMate XVE) compared with medical treatment. However, mortality rates at 2 years were high in both arms.[611] Other studies have not been randomized or compared different devices or post-implant strategies.[604,606,607,610,612,613] Prospective RCTs have been initiated to study strategies of early LVAD implantation vs prolonged medical treatment: Early-VAD (NCT02387112),[614] SweVAD,[615] AMBU-VAD (NCT04768322), and TEAM-HF (NCT06526195).

Histological examination of heart tissue after LVAD implantation or transplantation can identify potentially treatable or genetic causes of HF and is valuable for family screening and determining potential for myocardial recovery in LVAD patients.[616–619]

Recommendation Table 13 — Recommendations for durable mechanical circulatory support in advanced heart failure (see *Evidence Table 74*)

Recommendations	Class[a]	Level[b]
Durable MCS (LVAD) is recommended in selected[c] patients with advanced HFrEF, despite FMT and GDIT, as BTT, BTC, BTR, or as destination therapy to improve symptoms and reduce the risk of death.[604,611,613,620,621]	I	C
Histopathological examination of explanted heart tissue from LVAD or heart transplantation surgery should be considered in patients with non-ischaemic HF to identify an aetiological diagnosis that may be treatable or facilitate family screening.[616,618]	IIa	C

BTC, bridge to candidacy; BTR, bridge to recovery; BTT, bridge to transplantation; FMT, foundational medical therapy; GDIT, guideline-directed interventional therapy; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; LVAD, left ventricular assist device; MCS, mechanical circulatory support.
[a]Class of recommendation.
[b]Level of evidence.
[c]Eligibility criteria are reported in *Table 16*.

8.2.3. Heart transplantation

Heart transplantation, although never evaluated in RCTs, remains the gold-standard treatment for advanced HF in the absence of contraindications. Post-transplant 1-year survival is 80%–90% and median survival is around 12.5 years.[622,623] Transplantation significantly improves QoL and functional status. The main challenge after heart transplantation is the balance between efficacy and side effects of immunosuppression. Organ donor shortage remains the main limitation. Several countries have now started donation after circulatory death programmes, besides donation after brain death, with comparable mid-term results[624,625] and, as a result, the numbers of heart transplantations have increased. Nevertheless, careful recipient selection remains essential, based on pre-transplant and post-transplant life expectancy (both influenced by pre-operative status and comorbidities). The main indications and contraindications for heart transplantation are listed in *Table 17*.[580]

Although patients younger than 65 years of age might be more appropriate candidates due to their overall life expectancy, most programmes accept patients up to 70 years of age, and biological age as well as chronological age must be taken into account. Surgical complexity [previous sternotomies, mediastinal radiation, adult congenital heart disease (ACHD)] should also be considered. The decision pathway to transplantation or LVAD is rarely straightforward and is unique to each patient.

Table 17 Indications and contraindications for heart transplantation

Indications[a]
Advanced HF and no other therapeutic option (except for durable MCS as BTT)
Absolute contraindications
Inability to comply with the therapeutic regimen (e.g. dementia)
Serious comorbidities with poor prognosis, not reversible with heart transplantation
Other contraindications
Active infection[b]
Severe peripheral arterial or cerebrovascular disease
Elevated pulmonary vascular resistance (if pharmacologically irreversible)[c]
Cancer[d]
Irreversible liver dysfunction (cirrhosis) or irreversible kidney dysfunction[e]
Systemic disease with multiorgan involvement
BMI >35 kg/m^2 or severe cachexia
Alcohol or substance abuse or active smoking within the past 6 months
Psychological instability
Insufficient social support to achieve compliant care in the outpatient setting

BMI, body mass index; BTT, bridge to transplantation; CPET, cardiopulmonary exercise testing; HF, heart failure; LVAD, left ventricular assist device; MCS, mechanical circulatory support; RHC, right heart catheterization.
[a]Indication by heart transplantation centre includes assessment of HF severity by RHC and/or CPET.
[b]Active infection is a relative contraindication to transplantation, but infected LVAD may be an indication.
[c]LVAD as bridge to candidacy should be considered.
[d]Highly selected cases may be eligible, to be discussed with an oncologist.
[e]Combined heart–liver or heart–kidney transplantation may be considered.

Eligibility for each option may change according to the specific conditions of each patient, which may also change over time. Some younger patients prefer to remain on LVAD for a prolonged period, rather than proceeding to transplantation immediately, to increase the potential number of life years gained. Other factors not related to the patient, such as average time on the heart transplantation waiting list, the centre's surgical experience, and resources, can also influence decision-making.

Recommendation Table 14 — Recommendations for heart transplantation (see *Evidence Tables 75* and *76*)

Recommendation	Class[a]	Level[b]
Heart transplantation is recommended in selected[c] patients with advanced HF refractory to FMT and GDIT, and without contraindications, to improve QoL and survival.[622,626]	I	C

FMT, foundational medical therapy; GDIT, guideline-directed interventional therapy; HF, heart failure; QoL, quality of life.
[a]Class of recommendation.
[b]Level of evidence.
[c]Eligibility criteria are reported in *Table 17*.

8.2.4. Symptom control and end-of-life care

Advance care planning is recommended in parallel to advanced HF treatments to determine goals of care and improve QoL along the disease trajectory.[627] For indications and the core components of end-of-life care, see Supplementary data online, *Table S20*.

End-of-life care in advanced HF focuses on symptom management (including breathlessness, pain, and anxiety and depression), patient comfort, and maintaining QoL ensuring personalized, compassionate care. It involves clear communication, shared decision-making, and integrating palliative or hospice care to support both the patient and their family. For further details on symptom management, see Supplementary data online, *Section S5.2.3*.

Patients on durable MCS may request withdrawal of life-sustaining treatments because these are no longer consistent with their goals of care, because of poor QoL or newly developed serious comorbidities such as cancer. The MCS may be deactivated after careful evaluation of the patient's wish and by, or under the supervision of, a specialized team. This decision has to take national laws into account. For details regarding follow-up in patients with advanced HF see *section 11.6.2* and Recommendation Table 26.

9. Cardiovascular comorbidities

9.1. Arrhythmias and conduction disturbances

9.1.1. Atrial fibrillation

Heart failure and AF frequently coexist, with AF occurring in more than half of patients with HF, and HF occurring in more than one-third of patients with AF. The prevalence of AF is slightly higher in patients with HFpEF compared with HFrEF.[195,628–631] The two conditions are deeply interrelated with shared risk factors and pathophysiological mechanisms. The coexistence of HF and AF is associated with a high risk of death, HFH, and stroke regardless of LVEF.[195,628–631] HF induced by AF appears to have a more favourable outcome than HF causing AF.[13,632]

The management of patients with HF and AF include identification of triggers, prevention of embolic events, management of HF, and rate or rhythm control of AF.

9.1.1.1. Identification of triggers and risk factor management

Precipitating factors for AF – e.g. hyperthyroidism, toxic agents (e.g. including alcohol), valvular heart diseases, infection, diabetes, uncontrolled hypertension, obesity, sleep disorders, and volume overload – should be routinely identified and appropriately managed. Diuretic therapy is indicated to relieve congestion and may increase the chances of restoring sinus rhythm by reducing filling pressures and ventricular rate.

9.1.1.2. Prevention of embolic events

Oral anticoagulation is recommended in patients with HF and AF to reduce the risk of thromboembolism, according to the CHA_2DS_2-VA score (*Table 18*).[118,633–635] However, patients with HCM and CA are at higher risk of thromboembolism irrespective of CHA_2DS_2-VA score, and anticoagulation is recommended for all these patients with AF.[636–642] In the absence of mechanical prosthetic heart valves and/or moderate

Table 18 Updated definitions for the CHA_2DS_2-VA score

	Description	Point
C	Chronic HF stage B, C, D	1
H	Hypertension	1
A	Age ≥75 years	2
D	Diabetes mellitus	1
S	Stroke/transient ischaemic attack/arterial thromboembolism	2
V	Vascular disease (CAD and/or PAD)	1
A	Age 65–74 years	1

CAD, coronary artery disease; CHA_2DS_2-VA, congestive heart failure, hypertension, age ≥75 years (2 points), diabetes mellitus, prior stroke/transient ischaemic attack/arterial thromboembolism (2 points), vascular disease, age 65–74 years; PAD, peripheral artery disease.
A CHA_2DS_2-VA score of 2 or more is recommended as an indicator of elevated thromboembolic risk for decisions on initiating oral anticoagulation.
A CHA_2DS_2-VA score of 1 should be considered an indicator of elevated thromboembolic risk for decisions on initiating oral anticoagulation.

or severe mitral stenosis, direct-acting oral anticoagulants are recommended as the anticoagulant of choice.[643–646] Left atrial appendage closure can be an option for selected patients as described in the *2024 ESC Guidelines for the management of atrial fibrillation*.[118,647–651]

9.1.1.3. Management of heart failure and atrial fibrillation

All patients with coexisting HF and AF should be optimally treated with FMT, AMT, and GDIT regardless of AF (*Section 6.2.4*).[435]

In patients with AF and HFrEF, where there may be a high likelihood of LVEF recovery following rhythm control, evidence remains limited. However, given the well-established prognostic benefit of FMT on long-term prognosis in the general HFrEF population, initiation of FMT upfront seems reasonable.

There is ongoing debate regarding the optimal management of AF in patients with HF. Currently, there is insufficient evidence to support a rhythm-control strategy over a rate-control strategy.[337,652–658] Decisions with regard to choice of strategy must be made taking into account the cause–effect relationship between AF and HF, along with clinical presentation, symptom burden, stage of disease, comorbidities, and patient preference.

9.1.1.4. Rate control

Data to support strict vs lenient rate control in patients with HF and AF are inconclusive. Analyses from a large observational registry showed a significant association between heart rate in AF and long-term death only in patients with HFrEF and heart rate >100 b.p.m.[659,660] The RACE II trial demonstrated that lenient rate control (target heart rate <110 b.p.m.) was non-inferior to strict rate control (<80 b.p.m. at rest; <110 b.p.m. during exercise) in patients with permanent AF with a primary endpoint of death from CV causes, HFH, stroke, systemic embolism, bleeding, and life-threatening arrhythmic events.[307] A post-hoc combined analysis from the AFFIRM and the RACE trials showed similar results.[661] However, these trials were not focused on HF and only a minority of patients included had HF.

A large observational study showed that a lenient rate-control strategy and poor rate control are associated with a higher risk of death as compared with strict rate control in patients with AF and HF regardless of LVEF.[662] Lenient rate control, with resting heart rate <110 b.p.m., should be considered as initial target in both patients with and without HF, with re-evaluation based on symptoms.[118]

Beta-blockers have proven safety and efficacy in patients with AF and HFrEF and are recommended as the first-line approach.[663,664] If the ventricular rate control is suboptimal with beta-blockers, or if beta-blockers are not tolerated, digoxin or digitoxin should be considered.[665–667] In patients with HFrEF who are haemodynamically unstable, i.v. amiodarone or digoxin may be used to achieve acute control of heart rate and improve haemodynamics, although acute electrical cardioversion to restore sinus rhythm should be first choice.[668–671] There is no evidence on pharmacological strategies for rate control in patients with AF and HFpEF.

Atrioventricular node ablation combined with CRT was found to be superior to pharmacological therapy in reducing death and HFH and improving QoL in patients with severely symptomatic permanent AF and HF, regardless of LVEF.[672,673]

9.1.1.5. Rhythm control

The results of RCTs comparing catheter ablation vs pharmacological rhythm control in patients with HFrEF cannot be considered conclusive for hard outcomes on HFH and death, although catheter ablation has proven superior to antiarrhythmic treatment for AF recurrence.[674–682] Data on the role of catheter ablation in HFpEF are limited.[683,684] For a detailed description, see Supplementary data online, *Section S6.1.1*.[674–681,683–686] Based on current evidence, catheter ablation should be considered only in carefully selected patients with HFrEF and symptomatic AF. This Task Force suggests that these criteria should be used to guide the selection of patients for catheter ablation: high burden AF,[687] less than 1-year duration of continuous persistent AF, and a clear cause–effect relationship between AF and HF.

In patients presenting with DHF, AF with rapid ventricular rates, and haemodynamic instability, urgent cardioversion is recommended. Pharmacological and electrical cardioversion seem to have similar outcomes, although specific studies in HF populations are lacking.[688,689] Amiodarone is recommended in patients with HFrEF requiring pharmacological cardioversion. Other antiarrhythmic drugs, i.e. propafenone, flecainide, and dronedarone, are associated with poorer outcomes in HFrEF and should be avoided.[690–694] There are no data on pharmacological cardioversion in HFpEF.

Recommendation Table 15 — Recommendations for management of atrial fibrillation in patients with heart failure (see *Evidence Tables 77–81*)

Recommendations	Class[a]	Level[b]
Recommendations for anticoagulation		
Oral anticoagulation is recommended in patients with clinical AF at elevated thromboembolic risk, as determined by CHA_2DS_2-VA score[c], to prevent ischaemic stroke and thromboembolism.[635]	I	A

Continued

DOACs are recommended in preference to VKAs in patients with HF[d] to prevent stroke and thromboembolism.[643–646]	I	B1
Rate control		
Beta-blockers are recommended in stable patients with HFrEF and AF as first-line therapy for short- and long-term rate control.[663,665]	I	C
Digoxin should be considered in stable patients with HFrEF and AF when the ventricular rate remains high despite beta-blockers, or when beta-blockers are contraindicated/not tolerated, in order to obtain short- and long-term rate control.[665–667]	IIa	C
Atrioventricular node ablation combined with CRT should be considered in patients with severely symptomatic permanent AF and poor rate control despite medical therapy and at least one HFH to reduce symptoms, physical limitations, recurrent HFH, and death.[672,673]	IIa	B1
Intravenous amiodarone or digoxin may be considered in haemodynamically unstable patients with HFrEF and AF to stabilize the patient and achieve acute control of heart rate.[668–671]	IIb	C
Cardioversion		
Urgent cardioversion is recommended in the setting of DHF in patients presenting with rapid ventricular rates and haemodynamic instability to restore sinus rhythm.[669,671,692,695]	I	C
Atrial fibrillation catheter ablation		
Catheter ablation for AF should be considered in selected[e] patients with symptomatic AF and HFrEF to improve QoL and reduce the risk of HFH or death.[674–676,678,681,682,684,696]	IIa	C

AF, atrial fibrillation; CHA_2DS_2-VA, congestive heart failure, hypertension, age ≥75 years (2 points), diabetes mellitus, prior stroke/transient ischaemic attack/arterial thromboembolism (2 points), vascular disease, age 65–74 years; CRT, cardiac resynchronization therapy; DHF, decompensated heart failure; DOAC, direct-acting oral anticoagulant; HF, heart failure; HFH, heart failure hospitalization; HFrEF, heart failure with reduced ejection fraction; QoL, quality of life; VKA, vitamin K antagonist.
[a]Class of recommendation.
[b]Level of evidence.
[c]See *Table 18*.
[d]Except for patients with moderate or severe mitral stenosis and in patents with mechanical prosthetic heart valves where VKAs are recommended.
[e]All the following criteria are required: high burden AF, less than 1-year duration for continuous persistent AF, clear cause–effect relationship between AF and HF.

9.1.2. Ventricular arrhythmias

Ventricular arrhythmias may cause HF or be a consequence thereof. In sustained ventricular tachycardia, initial management should include stabilization (electrical cardioversion), followed by identification and correction of precipitating factors, and optimization of FMT. Although amiodarone reduces ventricular arrhythmias, it does not reduce SCD or death.[697] Patients with HF and resuscitated cardiac arrest or life-threatening ventricular arrhythmias have an indication for a secondary prevention ICD.[119]

Heart failure can occur because of frequent PVCs.[698] A burden of PVCs of about 10% precipitates an increased risk of HF and the risk increases with higher burden.[119,699–701] Thus, regular assessment of LVEF in this setting is indicated. Amiodarone may be considered to reduce recurrent arrhythmias and improve LV function,[697] with regular follow-up to assess possible side effects. Catheter ablation of PVCs may improve LV function and, possibly, outcomes in patients with PVCs.[702–705] For further details, please refer to the *2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death*.[119]

9.1.3. Bradyarrhythmias

Pacing indications in patients with HF do not differ from those without HF. However, long-term RV pacing can adversely impact LV function.[706] In patients with HFrEF, where there is an expectation of high pacing requirements, i.e. complete heart block or AF with slow ventricular response, CRT implantation should be considered to improve outcomes (see Recommendation Table 7).[409]

9.2. Chronic coronary syndromes

Obstructive CAD is a frequent cause of HF.[33] Coronary microvascular dysfunction affects up to 80% of patients with HFpEF and seems to be associated with poor prognosis.[707–709] Diagnostic work-up of chronic coronary syndromes in patients with HF is described in *Section 5*. Treatment of chronic coronary syndrom in patients with established HF is described below.

9.2.1. Medical therapy

Beta-blockers are recommended as first-line therapy in patients with HFrEF and CAD due to their prognostic effects, closely followed by other FMT drugs.[288,290,291,710–712] Ivabradine should be considered in patients with HFrEF in sinus rhythm with heart rate >70 b.p.m. despite beta-blockers at the highest tolerated dose or if beta-blockers are contraindicated.[294,713] Other medications such as amlodipine,[714] felodipine,[715] nicorandil,[716] and ranolazine[717] do not have effects on death but may improve symptoms. Trimetazidine may improve LV function and exercise capacity in patients with HFrEF and chronic coronary syndrome already on beta-blockers.[718–720] Importantly, initiation and/or uptitration of antianginal therapy should not lead to reduction in FMT. Short-acting nitrates can cause hypotension and should be used with caution. Non-dihydropyridine calcium channel blockers (verapamil and diltiazem) are not recommended in patients with HFrEF due to their negative inotropic effects which may precipitate the risk of HF events.[721] The use of beta-blockers or calcium channel blockers do not appear to be associated with worse outcomes in HFpEF.[722,723] Treatment of patients with HFpEF should be similar to that of patients without HF (see the *2024 ESC Guidelines for the management of chronic coronary syndromes*).[10]

9.2.2. Myocardial revascularization

Data to support the prognostic benefit of myocardial revascularization in patients with stable obstructive CAD and HF are limited. Two RCTs compared revascularization vs medical therapy in patients with LVEF ≤35% and multivessel coronary disease.[178–180] The STICH trial compared coronary artery bypass grafting (CABG) to medical therapy and showed survival benefit

for CABG at long-term follow-up.[179,180] The REVIVED-BCIS2 study compared percutaneous coronary intervention (PCI) and optimal medical therapy to optimal medical therapy alone and was neutral.[178] The patient populations differed between the two trials and patients in REVIVED-BCIS2 were 10 years older, making comparison between them difficult. For details of these results and other studies, see Supplementary data online, *Section S6.2.1*.[178,180,724–735]

Patients with HF and chronic coronary syndrome due to obstructive CAD must receive FMT before revascularization. A multidisciplinary Heart Team discussion including an HF specialist is recommended to decide whether conservative treatment or an invasive treatment strategy should be adopted. If revascularization is planned, the multidisciplinary Heart Team should provide an individualized recommendation on the revascularization strategy—CABG or PCI—depending on patient characteristics. In case of persistent angina despite FMT for HF and antianginal drugs, revascularization is recommended regardless of LVEF. If the Heart Team agrees that revascularization is the best treatment option, in patients with HFrEF, LVEF ≤35% and multivessel disease, CABG should be the first choice (*Figure 19*).

The Task Force recognizes an apparent discrepancy between the latter recommendation (class of recommendation IIa, level of evidence B1) and other recommendations in this context across other guidelines (e.g. *2024 ESC Guidelines for the management of chronic coronary syndromes*, class of recommendation I, level

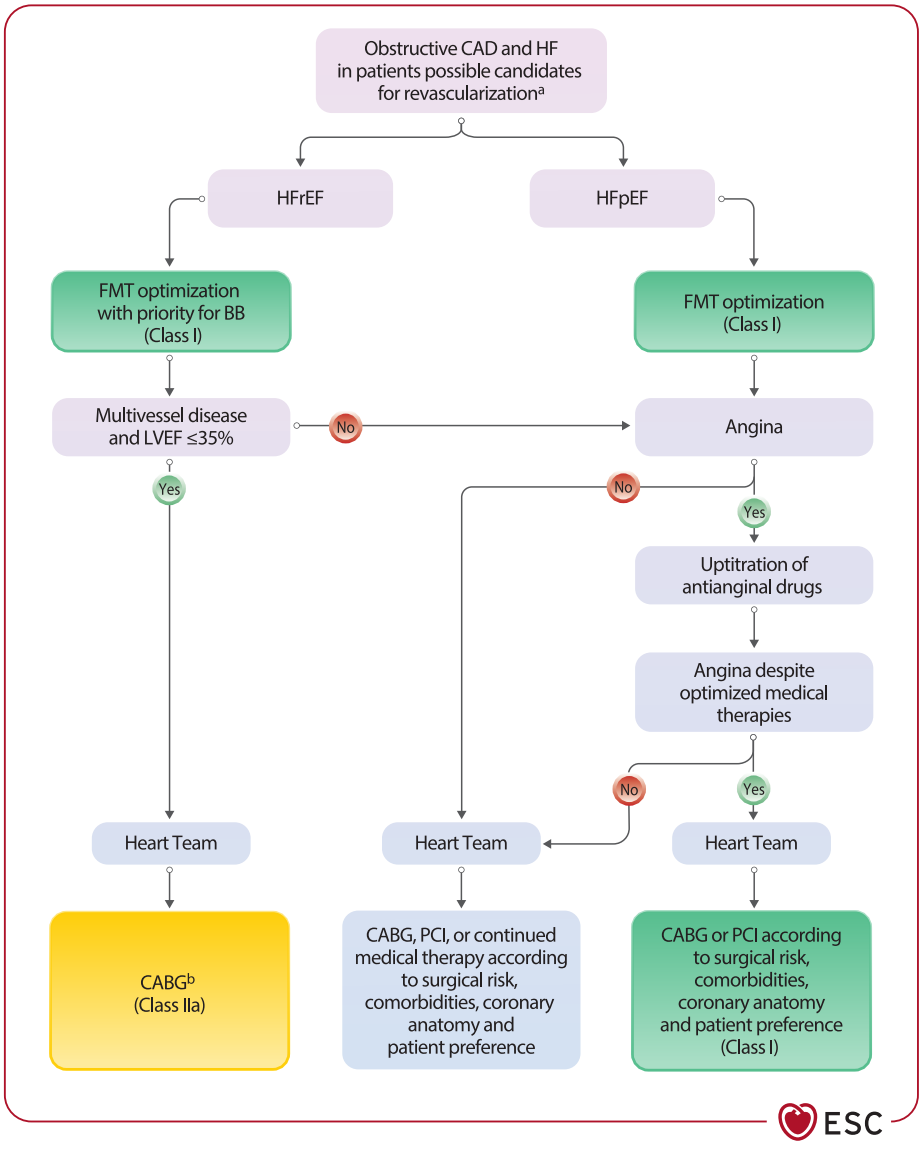

Figure 19 Management of coronary artery disease in patients with heart failure. BB, beta-blocker; CABG, coronary artery bypass grafting; CAD, coronary artery disease; FMT, foundational medical therapy; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention. Colours refer to class of recommendation. [a]Exclusion of frailty, severe and multiple comorbidities and limited life expectancy making the risk of revascularization higher than the expected benefit. [b]PCI or continued medical therapy are alternative treatments if the patient is not eligible for CABG.

of evidence B). However, the patient populations that were considered are slightly different in the chronic coronary syndrome guidelines (often patients with chronic coronary syndrome presenting with reduced LVEF) as compared to these guidelines (often patients with HFrEF presenting with CAD). In addition, according to the most recent system for level of evidence grading, proposed by the ESC, the Task Force considered STICHES, with all its limitations (mean age 60 years, limited number of events at 10 years, limited use of modern FMT), as the only possible study available to support the recommendation.[180]

Recommendation Table 16 — Recommendations for revascularization in chronic coronary syndrome in patients with heart failure (see *Evidence Table 82*)

Recommendations	Class[a]	Level[b]
Revascularization for symptom improvement (HFpEF and HFrEF)		
Coronary revascularization is recommended in patients with HF, obstructive CAD, and persistent angina, despite FMT for HF and antianginal drugs, to relieve symptoms.[734,735]	I	C
Revascularization for outcome improvement (HFrEF)		
If revascularization is planned after assessment by a Heart Team, CABG should be considered as the preferred revascularization strategy, in patients with LVEF ≤35% and multivessel CAD suitable for surgery, to improve long-term survival.[180]	IIa	B1

CABG, coronary artery bypass grafting; CAD, coronary artery disease; FMT, foundational medical therapy; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; LVEF, left ventricular ejection fraction.
[a]Class of recommendation.
[b]Level of evidence.

9.3. Valvular heart disease

9.3.1. Aortic stenosis

Aortic stenosis can contribute to or cause HF by increasing LV afterload.[736] Prevalence of aortic stenosis ranges between 3% and 7% in patients with chronic HF and is higher in patients with HFpEF as compared with those with HFrEF.[737] About 50% of patients with severe symptomatic aortic stenosis undergoing transcatheter aortic valve implantation (TAVI) have HF.[738] Once HF symptoms develop, prognosis is poor and timely valve intervention is mandatory. HF therapies may be used cautiously and should not delay valve intervention. After valve intervention, a clinical and echocardiographic reassessment is important to detect residual HF or risk of HF readmission. In this regard, further optimization of FMT as well as treatment of comorbidities and management of procedure-related factors is appropriate.[739] In the recent open-label DapaTAVI trial, 1222 patients with history of HF and at least one risk factor (diabetes, CKD, LV dysfunction) were randomly assigned to receive either dapagliflozin or standard of care. At 1-year follow-up, the risk of the primary endpoint (death from any cause or WHF events) was reduced by 28% in the treatment arm as compared with the control arm, mainly driven by WHF events.[740] Therefore, treatment with a SGLT2-I is reasonable in these patients.

Aortic valve intervention is recommended in all patients with HF and a life expectancy >1 year with high-gradient severe aortic stenosis, irrespective of LVEF, as well as in patients with severe low-flow low-gradient aortic stenosis and HFrEF. In patients with severe low-flow low-gradient aortic stenosis and HFpEF, aortic valve intervention should be considered. Details on diagnostic work-up, specific indications and the modality of intervention (TAVI vs surgery) are reported in the *2025 ESC/EACTS Guidelines for the management of valvular heart disease*.[9]

9.3.2. Aortic regurgitation

Severe aortic regurgitation can lead to LV dilatation and dysfunction which may progress to HF. Treatment with ACE-Is/ARNIs/ARBs/MRAs while awaiting aortic valve intervention can be beneficial.[741] Beta-blockers can prolong diastole and should be used only after careful consideration of risks and benefits.

Specific recommendations for intervention are reported in the *2025 ESC/EACTS Guidelines for the management of valvular heart disease*.[9]

9.3.3. Mitral regurgitation

9.3.3.1. Primary mitral regurgitation

Primary MR is caused by abnormalities of the valve apparatus and can lead to HF. In severe primary MR with HF symptoms, surgical repair is preferred over replacement whenever feasible.[739,742,743] Mitral transcatheter edge-to-edge repair (TEER) should be considered in patients at high surgical risk.[9,744,745]

9.3.3.2. Secondary mitral regurgitation

Secondary or functional MR is primarily a disease of the left cardiac chambers rather than the valvular apparatus. It is common in patients with HF, especially those with HFrEF in whom the disease has a prevalence of 25%.[746,747] In order to adequately assess the severity of MR, the patient should be euvolaemic or as close to euvolaemia as possible. The underlying aetiology and severity of MR needs to be assessed by cardiologists specialized in echocardiography and structural heart diseases.[748]

A new classification, differentiating between atrial secondary MR and ventricular secondary MR has been recently proposed.[9] Atrial secondary MR can be associated with HFpEF.[749] Indications for mitral valve treatment in atrial secondary MR are reported in the *2025 ESC/EACTS Guidelines for the management of valvular heart disease*.[9]

In patients with severe ventricular secondary MR and HFrEF, optimization of FMT and GDIT with CRT implantation (if indicated) is mandatory before considering any mitral valve intervention (*Figure 20*). In case of concomitant CAD requiring revascularization, specific recommendations on management are reported in the *2025 ESC/EACTS Guidelines for the management of valvular heart disease*.[9] In selected patients without need for coronary revascularization, TEER is recommended. *Table 19* provides the clinical and echocardiographic criteria for patient selection, which are based on inclusion criteria from RCTs. For the results of these studies, see Supplementary data online, *Section S6.3.1*.[750–754] If the criteria reported in *Table 19* are not fulfilled, other options can be considered. Specifically, in

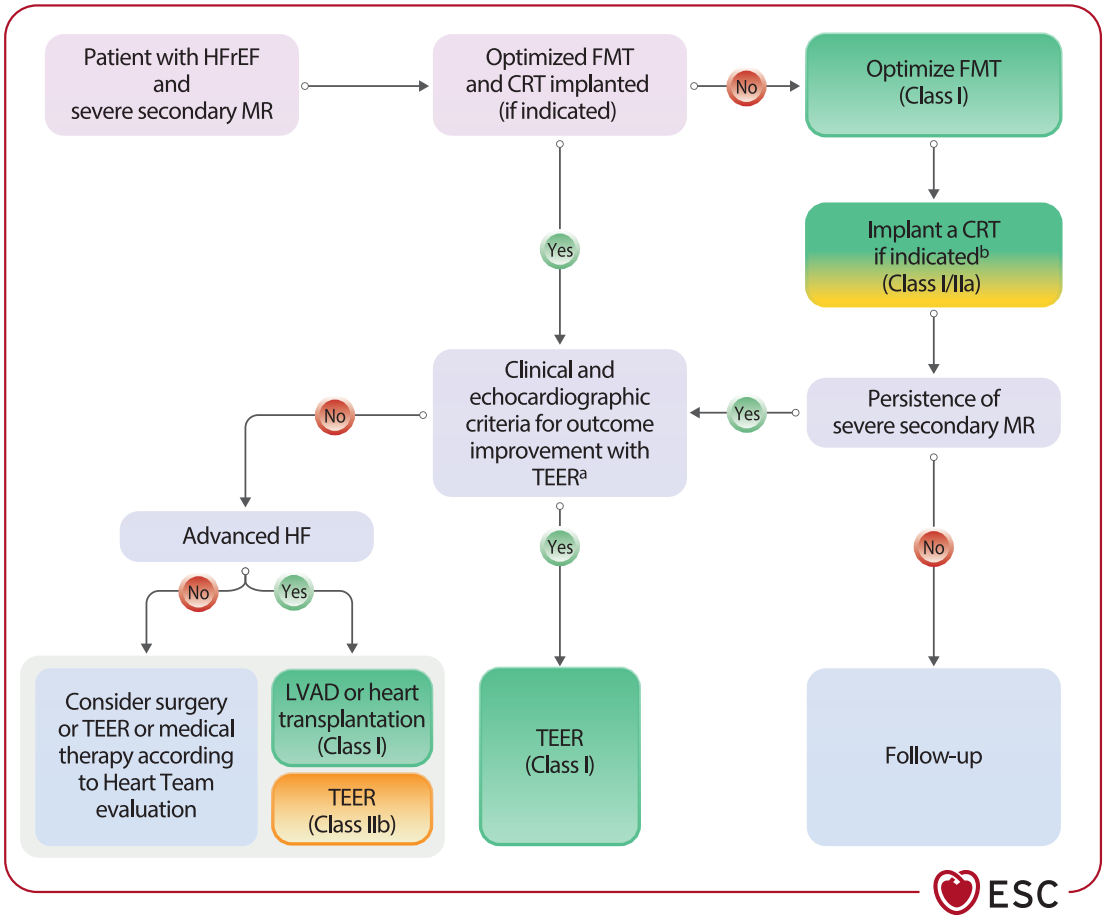

Figure 20 Management of secondary mitral regurgitation in patients with heart failure with reduced ejection fraction. CRT, cardiac resynchronization therapy; FMT, foundational medical therapy; HF, heart failure; LVAD, left ventricular assist device; MR, mitral regurgitation; TEER, transcatheter edge-to-edge repair. Colours refer to class of recommendation. [a]See *Table 19*. [b]See *Figure 10*.

Table 19 Selection criteria for mitral transcatheter edge-to-edge repair in heart failure with reduced ejection fraction

Clinical and echocardiographic criteria
Optimized FMT and other GDIT (i.e. CRT) if needed
NYHA class ≥II
At least one HFH within the last year OR Increased natriuretic peptide levels (BNP ≥300 pg/mL or NT-proBNP ≥1000 pg/mL)
No stage D (advanced) HF
No CAD requiring revascularization
No hypertrophic, restrictive, or infiltrative cardiomyopathies
LVEF 20%–50%
LVESD ≤70 mm
Anatomy deemed suitable for mitral TEER
sPAP ≤70 mmHg
No severe RV dysfunction
No severe aortic and/or tricuspid valve disease

BNP, B-type natriuretic peptide; CAD, coronary artery disease; CRT, cardiac resynchronization therapy; FMT, foundational medical therapy; GDIT, guideline-directed interventional therapy; HF, heart failure; HFH, heart failure hospitalization; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic diameter; TEER, transcatheter edge-to-edge repair; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; RV, right ventricular; sPAP, systolic pulmonary artery pressure.

patients with advanced HF, LVAD or heart transplantation is recommended as first choice and TEER may be considered for symptom improvement in patients not suitable or waiting for these therapies (see *Section 8*) (*Figure 20*). Notably, patients with ventricular secondary MR experience a higher residual risk of death or HFH despite TEER.[755,756] Thus, close follow-up in HF clinics is warranted.[757]

Recommendation Table 17 — Recommendations for valvular heart disease in patients with heart failure (see *Evidence Tables 83* and *84*)

Recommendations	Class[a]	Level[b]
Aortic stenosis		
Aortic valve intervention, SAVR or TAVI, is recommended in patients with severe aortic stenosis and HF[c] to improve symptoms and reduce the risk of death.[758–765]	I	B1
Secondary mitral regurgitation		
Mitral transcatheter edge-to-edge repair is recommended in haemodynamically stable, symptomatic patients with HFrEF and persistent severe secondary mitral regurgitation despite optimized FMT and CRT if indicated, who fulfil specific clinical and echocardiographic criteria,[d] in order to reduce the risk of HFH and improve QoL.[750–753]	I	B1
Mitral transcatheter edge-to-edge repair may be considered in selected symptomatic patients with HFrEF and persistent severe secondary mitral regurgitation despite optimized FMT and CRT if indicated (after excluding the option of LVAD or heart transplantation) who do not fulfil the clinical and echocardiographic criteria for outcome improvement,[d] in order to improve symptoms.[766–769]	IIb	C

CRT, cardiac resynchronization therapy; FMT, foundational medical therapy; HF, heart failure; HFH, heart failure hospitalization; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; LVAD, left ventricular assist device; LVEF, left ventricular ejection fraction; QoL, quality of life; SAVR, surgical aortic valve replacement; TAVI, transcatheter aortic valve implantation.

[a]Class of recommendation.

[b]Level of evidence.

[c]This recommendation refers to patients with severe high gradient aortic stenosis regardless of LVEF and to patients with low-flow low-gradient aortic stenosis and HFrEF. For details regarding low-flow low-gradient aortic stenosis in HFpEF, we refer to the *2025 ESC/EACTS Guidelines for the management of valvular heart disease*.[9]

[d]For clinical and echocardiographic criteria, see *Table 19*.

9.3.4. Tricuspid regurgitation

Severe TR has a high prevalence (9%–20%) in both patients with HFpEF and HFrEF.[747,770]

Tricuspid regurgitation is currently classified as primary TR, CIED-related TR, and secondary TR. Secondary TR is most common.[747,770] Medical therapy to target TR is limited.[747,771] The development of transcatheter devices to treat TR provides an alternative to surgery in selected patients. Three RCTs are currently available that investigated the role of transcatheter treatments in patients with severe symptomatic TR. They showed a significant benefit in terms of QoL in patients receiving device therapy as compared with those treated conservatively, but without reduction of death or HFH at 1-year follow-up.[772–774] Recently, a possible benefit in terms of HFH was reported in patients treated with tricuspid TEER, but with a high rate of crossover after 1-year follow-up.[775,776] It should be noted that all these studies were unblinded and did not focus on HFpEF or HFrEF populations.

Indications for TR treatment are reported in the *2025 ESC/EACTS Guidelines for the management of valvular heart disease*.[9]

9.4. Hypertension

Hypertension is common in patients with HF, especially those with HFpEF.[454,777,778] In hypertensive heart disease, LV remodelling and LV hypertrophy lead to both diastolic and systolic impairment. Specific blood pressure targets for patients with hypertension and HF have not been evaluated in RCTs.

In patients presenting with HF due to refractory hypertension, secondary causes [i.e. primary aldosteronism, renovascular hypertension, and obstructive sleep apnoea (OSA)] should be ruled out and treated.[62]

Indications for the treatment of hypertension in HF are reported in the *2024 ESC Guidelines for the management of elevated blood pressure and hypertension*.[62]

Lifestyle interventions, such as increasing physical activity, optimizing weight, reducing salt and alcohol intake, and smoking cessation, are beneficial in all cases.[62]

The optimal treatment strategy for hypertension in patients with HFpEF is uncertain. FMT with effect on blood pressure (i.e. MRA) should be started, continued, or uptitrated. Loop diuretics reduce congestion and decrease blood pressure. In addition, ACE-Is, ARBs, and calcium channel blockers cause LV regression and therefore may be beneficial in both controlling blood pressure and improving HFpEF symptoms.[62] Patients with HFpEF have limited preload reserve; therefore, normotension should be maintained and hypotension avoided.

In patients with HFrEF, treatment strategies are similar to those for normotensive patients, as FMT also lowers blood pressure. Once FMT has been initiated and uptitrated, suboptimal blood pressure control is rare in HFrEF. If additional agents are required, amlodipine or felodipine may be considered provided the patient is euvolaemic.[714,715] Alpha-blockers may be continued for the treatment of prostatic hyperplasia in the absence of hypotension but are not recommended for the treatment of hypertension in HFrEF. Non-dihydropyridine calcium channel blockers, e.g. verapamil and diltiazem, and central sympathetic agonists, e.g. moxonidine, are contraindicated due to poor outcomes in patients with HFrEF.[779] In patients with HFrEF, asymptomatic hypotension should be accepted in order to maintain target doses of FMT.[780]

9.5. Stroke

Heart failure and stroke share common risk factors. Approximately 10%–24% of patients with ischaemic stroke have concomitant HF either *de novo* or pre-existing.[781–784] Conversely, patients with HF have an increased risk of stroke compared with those without.[785] A history of stroke is reported

in 8%–11% patients with HF[785–789] with similar[790–794] or increased[795,796] prevalence in patients with HFpEF compared with HFrEF.

Poorer outcomes after stroke are observed in patients with HF with a 2.2–4.5 times higher rate of death compared with people without HF,[782,783,797] as well as an increased rate of recurrent stroke.[798]

The risk of stroke in patients with HF seems independent of rhythm, with an annualized stroke risk of 2.0 per 100 patient-years in patients in sinus rhythm and 2.87 per 100 patient-years in patients with AF.[799–802] However, RCTs failed to demonstrate a possible benefit of oral anticoagulation in patients with HFrEF in sinus rhythm.[803–806] Thus, in the absence of AF, there is no evidence to recommend routine anticoagulation for stroke prevention in patients with HFrEF.

Optimization of blood pressure, heart rate, and cardiac output immediately after a stroke is key to reducing the risk of DHF and improving outcomes. In patients already established on FMT, treatment with FMT should be maintained if possible and attention should be paid to dose modification in order to avoid both hypo- and hypertension as well as rebound tachycardia in patients in whom beta-blockers have been withdrawn.[807] Following the acute phase, treatment of HF in patients with stroke does not differ from treatment in patients without stroke.

10. Non-cardiovascular comorbidities

10.1. Obesity

Obesity contributes to the development of well-known CV and HF risk factors like hypertension, diabetes, and dyslipidaemia. Obesity has direct adverse effects on cardiac structure and function, and is associated with the development of CVD, including HF.[808] Patients with HF and obesity may have lower natriuretic peptide concentrations due to increased expression of clearance receptors, augmented peptide degradation by the adipose tissue,[155] and underestimation of circulatory congestion.[809] Peak oxygen consumption adjusted for body weight underestimates exercise capacity in obese patients, and an adjustment for lean body mass should be used for risk stratification pro-inflammatory.[810]

A stronger association between obesity and HFpEF rather than HFrEF has been described.[778,811] Among patients with HFpEF, the obesity-related phenotype has a high prevalence (30%–40% in Europe and 60%–70% in North America).[314,812] These patients display several pathophysiological mechanisms that differ from non-obese patients with HFpEF.[813] An increase in adipocyte mass induces a state of systemic inflammation and a proinflammatory transformation of epicardial adipose tissue that may lead to fibrosis. The capacity of the left ventricle to dilate in response to an increase in blood volume is impaired, and thus, even modest degrees of volume overload may lead to cardiac overfilling and disproportionate increase in cardiac filling pressures.[814] On average, patients with HFpEF and obesity are younger, experience worse HF signs and symptoms, poorer QoL, and worse functional capacity, than those without obesity.[815,816]

Weight-loss interventions in patients with HFpEF and obesity alleviate symptoms and may improve outcomes. Lifestyle interventions, such as caloric restriction, exercise, and patient education, have a significant impact on body weight and are recommended in all patients with HF.[817,818] Recent RCTs demonstrated favourable effects of the GLP-1 RA semaglutide and the dual GIP/GLP-1 RA tirzepatide in patients with HFpEF and obesity regardless of diabetes status, namely reduction of body weight, improvement of QoL, symptoms, and functional capacity (see Supplementary data online, *Section S7.1*).[315–317] Pooled and secondary analyses of RCTs, and the recent SUMMIT trial, have also suggested a potential benefit of these drugs on HF events.[317,819,820]

Dedicated RCTs are needed to evaluate safety and efficacy of these drugs in patients with HFrEF and to assess long-term follow-up.[821,822]

In propensity score-matched cohort studies, bariatric surgery was associated with weight loss and a lower risk of all-cause and CV death, HFH, and AF as compared to medical therapy in patients with HF and a BMI ≥35 kg/m^2, with consistent benefits observed among patients with HFrEF and HFpEF.[823,824]

Studies comparing bariatric surgery vs new anti-obesity medications are lacking, and the indications for bariatric surgery may change in the future.

Recommendation Table 18 — Recommendations for obesity in patients with heart failure (see *Evidence Tables 85 and 86*)

Recommendations	Class[a]	Level[b]
Semaglutide or tirzepatide should be considered for patients with symptomatic HF, LVEF ≥45%, and BMI ≥30 kg/m^2, regardless of diabetes status, to reduce body weight, and improve exercise capacity and QoL.[315–317,819,820,825]	IIa	B1
Bariatric surgery may be considered in obese patients with HF and a BMI ≥35 kg/m^2 to reduce body weight when repetitive and structured lifestyle changes combined with weight-reducing medications do not result in maintained weight loss.[823,824]	IIb	C

BMI, body mass index; HF, heart failure; LVEF, left ventricular ejection fraction; QoL, quality of life.
[a]Class of recommendation.
[b]Level of evidence.

10.2. Diabetes

Patients with HF who have T2DM have a poorer prognosis than patients who do not have T2DM.[826–828]

The diagnostic process and therapeutic approach to HF in patients with T2DM is the same as the population without T2DM. There is no evidence that the efficacy of FMT is altered by the presence of T2DM.[241,829–833 60] The *2023 ESC Guidelines for the management of cardiovascular disease in patients with diabetes* dedicated a specific section to the treatment of diabetes in patients with HF.[60]

Sodium–glucose co-transporter 2 inhibitors have been investigated in different populations with diabetes, ranging from patients with ASCVD or multiple ASCVD risk factors to patients with established HF across the entire range of LVEF or recently hospitalized for WHF, with greater absolute risk reduction of clinical events in patients at higher risk.[834] Thus, the use of

SGLT2-Is is recommended in all patients with HF and T2DM, independently of glycated haemoglobin levels or other concomitant glucose-lowering agents. SGLT2-Is are generally well tolerated, although they may cause urinary infections and genital fungal infections as vulvovaginitis and balanitis with a prevalence of up to 6.9% in women and 4.8% in men. They are not indicated in patients with type 1 diabetes mellitus due to the risk of diabetic ketoacidosis (reported incidence of 2%–3%).[835,836] Semaglutide or tirzepatide should be added if not contraindicated in patients with HFpEF and T2DM, especially if they are also obese.[316,317]

Metformin, despite its long history as first-line treatment of T2DM, has no dedicated CV outcome trials to assess its safety or efficacy; observational studies reported a lower risk of death or HFH in patients with HF when compared with insulin and sulfonylureas.[837–839] Metformin is not recommended in patients with an eGFR <30 mL/min/1.73 m^2 or hepatic impairment because of the risk of lactic acidosis.

In the context of T2DM, insulin glargine and insulin degludec have been evaluated in specific CV outcome trials, demonstrating a neutral effect on incident HF in patients with diabetes.[840–842] In post-hoc analyses of RCTs and retrospective registries, use of insulin was associated with poorer outcomes among patients with HF. Thus, if insulin is needed in a patient with HF, patients should be monitored for WHF after initiation of treatment.[843,844]

The dipeptidyl peptidase-4 inhibitor saxagliptin and thiazolidinediones (glitazones) have been associated with an approximately 30% increased risk of HFH and, thus, are contraindicated in patients with HF.[845,846] No consistent data are available for the use of sulphonylureas in patients with HF.[60]

10.3. Chronic kidney disease

Chronic kidney disease and HF frequently coexist.[847] They share common risk factors and may develop simultaneously. CKD may lead to worsening of cardiac function and vice versa. The incidence of CKD is five-fold higher in patients with HF as compared with those without.[848] About 30%–40% of individuals with chronic HF have CKD, with the highest proportions, up to 50%, in HFpEF.[778,849,850] CKD is a major independent determinant of increased mortality and morbidity in HF.[850] Albuminuria and low GFR are independently associated with an increased risk of major ASCVD, HF events, and CV death.[61,851–854] The presence of CKD might have an impact on FMT optimization, and it is often cited as a reason for FMT under-utilization in clinical practice.[855] Even in most patients with CKD the initiation of beta-blockers, ACE-Is/ARNIs/ARBs, SGLT2-Is, and MRAs is recommended.[164]

Several RCTs have shown that patients with HF and concomitant CKD are at higher risk of events as compared to those without CKD. However, no interaction between drug effects and kidney function was noted in subgroup analyses of these trials.[242–245,309] Furthermore, the beneficial effects of FMT are similar, or even higher, irrespective of CKD.[251,252,847,856–858]

An evidence gap remains for the treatment of HF in patients with severe CKD as these patients were generally excluded from RCTs.

Worsening kidney function in patients with chronic HF is not necessarily associated with worse outcomes. For example, after initiation of ACE-Is/ARNIs/ARBs, MRAs or SGLT2-Is, an initial decrease in the glomerular filtration pressure may decrease GFR and increase serum creatinine. These changes are generally transient and occur despite improvement in patient outcomes and may delay long term deterioration of kidney function.[243,250–253] Sacubitril–valsartan, compared with enalapril, led to a slower decline in kidney function, despite a slight increase in the UACR, and improved CV outcomes to a similar extent in patients with CKD vs other patients in the PARADIGM-HF trial.[279] In a participant-level pooled analysis of the DAPA-HF and DELIVER trials, patients experiencing worsening of eGFR to <25 mL/min/1.73 m^2 were at heightened risk for development of subsequent CV events. Continuation of dapagliflozin was associated with lower rates of the primary composite outcome.[859]

A prespecified secondary analysis of the FINEARTS-HF trial, in patients with HF and LVEF ≥40%, reported an acute decline in eGFR of −2.9 mL/min/1.73 m^2 (95% CI −3.4 to −2.4) during the first 3 months on finerenone vs placebo.[860] However, finerenone still reduced the risk of new-onset micro- and macroalbuminuria by 24% and 38%, respectively.[860]

Thus, a transient decrease in kidney function after the initiation of ACE-Is/ARNIs/ARBs and MRAs or SGLT2-Is should not prompt their interruption. An increase in serum creatinine of <50% above baseline, as long as eGFR remains >15 mL/min/1.73 m^2, is considered acceptable.

Notably, in patients with HFpEF, semaglutide and tirzepatide may acutely reduce eGFR; however, they exhibit a long-term protective effect on kidney function.[861,862]

Chronic kidney disease is highly prevalent in patients with DHF. Worsening or improvement of kidney function occurs commonly, affecting about 30%–50% of patients admitted with HF.[273] Adverse CV outcomes are observed in patients with worsening kidney function and poor diuretic response, but not in patients with good diuretic response.[506,863]

Data from the STRONG-HF trial showed that a decrease in eGFR within 1 week after discharge was associated with more evidence of congestion and with an increased incidence of HF readmissions.[864] Conversely, worsening kidney function is not associated with poor outcomes in the context of successful decongestion.[506,863] For further details refer to the 2026 ESC Guidelines on cardiovascular disease and chronic kidney disease.[122]

10.4. Iron deficiency and anaemia

Iron deficiency and anaemia are common in patients with HF and are associated with reduced functional capacity, and worse QoL and prognosis independently of each other.[778,865–868] Iron deficiency is slightly more prevalent in patients with HFpEF than in patients with HFrEF.[865,869]

In patients with HF, ID has been defined as either ferritin <100 ng/mL, or ferritin 100–299 ng/mL with TSAT <20%. This definition has been adopted by the *2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure*[3] and the *2023 Focused Update of the 2021 ESC Guidelines for the*

diagnosis and treatment of acute and chronic heart failure,[5] and has been used in almost all recent trials assessing the effects of i.v. iron supplementation in patients with HF and ID. However, it has recently been recognized that in patients with HF this definition does not reliably identify patients with absolute or functional ID. The current definition of ID may include patients with TSATs (≥20%) and serum ferritin levels (20–100 mg/L) in the normal range, who are probably not iron deficient, exhibit a better prognosis, and might not respond to i.v. iron therapy.[870] Moreover, serum ferritin levels are highly sensitive to inflammation and oxidative stress. Thus, an alternative definition of ID—TSAT <20%—has been proposed, mainly based on evidence from explorative analyses and meta-analyses of RCTs. A TSAT <20% has higher sensitivity and specificity compared with the previous definition of ID and is associated with higher mortality rates, independently of HF phenotype.[869–871] Moreover, some meta-analyses of large RCTs reported that lower TSAT values better identify patients that will respond favourably to i.v. iron supplementation.[872–874] The Task Force supports the use of this most recent definition of ID in patients with HF and recognizes the need for new trials investigating the efficacy of i.v. iron supplementation in patients with HF and ID as defined by TSAT <20%.

Several trials, including AFFIRM-AHF,[496] CONFIRM-HF,[875] FAIR-HF,[876,877] EFFECT-HF,[878] and IRONMAN[879] (where ID was defined as either ferritin <100 ng/mL, or ferritin 100–299 ng/mL with TSAT <20%), have demonstrated that iron supplementation with i.v. ferric carboxymaltose is safe and effective in improving symptoms and QoL in patients with HF and LVEF <40%–45%.

Thus, i.v. iron supplementation is recommended in patients with symptomatic HFrEF and ID to alleviate HF symptoms and improve QoL. Data in patients with HFpEF are scarce.[880]

The prognostic benefit of i.v. iron supplementation in patients with HF has been investigated in several RCTs and meta-analyses (see Supplementary data online, *Section S7.2*).[496,872,873,879,881–886] Given the conflicting results of major RCTs, the position of the Task Force is that evidence regarding the benefits of i.v. iron supplementation on strong endpoints is not conclusive. This is primarily due to the use of the old definition of ID as an enrolment criterion in almost all trials, the heterogeneity of RCTs in terms of enrolled populations as well as of i.v. iron doses and timing of administration and that some major RCTs were affected by the coronavirus disease 2019 pandemic. Thus, i.v. iron supplementation with ferric carboxymaltose or ferric derisomaltose should be considered in patients with symptomatic HFrEF and ID to reduce the risk of HFH, taking into account that patients with TSAT <20% might benefit most. Further trials using TSAT <20%, or other criteria that do not rely on ferritin levels as inclusion criteria, are warranted.

In patients with HFrEF and mild to moderate anaemia enrolled in the RED-HF trial,[887] darbepoetin-alpha failed to reduce all-cause death or HFH and showed an increased risk of thromboembolic events. Thus, erythropoietin-stimulating agents should be avoided for the treatment of anaemia related to HF.

Recommendation Table 19 — Recommendations for iron deficiency in patients with heart failure (see *Evidence Tables 87 and 88*)

Recommendations	Class[a]	Level[b]
Intravenous iron supplementation is recommended in patients with symptomatic HFrEF and iron deficiency to alleviate HF symptoms and improve QoL.[875–879]	I	B1
Intravenous iron supplementation should be considered in patients with symptomatic HFrEF and iron deficiency to reduce the risk of HFH.[872–874,879,881,885,886,888]	IIa	B1

HF, heart failure; HFH, heart failure hospitalization; HFrEF, heart failure with reduced ejection fraction; QoL, quality of life.
[a]Class of recommendation.
[b]Level of evidence.

10.5. Cancer

In patients with cancer, HF may occur as a result of the interactions between cancer therapy, cancer itself, and/or patients' CV backgrounds (risk factors and coexisting CVD). Current cancer treatments may cause HF through direct cardiotoxic effects, or indirectly, favouring the occurrence of pathological conditions predisposing to HF, such as volume overload from i.v. infusions and corticosteroids, myocarditis, myocardial ischaemia, systemic or pulmonary hypertension, thromboembolism, arrhythmias, or valve disease.[6,889,890]

The definition of symptomatic and asymptomatic cancer therapy-related cardiac dysfunction is reported in Supplementary data online, *Table S21*. Cancer drugs causing HF are reported in Supplementary data online, *Table S22*.

In patients who develop symptomatic HF during cancer therapy, FMT is recommended, regardless of LVEF.[6] Discontinuation vs continuation of cardiotoxic drugs should be discussed by a multidisciplinary team. Severity of cancer therapy-related cardiac dysfunction guides the decision.[6,891] Initiation of FMT for HFrEF is recommended in patients with asymptomatic moderate-to-severe cancer therapy-related cardiac dysfunction and should be considered in asymptomatic patients with mild presentations.

For details regarding CV toxicity risk assessment process, diagnostic work-up, follow-up procedures, and therapeutic management of cardiotoxicity, we refer to the *2022 ESC Guidelines on cardio-oncology*.[6]

10.6. Lung disease and sleep-disordered breathing

Chronic obstructive pulmonary disease is common among patients with HF.[892–894] Due to the overlap in symptoms and signs, the differentiation between HF and COPD may be difficult.[895]

Chronic obstructive pulmonary disease significantly impacts on symptoms and QoL, has been associated with HF undertreatment, and negatively influences prognosis of HF.[893,896]

Treatment of HF is generally well tolerated in COPD. The use of cardioselective beta-blockers (bisoprolol, metoprolol succinate, or nebivolol) should be preferred. In patients with asthma,

these medications require more caution and should be started at low doses after consideration of the risks and benefits, with close monitoring for signs of airway obstruction, and appropriate supervision.[897] Chronic obstructive pulmonary disease exacerbations should not be a cause of beta-blocker discontinuation.[898] Inhaled corticosteroids and beta-adrenergic agonists have not been specifically studied in patients with HF; however, they do not seem to increase CV risk.[899,900] In addition, appropriate management of COPD can improve cardiac function.[901]

Sleep-disordered breathing is found in over one-third of patients with HF and is even more prevalent in DHF. Sleep-disordered breathing includes OSA, central sleep apnoea (CSA), and mixed disease. SDB negatively impacts disease progression and prognosis.[902,903] Patients with a suspicion of SDB should be referred for overnight polysomnography to definitively diagnose SDB, and to document the predominant type of sleep apnoea (central vs obstructive).[902] The therapeutic approach to SDB includes the correction of underlying causes, when identified.

The use of adaptive servo-ventilation (ASV) in patients with HFrEF and predominantly CSA is not recommended, based on the results of the SERVE-HF trial,[904] which showed an increase in both all-cause and CV death in patients with chronic HF, LVEF ≤45%, and SDB with predominant CSA.[904]

The ADVENT-HF trial randomized 731 patients with HF, LVEF ≤45%, and coexisting SDB, mostly OSA (73%) to standard optimal treatment alone or standard optimal treatment and ASV (1:1). Over a mean follow-up period of 3.6 years, ASV had a neutral effect on the primary composite outcome (the cumulative incidence of all-cause death, first CV hospitalization, new-onset AF/flutter, and delivery of an appropriate ICD shock).[905] However, ASV improved sleep quality and structure, health-related QoL, and symptoms of patients with SDB.[905]

Thus, in patients with SDB and predominant OSA, nocturnal hypoxaemia can be treated with nocturnal oxygen supplementation, continuous positive airway pressure (CPAP), bilevel positive airway pressure, and ASV.

When SDB is caused by CSA, implantable phrenic nerve stimulation was found to be safe and effective in reducing the apnoea–hypopnoea index in a small RCT.[906–908]

Recommendation Table 20 — Recommendations for lung disease and sleep-disordered breathing (see *Evidence Table 89*)

Recommendations	Class[a]	Level[b]
Adaptive servo-ventilation may be considered in patients with HFrEF and sleep-disordered breathing with predominant obstructive sleep apnoea to improve sleep quality, health-related QoL and symptoms.[905]	IIb	C
Adaptive servo-ventilation is not recommended in patients with HFrEF and sleep-disordered breathing with predominant central sleep apnoea because of an increased risk of CV and all-cause death.[904]	III	A

CV, cardiovascular; HFrEF, heart failure with reduced ejection fraction; QoL, quality of life.
[a]Class of recommendation.
[b]Level of evidence.

10.7. Anxiety, depression, and cognitive impairment

Anxiety and depression are common findings in patients affected by chronic and disabling conditions, such as HF, and need to be promptly identified to minimize psychological distress and its negative consequences.[909] Depression affects 20% of patients with HF, and it may affect adherence to FMT. Its prevalence is higher in women, and it is associated with worse clinical status and poorer prognosis.[910–912]

The diagnosis of depression typically relies on standardized questionnaires and clinical interviews. Symptom overlap between HF and depression can complicate diagnosis, as both conditions may present with cognitive issues (e.g. difficulty concentrating) and physical symptoms (e.g. fatigue). Several validated questionnaires are available for screening clinically significant depressive symptoms[911] (see Supplementary data online, *Section S7.4, Table S23*).

Cognitive impairment in these patients has been reported.[911,913] However, there is still no consensus on the best therapy for patients with HF and depression.

Cognitive behavioural therapy has demonstrated significant favourable long-term (4–9 months) reduction of anxiety and depression and improvement in QoL compared with non-treated patients.[914,915] The safety of sertraline and escitalopram has been demonstrated, although without a significant reduction in depression compared with placebo.[916,917] Tricyclic antidepressants should be avoided for the treatment of depression in HF as they may cause hypotension, WHF, and arrhythmias.[911,912]

10.8. Frailty

Frailty is defined as a multidimensional, dynamic, and potentially reversible state, related to, but independent of, age, that makes individuals more vulnerable to the effects of stressors and at increased risk of poor outcomes. A score assessing frailty including four domains (clinical, functional, psychocognitive, and social) has recently been proposed.[918]

The presence of frailty might have an impact on disease management and is associated with higher rates of death and hospitalizations, and reduced health-related QoL, regardless of which tool was used to assess frailty.[919–923] In patients with HF, frailty is particularly prevalent in older adults. When frailty is suspected or identified, a multidisciplinary approach to facilitate an individualized management is warranted.[918,922,924]

Recommendation Table 21 — Recommendations for anxiety, depression, and frailty (see *Evidence Tables 90* and *91*)

Recommendation	Class[a]	Level[b]
Assessment of anxiety, depression and frailty should be considered in patients with HF to support the development of personalized care plans and to identify factors that may contribute to adverse outcomes.[909,914,915,920,923]	IIa	C

HF, heart failure.
[a]Class of recommendation.
[b]Level of evidence.

10.9. Other non-cardiovascular comorbidities

Infections may cause WHF and can precipitate HFH.[925,926] Infections should ideally be prevented or, if present, promptly recognized and treated to avoid disease progression.[927–930]

Influenza vaccination is associated with a reduced risk of pneumonia and all-cause death in patients with HF.[931–936] Thus, influenza and pneumococcal vaccination should be considered in all patients with HF in order to reduce the risk of infection-related complications.[935]

Thyroid dysfunction can cause changes in cardiac function and structure and may precipitate DHF.[937,938] Assessment of thyroid function is recommended in patients with *de novo* HF or DHF and should be regularly assessed during follow-up of patients with HF. Treatment of thyroid dysfunction should be guided by endocrine guidelines.[939–942]

Hyperuricaemia and consequent gout attacks can be frequent in patients with HF, mainly caused or precipitated by diuretic treatment.[943,944] Allopurinol is recommended as the first choice to chronically reduce uric acid levels in patients with HF,[945] whereas colchicine can be used for acute gout attacks. Non-steroidal anti-inflammatory drugs and selective cyclooxygenase-2 inhibitors are not recommended in patients with HF because they may precipitate decompensation and worsen kidney function.[942,946–948]

Heart failure and erectile dysfunction frequently coexist.[949,950] Cardioselective beta-blockers should be preferred in patients with HF and erectile dysfunction, mainly bisoprolol and nebivolol, started at the lowest doses.[897] In the presence of erectile dysfunction symptoms, phosphodiesterase-V inhibitors are generally safe and can be considered in patients who are compensated,[951] avoiding their concomitant use with nitrates.[952]

Recommendation Table 22 — Recommendations for other non-cardiovascular comorbidities (see *Evidence Tables 92 and 93*)

Recommendations	Class[a]	Level[b]
Influenza and pneumococcal vaccination should be considered in patients with HF to reduce the risk of pneumonia complications, hospitalization, and death.[931–934,936,953,954]	IIa	C
NSAIDs and COX-2 inhibitors are not recommended in patients with HF as they increase the risk of HF worsening and HFH.[942,946–948]	III	B2

COX-2, cyclooxygenase-2; HF, heart failure; HFH, heart failure hospitalization; NSAID, non-steroidal anti-inflammatory drug.
[a]Class of recommendation.
[b]Level of evidence.

11. Multidisciplinary team management, long-term follow-up, and patient care

11.1. Multidisciplinary management of heart failure

Multidisciplinary care for HF combines the expertise of various professionals to provide integrated, patient-centred care that improves both clinical outcomes and QoL for patients (*Figure 21*).

Access to healthcare professionals with awareness of HF and expertise in its diagnosis and management is essential for early detection and better outcomes. Multidisciplinary HF care involves generalist and specialist healthcare professionals,[955] including cardiologists, cardiothoracic surgeons, specialist nurses, pharmacists, and physiologists (*Figure 21*) (see Supplementary data online, *Section S8.1*).[17,956–963]

Management by an HF multidisciplinary team (HF-MDT) across outpatient and inpatient settings improves outcomes for people with HF.[962,964–967]

The literature evaluates various methods of delivering HF management programmes enabling local HF services to design services tailored to their HF-MDT and the structure of their healthcare system. A meta-analysis of 16 RCTs with 3999 eligible patients evaluating the benefits of multidisciplinary HF clinics compared with usual care demonstrated a reduction in HFH.[967] A meta-analysis of eight RCTs with 1764 patients indicated that multidisciplinary teams may have the potential to reduce death, although a definitive RCT is needed.[964] The benefits were more evident in patients with a recent emergency department presentation or HFH.[966] Other methods of delivery, including home visits and transitional care models, are given in Supplementary data online, *Section S8.1*.[145,962,965,968–972]

Healthcare professionals involved in the management of HF, whether specialist or generalist, should be equipped with the knowledge required to effectively assess and manage HF through appropriate education and training.[958,973,974] Malnutrition has been associated with worse prognosis in patients with HF.[738] Thus, nutritional assessment and dietary interventions can be useful.[588,589] No evidence supports fluid restriction in chronic HF.[975,976]

Recommendation Table 23 — Recommendations for the multidisciplinary management of heart failure (see *Evidence Tables 94–96*)

Recommendations	Class[a]	Level[b]
A multidisciplinary HF management programme is recommended in patients with HF to reduce the risk of HFH and death.[964–967]	I	B1
HF education and self-management strategies in patients with HF are recommended to reduce the risk of HFH or death.[977]	I	A
Multidisciplinary interventions to improve adherence, including assessment of health literacy and polypharmacy review, are recommended in patients with HF to reduce the risk of hospitalization and death.[978–981]	I	B2

HF, heart failure; HFH, heart failure hospitalization.
[a]Class of recommendation.
[b]Level of evidence.

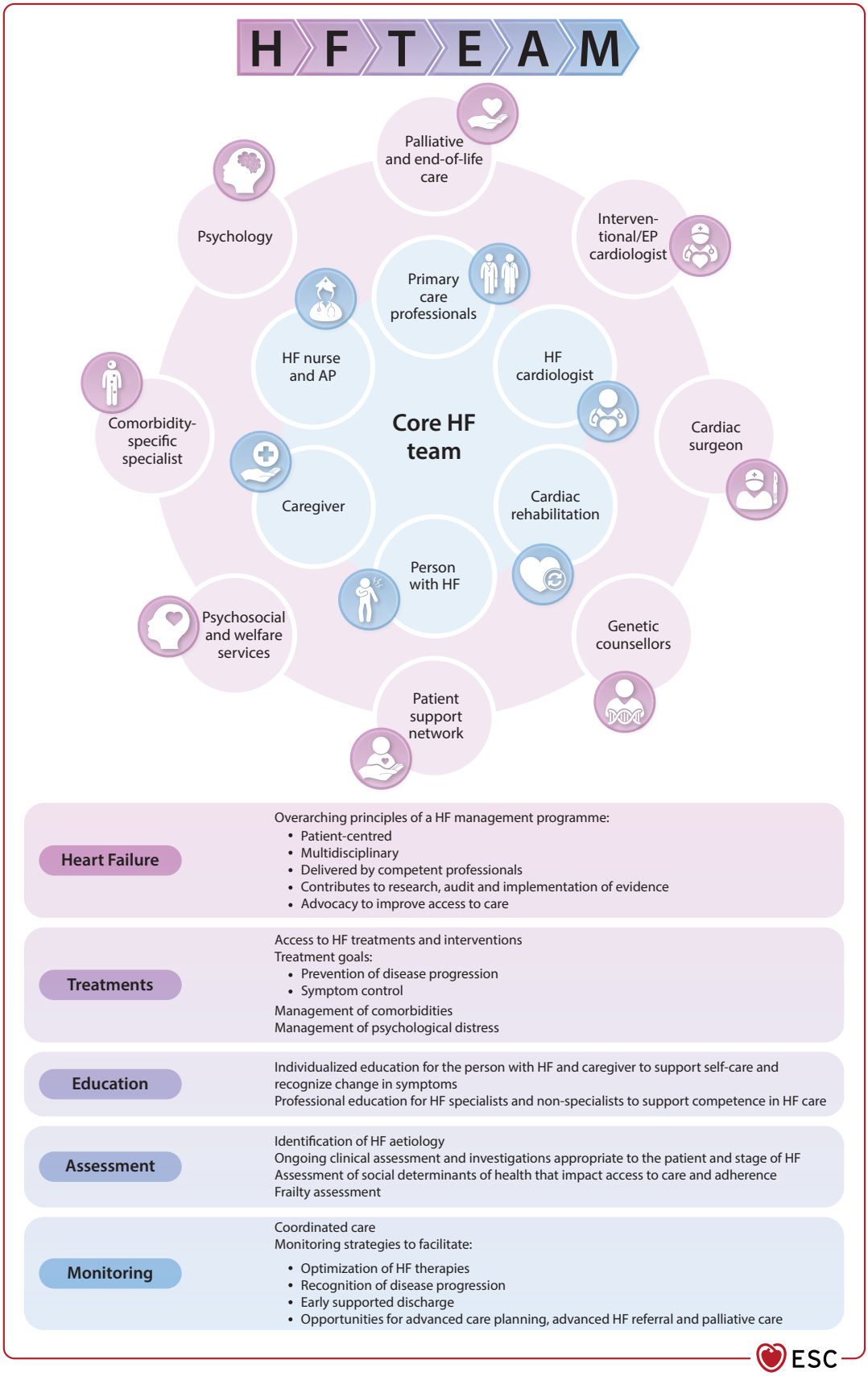

Figure 21 Core members of the heart failure team with expanded team members depending on patient needs and local availability. AP, allied professional; EP, electrophysiology; HF, heart failure.

11.2. Patient education, self-care, and lifestyle advice

Education, self-care, and lifestyle advice empower patients and their caregivers in managing HF and engage in shared decision-making. Self-care incorporates education and strategies to support maintenance, monitoring, and management of HF.[973] The aim is to ensure people with HF and their caregivers are equipped with knowledge and skills and be partners in their care and not simply recipients of information and treatments. The benefits of self-care are described in a meta-analysis of 20 RCTs including 5624 patients.[977] Self-management interventions on the background of usual HF care improved QoL and reduced time to HFH or all-cause death. There may be some barriers to self-care, but these can be overcome by careful design of programmes[982,983] (see Supplementary data online, *Section S8.2*).

Effective self-care enhances QoL, reduces symptom severity, and lowers the risk of hospitalization. It is essential that HF professionals collaborate with patients and caregivers, using shared decision-making to develop personalized self-care plans (Supplementary data online, *Table S24*).

11.3. Implementation and adherence to therapy

11.3.1. Implementation and optimization

Implementation of HF therapies should be individualized, based on available evidence, and involve the HF-MDT and patients and caregivers. Yet, there remain delays to implementation and optimization of treatments.[984–986] Multivariable adjusted large observational studies suggest that among the strongest factors associated with improved FMT, AMT, and GDIT use is access to cardiologist specialists.[987–990] For barriers and facilitators to improved implementation of HF therapies, including clinical inertia, impact of race, ethnicity, gender, and health literacy, see Supplementary data online, *Table S25*.

Evidence supports the role of HF nurses and pharmacists in the implementation and optimization of HF therapies and avoidance of unnecessary side effects of polypharmacy.[991–994]

Pharmacists play a key role in ensuring safe and effective use of medicines, including medication reconciliation and the optimization of therapies for comorbidities. Development of the HF-MDT to support the implementation and optimization of HF and to address the barriers that exist is key to improving outcomes for patients.

11.3.2. Long-term adherence

Adherence to self-care strategies and therapies is essential to control symptoms, limit disease progression, and reduce hospitalization and death.[981] Factors that impact adherence and affect clinical outcomes include health literacy, polypharmacy, and managing multiple health conditions.[978,979,995] Strategies to improve adherence in the context of HF have been described elsewhere and provide guidance on the use of education tailored to the individual, communication skills, polypharmacy review, and co-ordinated care.[980,996] Central to these is the importance of the HF-MDT recognizing the barriers to adherence, assessing those barriers, and utilizing other members of the health and social care team to address them.

11.4. Exercise training and cardiac rehabilitation

11.4.1. Benefits of exercise training according to heart failure stage and phenotype

There is consistent evidence that exercise training improves exercise tolerance and health-related QoL in patients with HF.[94] HF-ACTION was the largest RCT on exercise training in HF including 2331 patients with LVEF ≤35% (NYHA classes II–IV). Compared with usual care, supervised exercise training plus usual care showed modest, non-significant reductions in all-cause death and hospitalizations. However, prespecified adjustments revealed significant reductions in CV death and HFH.[997] A systematic review of 60 trials with 8728 patients (mean age 63 years, mean LVEF 32%) confirmed improvements in functional capacity, QoL, and reductions in HFH with exercise training but found no reduction in death.[998] Similar findings were reported by another systematic review focusing on HFrEF (LVEF <40%).[94,999]

In HFpEF, exercise training is safe and significantly enhances exercise capacity and QoL, with no significant impact on diastolic function, arterial stiffness, or vascular function, and insufficient data exist to assess its impact on clinical events, such as death and hospital admissions, due to small sample sizes and short follow-up times.[1000,1001]

Most trials in HF, except for HF-ACTION, are too small to reliably evaluate the effects of exercise rehabilitation across subgroups (see Supplementary data online, *Section S8.4*).[1002,1003]

In patients with long-term mechanical support, the benefit of exercise training on functional capacity has been demonstrated.[1004,1005] The Rehab-VAD trial showed that moderate intensity aerobic training was safe in patients with continuous-flow LVADs and yielded significantly improved health status, treadmill time, and leg strength, without significant improvements in peak oxygen consumption.[1006] If a patient with advanced HF can tolerate physical activity, exercise training can improve QoL.[1007] Exercise training before and after heart transplantation should follow recommendations according to the consensus document.[1008]

11.4.2. Safety and contraindications

No major adverse effects of exercise training were reported in the included studies of above systematic reviews and meta-analyses.[1001,1009] However, exercise interventions should only be initiated in stable individuals after initiation of FMT.

Exercise training is contraindicated in patients with refractory/unstable angina and other high-risk CV conditions (e.g. high-grade arrhythmias, DHF, active thromboembolic disease) and in any other unstable non-cardiac condition (e.g. active infection, uncontrolled diabetes, end-stage cancer, COPD exacerbation).[94]

11.4.3. Exercise prescription

A personalized training programme, with the mode of delivery, type, and intensity tailored to the patient's preferences, risk level, and comorbidities, is recommended to improve uptake of exercise-based cardiac rehabilitation. Exercise training should be started as part of cardiac rehabilitation and be individually prescribed according to the FITT model (frequency, intensity,

time, type) for aerobic training, resistance training, and inspiratory muscle training[1010,1011] (see Supplementary data online, *Section S8.4*).[998,1012–1016]

Adherence to the prescribed exercise regimen is crucial (see Supplementary data online, *Section S8.4*).[1017–1020]

Recommendation Table 24 — Recommendations for exercise training and cardiac rehabilitation (see *Evidence Tables 97–99*)

Recommendations	Class[a]	Level[b]
Personalized exercise training, in the context of multidisciplinary exercise-based cardiac rehabilitation, is recommended for all stable patients, unless there are specific contraindications, in order to improve exercise capacity and QoL, and reduce the risk of all-cause hospitalization.[1021]	I	B1
Personalized exercise training outside exercise-based cardiac rehabilitation is recommended for all stable patients on a long-term basis, unless there are specific contraindications, in order to improve exercise capacity and QoL, and reduce the risk of all-cause hospitalization.[1022]	I	B2
Cardiac rehabilitation[c] is recommended in patients with an LVAD to improve functional capacity and QoL.[1005,1023]	I	B1
Cardiac rehabilitation[c] should be considered in patients with DHF, as soon as safely possible, to improve functional capacity and QoL.[1002,1024–1026]	IIa	B1

DHF, decompensated heart failure; LVAD, left ventricular assist device; QoL, quality of life.
[a]Class of recommendation.
[b]Level of evidence.
[c]Either comprehensive or exercise-based.

11.5. Telemonitoring

Advances in digital technology and telemonitoring have, in recent years, contributed substantially to the transformation of (remote) care delivery, from a hospital-centred approach to a patient-oriented approach. Telemonitoring can involve non-invasive and invasive monitoring modalities. Non-invasive telemonitoring relies on traditional vital parameters measured remotely (e.g. weight, heart rate, and blood pressure), which can be used to guide patients remotely to adjust therapy or seek advice either through telephone consultations or eHealth-based environments. Recent systematic reviews and meta-analyses report significant reductions in all-cause death and HFH with non-invasive telemonitoring.[1027–1029] However, despite a growing body of evidence, results from individual trials are inconsistent and limited mainly by considerable heterogeneity in terms of patient population, modality, and intervention (see Supplementary data online, *Section S8.5*).[1027–1031] At present, non-invasive telemonitoring may be considered for patients with HF in order to reduce the risk of HFH.

Device-based monitoring modalities (pacemaker/ICD/CRT) based upon thoracic impedance, heart sounds, and breathing patterns, aim to assist in the selection between stable patients and those that need rapid access to care.[1032,1033] Many implanted devices can provide remote information either on the device itself (generator and lead function), arrhythmias, or on patient physiology (heart rate, heart sounds, bio-impedance). There is evidence that monitoring can detect device malfunction/integrity and that it may be useful for detecting arrhythmias. However, there is currently little evidence that device monitoring improves clinical outcomes, although ongoing RCTs are awaited.[1029,1033–1039]

Invasive monitoring modalities consist of several specifically designed telemonitoring sensor technologies measuring remote haemodynamic parameters. Currently, only pulmonary artery sensor-guided therapy has been studied in multiple RCTs and has shown a benefit in reducing HFH in patients in NYHA class III and a HFH within the past 12 months.[1029,1040–1047] Additionally, several prospective studies have confirmed the safety and efficacy of pulmonary artery-guided therapy in reducing HFH in multiple settings.[1037,1048–1052] Remote haemodynamic monitoring by pulmonary artery-guided therapy should be considered in selected patients with moderate-to-severe HF with NYHA class III and a HFH within the past 12 months in order to reduce the risk of HFH.

Recommendation Table 25 — Recommendations for invasive and non-invasive telemonitoring (see *Evidence Table 100*)

Recommendations	Class[a]	Level[b]
Remote haemodynamic monitoring of PA pressure should be considered in symptomatic patients with HF, NYHA class III, and an HFH in the past 12 months in order to reduce the risk of HFH.[1029,1043,1045]	IIa	B1
Non-invasive telemonitoring modalities may be considered for patients with HF in order to reduce the risk of HFH.[1027,1029,1053]	IIb	B1

HF, heart failure; HFH, heart failure hospitalization; NYHA, New York Heart Association; PA, pulmonary artery.
[a]Class of recommendation.
[b]Level of evidence.

11.6. Long-term follow-up

11.6.1. Follow-up

Patients with HF, even when symptoms are stable and well controlled, require regular in-person follow-up to ensure ongoing optimization of therapy, detect asymptomatic disease progression or comorbidities, and discuss new advances in care. For follow-up intervals of patients with a recent episode of DHF undergoing optimization or uptitration of FMT, see *Section 7*.

For symptomatic patients with HF with no recent DHF, these guidelines recommend assessment of symptom severity, pharmacological adherence, arrhythmias, changes in the ECG and, if deemed relevant, echocardiography and laboratory parameters (including full blood count, electrolytes, iron

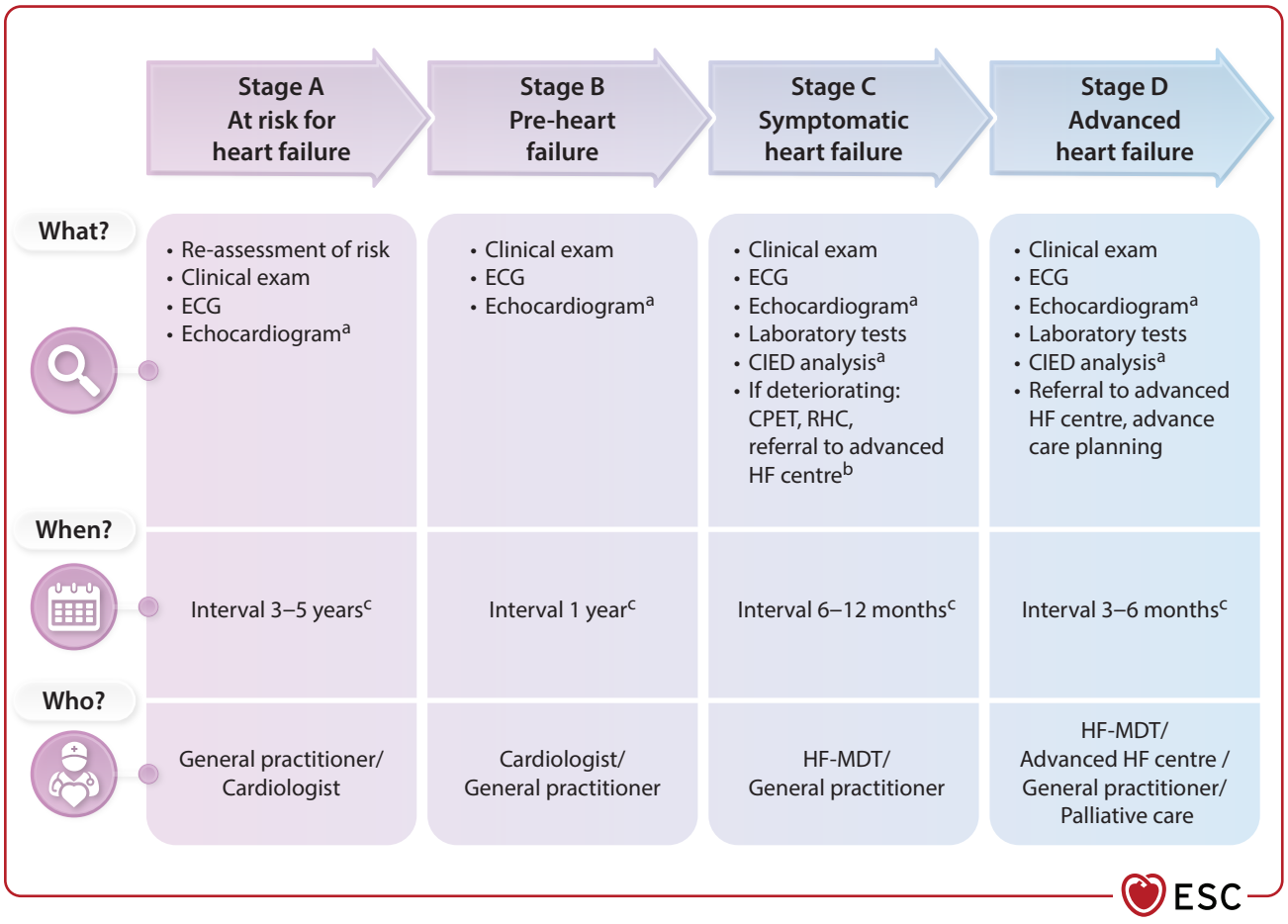

Figure 22 Long-term follow-up of patients with stable heart failure—what—when—who. CIED, cardiac implantable electronic device; CPET, cardiopulmonary exercise testing; ECG, electrocardiogram; HF, heart failure; HF-MDT, heart failure multidisciplinary team; RHC, right heart catheterization. [a]If deemed clinically relevant. [b]Check 'I NEED HELP' criteria, *Figure 16*; *Table 15* (*Section 8*). [c]Intervals may be shorter.

status, liver, kidney, and thyroid function). What is needed, at which interval and who has to perform the follow-up assessment depend on HF stage (*Figure 22*). The necessity of cardiologist-led follow-up for these patients remains uncertain, with some studies suggesting that primary care follow-up may be appropriate.[1054] However, evidence-based intervention uptake is low in many settings, and studies indicate that follow-up by an HF clinic, alongside quality improvement registries, may lead to better therapy optimization and improved outcomes.[990,994,1054–1057]

An ECG is recommended to detect QRS prolongation, which may qualify patients for CRT, as well as to identify conduction disturbances, AF, and other arrhythmias. Echocardiography should be performed if there is clinical deterioration or if otherwise deemed relevant. Trials investigating the use of biomarkers, such as BNP and NT-proBNP, to guide therapy in HFrEF have yielded inconsistent results.[1058–1060] Although these biomarkers are strong prognostic indicators, it remains unclear what additional value a biomarker-guided strategy offers beyond strict adherence to FMT. As such, routine biomarker measurement for guidance on diuretic therapy is not currently supported by the evidence.

11.6.2. Advance care planning and palliative care

While the disease trajectory of each patient with HF is unique, there is a generalizable pattern of gradual decline, punctuated by episodes of acute deterioration leading to death. Communication about disease trajectory and advance care planning should be incorporated by all healthcare professionals throughout the course of the disease.[1061,1062]

Advance care planning is a structured process that facilitates the exploration and communication of the patient's personal values, life goals, and preferences regarding future medical care, and may include preferences for place of death and resuscitation (which may include deactivating devices, such as ICD or durable MCS). Advance care planning should be documented, regularly reviewed, and routinely communicated to all those involved in the patient's care. Evidence shows that proactive advance care planning can reduce hospitalizations and improve QoL and end-of-life care, yet many patients with HF lack formalized plans, highlighting the need for better implementation.[627]

Palliative care, defined as patient- and family-centred care aimed at optimizing health-related QoL by anticipating, preventing, and alleviating suffering, should be integrated into the management of patients with HF in an advanced stage of the

disease. The role of palliative and supportive care spans the entire course of HF, beginning early in the disease, intensifying as the condition progresses, and extending into caregiver bereavement. Evidence supports the use of multidisciplinary palliative care in people with advanced HF to improve patient-reported outcomes (symptom burden, depression, functional status, QoL), but trials do not identify who would benefit most from specialist palliative referral.[1063–1065] There are no sufficiently robust multicentre evaluation phase trials to provide generalizable findings.

Recommendation Table 26 — Recommendations for long-term follow-up (see *Evidence Tables 101 and 102*)

Recommendations	Class[a]	Level[b]
Proactive discussion regarding HF trajectory, goals of care, and advance care planning is recommended in patients with advanced HF to facilitate communication on end of life and QoL.[627]	I	B1
Access to an integrated HF palliative care multidisciplinary team is recommended for patients in an advanced HF stage to improve QoL and reduce symptom burden.[1066–1068]	I	B2

HF, heart failure; QoL, quality of life.
[a]Class of recommendation.
[b]Level of evidence.

12. Specific conditions

12.1. Pregnancy and heart failure

Heart failure in pregnancy requires careful multidisciplinary management.[1069–1071] The core components of HF care in pregnancy involves multiple aspects from pre-conception to postpartum (see Supplementary data online, *Table S26*).

Specific recommendations for pre-conception care and management of HF during pregnancy can be found in *Recommendation Table 27*. For an overview of managing HF in pregnancy, see Supplementary data online, *Section S9.1*. For a comprehensive and detailed guidance, we refer to the *2025 ESC Guidelines for the management of cardiovascular disease and pregnancy*.[7]

Recommendation Table 27 — Recommendations for heart failure and pregnancy (see *Evidence Tables 103–107*)

Recommendations	Class[a]	Level[b]
Pre-conception care and counselling is recommended for patients with HF to facilitate decision-making surrounding HF treatments, pregnancy, contraception, pre-implantation genetic screening, and assisted reproductive therapies.	I	C
In pregnant women with HFrEF, it is recommended that non-selective beta-blockers are switched to beta$_1$-selective blockers (metoprolol, bisoprolol) with close mother and foetus monitoring to reduce the risk of adverse foetal events and a lower birth weight.[1072,1073]	I	C
ACE-Is, ARBs, ARNIs, MRAs, ivabradine, and SGLT2-Is are not recommended during pregnancy due to the risk of foetotocixity or teratogenicity.[1074–1076]	III	C

ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; ARNI, angiotensin receptor–neprilysin inhibitor; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; MRA, mineralocorticoid receptor antagonist; SGLT2-I, sodium–glucose co-transporter 2 inhibitor.
[a]Class of recommendation.
[b]Level of evidence.

12.2. Cardiomyopathies

Cardiomyopathies are a common and specific cause of HF.[124] The *2023 ESC Guidelines for the management of cardiomyopathies* described cardiomyopathy phenotypes based on structural (e.g. ventricular hypertrophy, dilatation, or scar) and functional (e.g. systolic or diastolic dysfunction) features.[124] Detailed recommendations and algorithms for the diagnosis and management of cardiomyopathies are provided in the *2023 ESC Guidelines for the management of cardiomyopathies*.[124]

12.2.1. Hypertrophic cardiomyopathy

Patients with HCM may develop HFrEF; in such cases, they should in general be treated as other patients with HFrEF. However, many patients develop symptoms of HF without having HFrEF, and these should be treated according to the cardiomyopathy guidelines (see Supplementary data online, *Section S9.2*).[124]

12.3. Amyloidosis

12.3.1. Epidemiology and diagnosis

Cardiac amyloidosis is an infiltrative cardiomyopathy caused by amyloid fibril deposition in the extracellular space, resulting in increased myocardial thickness and stiffness, leading to a restrictive physiology.[1077,1078] The two most prevalent forms of CA are immunoglobulin light chain CA (AL-CA) and transthyretin amyloidosis (ATTR). Transthyretin amyloidosis includes the wild-type (>90% of cases), and the hereditary or variant forms.[1077] Greater awareness of CA, streamlined diagnostic processes, and the emergence of new treatments has led to an increase in the prevalence of CA.[1079,1080] The prevalence of CA is higher in males.[1081]

Cardiac amyloidosis should be suspected in patients with HF and increased LV wall thickness in the presence of specific red flags (*Table 20*), particularly in patients aged >65 years.

A timely, definitive diagnosis should be obtained as patient outcomes depend largely on early initiation of therapy (particularly in AL-CA). Cardiac amyloidosis can be diagnosed using both invasive and non-invasive diagnostic criteria. Invasive diagnostic criteria apply to all forms of CA, whereas non-invasive criteria are accepted only for transthyretin CA (ATTR-CA).[1077] *Figure 23* displays the diagnostic work-up and treatment options. For more diagnostic details, the Task Force refers to the 2021 ESC position statement on CA.[1077]

Table 20 'Red flags' for most common forms of cardiac amyloidosis

Category	Red flag	TTR	AL
Extracardiac	Polyneuropathy	X	X
	Dysautonomia	X	X
	Skin bruising	–	X
	Macroglossia	–	X
	Deafness	X	–
	Bilateral carpal tunnel syndrome	X	–
	Ruptured biceps tendon	X	–
	Lumbar spinal stenosis	X	–
	Vitreous deposits	X[a]	–
	Family history	X[a]	–
	Kidney insufficiency	X	X
	Proteinuria	X	X
Cardiac clinical	Hypotension or normotension if previously hypertensive	X	X
ECG	Pseudo-infarct ECG pattern	X	X
	Low/decreased QRS voltage relative to LV thickness	X	X
	AV conduction disease	X	X
Laboratory	Disproportionally elevated NT-proBNP relative to HF severity	X	X
	Persistently elevated cardiac troponin levels	X	X
Echocardiography	Granular sparkling of myocardium	X	X
	Increased right ventricular wall thickness	X	X
	Increased valve thickness	X	X
	Increased interatrial septum thickness	X	X
	Pericardial effusion	X	X
	Reduced longitudinal strain with apical sparing pattern	X	X
CMR[b]	Global subendocardial or transmural LGE	X	X
	Elevated native T1 values	X	X
	Increased extracellular volume	X	X
	Abnormal gadolinium kinetics	X	X

AL, immunoglobulin light chain; CA, cardiac amyloidosis; CMR, cardiac magnetic resonance; ECG, electrocardiogram; HF, heart failure; LGE, late gadolinium enhancement; LV, left ventricular; NT-proBNP, N-terminal-pro-B-type natriuretic peptide; TTR, transthyretin.
[a]Hereditary TTR-CA.
[b]CMR can be diagnostic for CA.

12.3.2. Disease-specific treatments

12.3.2.1. Immunoglobulin light chain cardiac amyloidosis

Treatment of AL-CA includes chemotherapy or autologous stem cell transplantation with careful monitoring of haematological response, cardiac and organ function. Management of AL-CA should be undertaken by a multidisciplinary team involving oncohaematology specialists and cardiologists, and whenever possible, patients should be referred to specialized centres.

12.3.2.2. Transthyretin cardiac amyloidosis

Therapeutic agents for ATTR-CA include drugs that inhibit hepatic synthesis of transthyretin (TTR), stabilize the tetramer, or disrupt the amyloid fibrils. Based on the results of large RCTs, the Task Force recommends treatment with a TTR stabilizer or a TTR silencer with proven safety and efficacy on morbidity and mortality, in patients with either wild-type or hereditary ATTR-CA and a clinical history of HF with NYHA classes I–III. These drugs include the TTR stabilizers tafamidis and acoramidis and the TTR silencer vutrisiran.[1082–1084]

In the ATTR-ACT trial, tafamidis reduced all-cause death and CV hospitalizations over 30 months in both hereditary and wild-type ATTR-CA.[1082] Benefits on functional capacity occurred within 6 months, whereas reduction in all-cause death was observed from 18 months onwards. It showed limited impact in advanced cases (NYHA class III).

In the ATTRibute-CM trial, after 30 months of treatment, acoramidis was superior to placebo in a hierarchical analysis (all-cause death, CV hospitalization, change from baseline in NT-proBNP, and change from baseline in 6-min walk test).[1083] Although it did not independently lower death at 30 months, it did reduce the combined endpoint of all-cause death or CV hospitalizations. Notably, survival rates in the placebo arm were higher than in the treatment group of ATTR-ACT, possibly reflecting earlier disease stage and the improvements in earlier diagnosis and access to specialist care. Furthermore, in the open-label extension study, early initiation and continuous use of acoramidis significantly reduced death at 42 months, as compared with the later initiation of acoramidis.[1085]

In the APOLLO-B trial, patisiran (i.v.) reduced functional decline over 12 months.[1086] However, no data are available regarding morbidity and mortality. In the HELIOS-B trial, vutrisiran (subcutaneous) reduced the risk of the combined endpoint of all-cause death and recurrent CV events vs placebo.[1084] Also, the risk of all-cause death through 42 months was lowered with vutrisiran. These benefits persisted regardless of background tafamidis use at baseline (~40% of the trial population).[1084]

None of the studies provided a head-to-head comparison of TTR silencers vs stabilizers nor a head-to-head comparison of monotherapy vs combination therapies. Several studies are ongoing with further therapeutical options acting on gene editing, RNA silencing, or the repletion of amyloid deposits, and might change the management of ATTR-CA in the future.

12.3.3. Treatment of heart failure and cardiovascular comorbidities

Evidence for the use of FMT in patients with CA is still scarce and limited to post-hoc analyses of RCTs or retrospective studies.[1087–1092] Patients with CA may poorly tolerate standard HF therapies due to restrictive physiology, autonomic dysfunction, atrioventricular conduction disturbance, and kidney impairment. Diuretics remain central for congestion management but must be used cautiously within a narrow euvolaemic window.[1089,1090] Increasing diuretic dose is a signal of disease progression with worse outcomes.[1093,1094] Evidence supports the safety and benefit of SGLT2-Is.[73,1089–1092] MRA might also be useful.[1092]

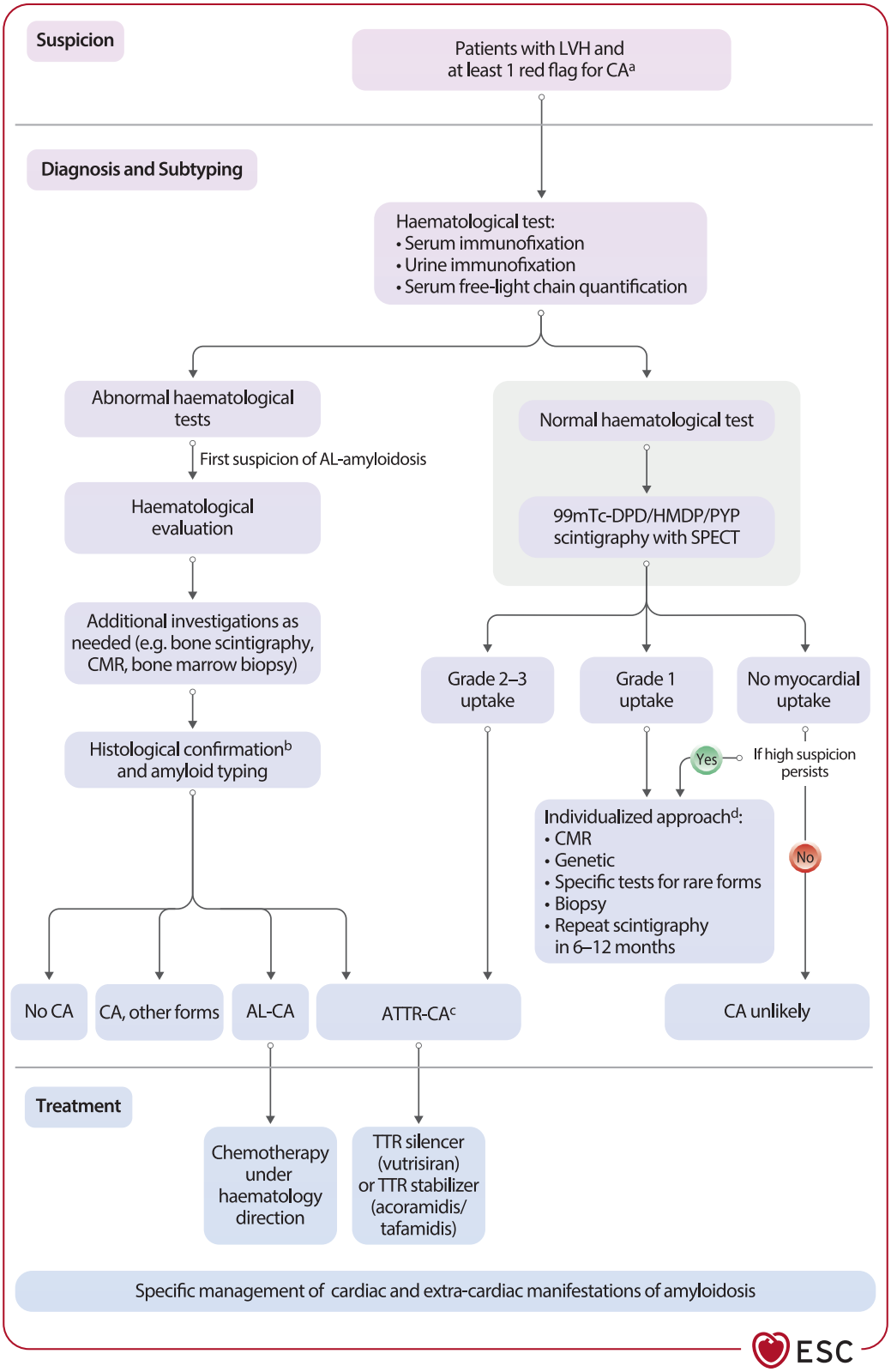

Figure 23 Diagnosis and treatment of cardiac amyloidosis in heart failure patients. ^{99m}Tc, technetium-99m; AL, immunoglobulin light chain; AL-CA, immunoglobulin light chain cardiac amyloidosis; ATTR-CA, transthyretin cardiac amyloidosis; CA, cardiac amyloidosis; CMR, cardiac magnetic resonance; DPD, 3,3-diphosphono-1,2-propanodicarboxylic acid; HMDP, hydroxymethylene diphosphonate; LVH, left ventricular hypertrophy; PYP, pyrophosphate; SPECT, single-photon emission computed tomography; TTR, transthyretin. [a]See *Table 20*. [b]Usually an extracardiac biopsy is performed first. [c]Perform TTR genetic testing. [d]Diagnosis will be based on the results from the individualized approach.

Beta-blockers and ACE-I/ARNI/ARB use requires caution, individualized decisions, and close monitoring.

In patients with CA and AF, anticoagulation is indicated regardless of CHA_2DS_2-VA score, due to high thromboembolic risk.[1077,1095–1097] Transoesophageal echocardiography is necessary before cardioversion to exclude intracardiac thrombus, regardless of the duration of anticoagulation before the procedure.[1098] The use of digoxin is generally discouraged due to high risk of toxicity. Few patients with CA and advanced symptoms may be eligible for heart transplantation in line with international criteria.[580]

Recommendation Table 28 — Recommendations for cardiac amyloidosis (see *Evidence Tables 108–111*)

Recommendation	Class[a]	Level[b]
Treatment with a TTR silencer (vutrisiran) or stabilizer (tafamidis or acoramidis) for patients with variant or wild-type transthyretin cardiac amyloidosis and NYHA classes I–III is recommended to reduce progression of symptoms and the risk of CV hospitalization and all-cause death.[1082–1084]	I	A

CV, cardiovascular; NYHA, New York Heart Association; TTR, transthyretin.
[a]Class of recommendation.
[b]Level of evidence.

12.4. Myocarditis

12.4.1. Epidemiology and diagnosis

The contribution of myocarditis as a cause of HF is estimated to be less than 5%.[1099] When patients with myocarditis present with DHF, LVEF <40%, life-threatening arrhythmias (ventricular tachycardia/fibrillation, third-degree atrioventricular block), and/or extensive LGE on CMR, they should be viewed as high risk.[1100,1101] High-risk patients may require an endomyocardial biopsy in order to tailor treatment,[8] whereas lower-risk patients may be examined with CMR imaging. The clinical presentation ranges from impaired LV function to refractory HF, CS (fulminant myocarditis), or sudden cardiac arrest. Some patients present primarily with arrhythmias. Prognosis depends on initial presentation.[1100,1101] Patients with fulminant myocarditis should be transferred or discussed with a center that has the possibility to perform endomyocardial biopsy and provide MCS support. High-risk patients have a high mortality and may need temporary MCS and/or in the long term heart transplantation or durable MCS.[1102–1104]

12.4.2. Treatment

The treatment algorithm is reported in the *2025 ESC Guidelines for the management of myocarditis and pericarditis*.[8] Patients with myocarditis and HFrEF should be empirically treated with FMT for HFrEF (see *Section 7*). Routine immunosuppression is not recommended in patients with preserved LVEF and should be reserved for fulminant, non-infectious forms of myocarditis to stabilize the patients.[8]

12.5. Adult congenital heart disease

Adult congenital heart disease is a heterogeneous group of structural heart abnormalities varying in complexity. There has been an improvement in survival with contemporary care.[1105] Consequently, HF in ACHD is increasingly common,[1106,1107] and represents a major contributor to morbidity and mortality, accounting for 26%–46% of deaths, with higher rates seen in more complex lesions.[1108–1110]

Managing HF in ACHD poses specific challenges related to original anatomy, presence of haemodynamic lesions, previous interventions, and extracardiac complications such as kidney and liver dysfunction.[1111,1112]

Specific indications on the management of these patients are reported in the *2020 ESC Guidelines for the management of adult congenital heart disease*[1111] and in a recent ESC clinical consensus statement.[1113]

13. Key messages

New classifications

- Heart failure has been redefined with two distinct phenotypes:
  - HFrEF: LVEF <50% + symptoms and/or signs of HF.
  - HFpEF: LVEF ≥50% + symptoms and/or signs of HF + objective evidence of cardiac structural and/or functional abnormalities.
- Stages of HF (A–D) have been adopted:
  - Stage A: individuals at risk for HF but without signs, symptoms, and cardiac abnormalities.
  - Stage B: pre-HF, defined as the presence of cardiac abnormalities without signs and symptoms of HF.
  - Stage C: symptomatic HF, defined as the presence of cardiac abnormalities and current or prior signs and/or symptoms of HF.
  - Stage D: advanced HF.
- New classifications for medical and interventional HF therapies have been introduced. The terms are designed to be dynamic and may therefore remain contemporary over time:
  - FMT—Foundational medical therapy: medical therapies for unselected patients with HF with Class I recommendation for reducing HFH and/or death.
  - AMT—Additional medical therapy: medical therapies with Class IIa/IIb recommendations or Class I recommendations for improving symptoms/QoL or reducing morbidity or mortality in specific subsets of patients with HF.
  - GDIT—Guideline-directed interventional therapy: all guideline-recommended implantable devices or interventional therapies.

Prevention of heart failure

- A strict control of HF risk factors is recommended to prevent HF.

Diagnosis of heart failure

- Measurement of natriuretic peptides and echocardiography have key roles in the diagnosis of HF. Additional testing is useful for aetiologies and phenotypes.
- Multimodality aetiology assessment should be sought to find potential treatable causes of HF.

Guideline-recommended therapies

- ARNIs or ACE-Is (ARB in case of intolerance) beta-blockers, MRAs, and SGLT2-Is are recommended as FMT for patients with HFrEF, whereas MRAs and SGLT2-Is are recommended as FMT for patients with HFpEF.
- ICDs are recommended in selected patients with HFrEF, LVEF ≤35%, and an ischaemic aetiology, and should be considered in those with a non-ischaemic aetiology.
- CRT-P or CRT-D is recommended in patients with HFrEF, LVEF ≤35%, in sinus rhythm, with an LBBB ≥150 ms and should be considered in those with an LBBB ≥130–149 ms or non-LBBB ≥150 ms.

Decompensated heart failure

- Decompensated heart failure refers to acute or gradual onset of symptoms and/or signs of HF, severe enough to deserve urgent medical attention, leading to an unplanned hospital admission or an emergency department visit or an ambulatory visit, and requiring subsequent initiation or intensification of treatment.
- Treatment of DHF is based on addressing any associated triggers urgently, diuretics for congestion with the addition of vasodilators for high blood pressure, inotropes, and/or temporary MCS for hypoperfusion.
- Patients hospitalized for HF should be carefully evaluated to exclude persistent signs of congestion. FMT must be started or optimized before discharge and close visits in the early post-discharge period must be planned.

Advanced heart failure

- Patients with advanced HF refractory to FMT and GDIT who do not have absolute contraindications must have timely referral for consideration of heart transplantation or MCS.

Cardiovascular comorbidities

- Catheter ablation should be considered only in carefully selected patients with HFrEF and symptomatic AF. Selection criteria include high-burden AF, less than 1-year duration of continuous persistent AF, and a clear cause–effect relationship between AF and HF.
- Patients with obstructive CAD and HF need to be treated conservatively or invasively (CABG or PCI) according to clinical and anatomical suitability for revascularization, HF phenotype and history, presence of angina, comorbidities, frailty, and patient preference.
- Surgical aortic valve replacement or TAVI, as assessed by the Heart Team, is recommended in patient with severe low-flow low-gradient aortic stenosis and HF regardless of LVEF and in patients with severe low-flow low-gradient aortic stenosis and HFrEF.
- Mitral TEER is recommended in selected patients with severe ventricular secondary MR and HFrEF after optimization of FMT and CRT implantation (if needed).

Non-cardiovascular comorbidities

- Patients should be routinely screened and treated for non-CV comorbidities (e.g. diabetes, CKD, obesity, ID, anxiety and depression) and frailty.
- Lifestyle interventions, exercise, diet, and patient education are fundamental steps for body-weight management in patients with HF and obesity, followed by pharmacological and surgical interventions.
- It is recommended to switch glucose-lowering treatment from agents without proven CV efficacy or safety to agents with proven CV benefit in patients with HF and diabetes.

Multidisciplinary management

- A multidisciplinary HF management programme is recommended.
- Cardiac rehabilitation, with exercise training, is a key tool to reduce hospitalizations and improve functional capacity and QoL in patients with HF.
- Remote haemodynamic monitoring of PA pressure should be considered in selected patients; non-invasive telemonitoring modalities may be considered.

Specific conditions

- Pre-conception care and counselling is recommended for patients with stage B or C HF to facilitate decision-making surrounding pregnancy.
- Specific disease-modifying therapies are recommended in patients with CA.

14. Gaps in evidence

Despite advances in the management of HF, multiple areas of uncertainty remain. Future research should address the following gaps.

(1) Definitions and prevention
   - Consensus regarding normal values/ranges of ejection fraction.
   - More information on the incidence, prevalence and prognostic importance of HF with improved LVEF, and a need to validate and evaluate the clinical importance of the new definition proposed by the Second Universal Definition of HF.[47]
   - The benefits and risks of various weight-loss methods for HF risk reduction in obesity need further studies.
   - More research is needed to understand if SGLT2-Is and MRAs prevent HF in patients without diabetes but with comorbidities like obesity, hypertension, and/or CKD.
   - Studies are needed to better understand if CPAP therapy lowers risk of HF in patients with sleep apnoea.

(2) Diagnosis and phenotyping
- Further research into the underlying characteristics, pathophysiology, diagnosis, and phenotyping of HFpEF.
- Role of artificial intelligence in the diagnostic pathway for HF as well as for patient inclusion in RCTs.
- Validated diagnostic protocols including deeper phenotyping for the diagnosis of HFpEF.
- Validation of the historic exercise-induced pulmonary capillary wedge pressure cut-offs used in the diagnosis of HFpEF.
- Prospective validation of age-related natriuretic peptide cut-offs in chronic HF.
- Degree of influence of BMI on natriuretic peptides to allow for individual adjustment of expected ranges.
- Prospective studies to test the diagnostic yield for endomyocardial biopsy, and whether a biopsy would affect treatment decisions and outcomes in patients with unexplained cardiomyopathy and evidence of inflammation/infiltration/storage on CMR or CT-positron emission tomography.

(3) Medical treatment and devices
- Contemporary reproducibility of old trials on medical and device therapies.
- Future trials on medical/device therapy for HF should adhere to contemporary FMT.
- Randomized clinical trials comparing different MRAs in both HFrEF and HFpEF.
- Randomized clinical trials investigating the optimal medical therapy for HFpEF.
- Randomized clinical trials comparing different GLP-1 RAs.
- Randomized clinical trials on the optimal sequencing when initiating FMT both in HFrEF and HFpEF.
- More data on the role of potassium binders, both in patients with and without CKD.
- Management strategies and therapies for HF with improved LVEF.
- Indications for ICDs in specific subgroups of patients, and optimal selection of ICD candidates in HFrEF, including patients with ischaemic and non-ischaemic HF.
- Efficacy of CRT in AF.
- Randomized controlled trials with morbidity and mortality endpoints and long-term follow-up, comparing CSP and trans-coronary vein CRT in patients with HFrEF.
- Randomized controlled trials with morbidity and mortality and long-term follow-up on interatrial shunt devices in patients with HFrEF and HFpEF.

(4) Decompensated heart failure
- Evidence on medical therapy with prognostic benefit in DHF.
- Evidence for best decongestion protocols in patients with and without CKD and in the setting of continued/initiation of FMT.
- Evidence-based use of imaging techniques and biomarkers that have an impact on patients' clinical course in DHF.
- Definition of evidence-based treatment options and therapeutic algorithms for patients with CS.
- Better definition of the role of MCS in CS.
- Better definition of the role of inotropes, vasopressors and vasodilators in DHF.
- Studies on the best early post-discharge risk-based management protocols to reduce early readmission to hospital.

(5) Advanced heart failure
- Benefit of FMT, AMT, and GDIT in advanced HFrEF needs further investigation.
- Which medication to down-titrate/stop first in patients with advanced HF who no longer tolerate all FMT.
- Durable MCS (LVADs) vs medical treatment in INTERMACS >4 without high-risk features.
- Optimal lifetime management strategies in very young adults with advanced HF.
- Advances in durable MCS, including strategies to reduce the risk of infection.
- Advances in medical treatment for the many patients who cannot undergo MCS or heart transplantation, including development of treatment strategies, and novel inotropes or myotropes for patients with advanced HF.

(6) Cardiovascular comorbidities
- Adequately powered RCTs showing the best strategy for management of AF in patients with HF.
- Selection of patients with HFrEF and HFpEF that may benefit from AF ablation.
- Better characterization of patients with arrhythmia-associated HF, especially patients with AF-associated HF.
- Randomized controlled trials investigating best management options for patients with AF-associated HF, both in terms of HF management and management of AF.
- Randomized controlled trials to assess the role of coronary revascularization and different revascularization strategies in patients with HFrEF and HFpEF on current FMT.
- Longer-term follow-up results for mitral TEER interventions in HFrEF.
- Role of mitral TEER in patients with HFrEF who do not fulfil specific echocardiographic and clinical criteria.
- Treatment of atrial secondary MR in patients with HFpEF.
- Further RCTs to assess the role of transcatheter valve intervention in patients with HF and TR.

(7) Non-cardiovascular comorbidities
- More clinically appropriate definition of ID in HF.
- Further RCTs, using the novel definition of ID as an inclusion criterion, to assess the prognostic role of i.v. iron supplementation.
- The prognostic role of HF treatment in patients with severe kidney dysfunction (i.e. eGFR <30 mL/min/1.73 m^2), excluded from RCTs.
- The effects of GLP-1 RAs and tirzepatide on morbidity and mortality in patients with HFpEF and HFrEF.
- Treatment of SDB, both central and obstructive, needs further investigation to clarify benefit and safety concerns.

(8) Multidisciplinary management
- Studies on optimal models for follow-up of patients with stable HF.

- Long-term trials on exercise in patients with HF.
- Studies to determine personalized approach for palliative care to improve patient-centred outcomes.
- Models of care that incorporate contemporary patients with HF and the wider multidisciplinary team including cardio-kidney-metabolic professionals in HF care.
- Patient selection for telemonitoring.

(9) Specific conditions
- Randomized clinical trials for the treatment of peri-partum cardiomyopathy.
- Head-to-head comparison between different disease-modifying drugs in ATTR-CA.
- Evidence for the combined use of disease-modifying drugs in ATTR-CA.
- Evidence for gene editing and antibodies for the removal of amyloid deposits.
- Efficacy of traditional HF therapies in patients with CA.
- Identification of patients with ATTR-CA who could benefit from device therapy (e.g. ICD/CRT).
- Data collection to support advice on screening for *TTR* gene carriers—when to initiate and follow-up interval.

15. Evidence tables

Evidence tables are available at *European Heart Journal* online.

16. Data availability

No new data were generated or analysed in support of this research.

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18. Appendix

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