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2023 National Heart Center/Saudi Heart Association Focused Update of the 2019 Saudi Heart Association Guidelines for the Management of Heart Failure

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Abstract

Background: **The burden of cardiovascular diseases is undeniable in local populations, who have high mortality rates and a young age of disease onset. A systematic review of emerging evidence and update of the Saudi Heart Association (SHA) 2019 heart failure (HF) guidelines was therefore undertaken.**

Methodology: **A panel of expert cardiologists reviewed recommendations of the 2019 guidelines following the Saudi Heart Association methodology for guideline recommendations. When needed, the panel provided updated and new recommendations endorsed by the national heart council that are appropriate for clinical practice and local resources in Saudi Arabia.**

Recommendations and conclusion: **The focused update describes the appropriate use of clinical assessment as well as invasive and non-invasive modalities for the classification and diagnosis of HF. The prevention of HF was emphasized by expanding on both primary and secondary prevention approaches. Pharmacological treatment of HF was supplemented with recommendations on newer therapies, such as SGLT-2 inhibitors. Recommendations were also provided on the management of patients with cardiovascular and non-cardiovascular co-morbidities, with a focus on cardio-oncology**

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and pregnancy. Updated clinical algorithms were included in support of HF management in both the acute and chronic settings. The implementation of this focused update on HF management in clinical practice is expected to lead to improved patient outcomes by providing evidence-based comprehensive guidance for practitioners in Saudi Arabia.

Keywords: Heart failure, Saudi Arabia, NHC/SHA clinical practice guidelines, Focused update, Diagnosis, Prevention, Therapeutics, Surgery

1. Introduction

The global burden of cardiovascular diseases continues to increase, with an estimated 523 million prevalent cases of cardiovascular disease (CVD) and 197 million prevalent cases of ischemic heart disease in 2019 [1]. Heart failure (HF) is a global pandemic estimated to affect 64.3 million people in 2017 [2]. Countries in the Gulf region have some of the highest age-standardized prevalence rates of HF around the world [3]. Several local registries provided nascent insights into the epidemiology of HF in the Gulf and Middle East region (Table 1). Local populations are distinct from their Western counterparts in that they have higher mortality rates and a younger age of disease onset; on average, people with heart failure in the region are 10 years younger than patients in Western countries [4]. Data from Saudi registries and studies paint a similar picture. The HEARTS and HEARTS-Chronic registries reported that the mean age of patients was relatively young (60.6 years in HEARTS, and 55.6 years in HEARTS-Chronic) [5,6]. Moderate to severe left ventricular (LV) dysfunction is observed in the majority of patients and coronary artery disease (CAD) is the main etiology of HF [5,6]. Mortality and re-hospitalization rates are high [5,6], and the risk of death is higher in patients with chronic HF who experience acute HF events [7]. Moreover, HF carries a significant economic burden. The annual per-patient cost reaches approximately $9563 and is mainly driven by procedures and hospitalizations [8,9]. Disease progression to Class IV HF naturally incurs higher medical costs, which are estimated at almost double that of other patients [8]. While underrepresentation of heart failure with preserved ejection fraction (HFpEF) and smaller patient numbers remain a limitation of local registries, generated data pave the way for future structured studies and healthcare initiatives to improve HF management. This is important considering that lower health-related quality of life predicts mortality and re-hospitalization in HF regardless of symptoms severity and LV dysfunction [10]. This was reflected among Saudi HF patients among whom impaired quality of life was reported [11] and involvement in a structured management program for HF improved

Abbreviations list

ACEi	Angiotensin-converting enzyme inhibitors
AF	atrial fibrillation
AHF	acute heart failure
ARB	Angiotensin receptor blockers
ARNI	Angiontensin Receptor Neprilysin Inhibitor
ARVC	arrhythmogenic right ventricular cardiomyopathy
BNP	B-type natriuretic peptide
CABG	Coronary artery bypass graft surgery
CAD	coronary artery disease
CCS	chronic coronary syndrome
CCTA	Cardiac computed tomography angiography
CKD	chronic kidney disease
CMR	cardiac magnetic resonance
CPET	Cardiopulmonary Exercise Testing
CRT	cardiac resynchronization therapy
CTRCD	cancer therapy-related cardiac dysfunction
CV	cardiovascular
CVD	cardiovascular disease
DCM	dilated cardiomyopathy
DOAC	direct oral anticoagulant
EF	ejection fraction
eGFR	estimated glomerular filtration rate
EMB	Endomyocardial biopsy
GLS	Global Longitudinal Strain
HCM	hypertrophic cardiomyopathy
HF	heart failure
HFmrEF	heart failure with mildly preserved ejection fraction
HFpEF	heart failure with preserved ejection fraction
HFrEF	heart failure with reduced ejection fraction
ICA	invasive coronary angiography
ICD	implantable cardioverter defibrillators
LBBB	left bundle branch block
LGE	late gadolinium enhancement
LMWH	low molecular weight heparin
LV	left ventricular
LVAD	LV assist device
LVEF	left ventricular ejection fraction
MCS	Mechanical circulatory support
MRA	Mineralocorticoid receptor antagonist
NHC	national heart center
NT-pro BNP	N-terminal pro- B-type natriuretic peptide
PCI	Percutaneous coronary intervention
PET	Positron emission tomography
RAASi	Renin–angiotensin–aldosterone system inhibitor
RCT	randomized controlled trial
SFDA	Saudi Food and Drug Administration
SGLT-2	Sodium-glucose Cotransporter-2
SHA	Saudi Heart Association
SPECT	single photon emission computed tomography
VKA	vitamin K antagonist

Table 1. Saudi Heart Association classes of recommendations.

Color	Class	Definition
	Recommended	The usefulness and efficacy of a particular treatment/procedure/action is supported by available evidence.
	Should be considered	The usefulness and efficacy of a particular treatment/procedure/action is established by favorable expert opinion on conflicting evidence.
	May be considered	The usefulness and efficacy of a particular treatment/procedure/action is not well established by evidence and expert opinion.
	Not recommended	A particular treatment/procedure/action is not useful nor effective and is potentially harmful based on available evidence and/or general agreement.

quality of life, reduced mortality as well as hospitalization [12,13]).

Since the publication of the Saudi Heart Association (SHA) Heart Failure Guidelines in 2019, new studies have been published. This required systematic review and update of the guidelines. In these guidelines, health practitioners can find evidence-based recommendations supplemented by expert opinion where needed for the diagnosis, prevention, therapeutic and surgical management of both chronic and acute HF, as well as special patient populations.

2. Methods

A panel of expert cardiologists met in a series of meetings and reviewed recommendations of the 2019 guidelines in light of emerging evidence. The guidelines followed the Saudi Heart Association methodology for guideline recommendations (Table 1). Updated and new recommendations appropriate for clinical practice and local resources in Saudi Arabia were provided based on available data from clinical studies and meta-analyses, as well as local experience (Table 2). Unchanged recommendations are shown in their respective section in the text. These recommendations are endorsed by the national heart center (NHC).

3. Results - guideline statements

3.1. Definition and classification

Consistent with current practice, left ventricular ejection fraction (LVEF) measurement is adopted as a practical approach to define HF. The definition of HF in its three types is included in Table 3; LVEF $\leq$40% is indicative of heart failure with reduced ejection fraction (HFrEF), LVEF 41–49% defines heart failure with mildly reduced ejection fraction (HFmrEF) while heart failure with preserved ejection fraction (HFpEF) is defined as LVEF $\geq$50%.

Other relevant terminology and concepts should also be noted:

(1) asymptomatic LV systolic dysfunction refers to a patient who has never exhibited the typical signs and/or symptoms of HF and with a reduced LVEF); (2) stable HF refers to a treated patient with signs and symptoms that have remained generally unchanged for at least 1 month); (3) decompensated HF is used to describe deterioration of a chronic stable HF patient—this may happen suddenly or slowly; (4) heart failure with improved ejection fraction refers to patients with previously reduced ejection fraction that was improved at later measurement (by > 10%); and (5) heart failure with recovered ejection fraction refers to patients with recovery of LV dysfunction (LVEF >55%). Improved ejection fraction is not necessarily indicative of full myocardial recovery or normalization of LV function (heart failure with recovered ejection fraction (EF). There is currently no consensus on the definition, diagnosis, nor management of heart failure with recovered EF. However, it is recognized that guideline-directed medical and device therapy should be continued indefinitely considering the high rates of LV dysfunction recurrence, despite the improved clinical outcomes in this patient population [14].

Table 2. Updated and new recommendations in the 2023 SHA focused update.

Recommendation	SHA 2022	SHA 2019
Definition and classification		
Classification of HF	HFrEF: EF ≤40% **HFmrEF**: EF 41-49% HFpEF: EF >50%	HFrEF: EF ≤40% **HFbEF**: EF 41-49% HFpEF: EF >50%
I- Chronic HF		
Diagnosis		
Diagnostic tests	BNP/NTpro-BNP cutoff levels: NTproBNP: 125 pg/mL BNP: 35pg/mL	BNP/NTpro-BNP cutoff levels: NTproBNP: 100 pg/mL BNP: 40pg/mL
Non-invasive imaging		
TTE	TTE is recommended for the assessment of myocardial structure and function in patients with suspected HF to establish a diagnosis of HFrEF, HFmrEF, or HFpEF and to identify patients for the most appropriate pharmacological and device therapy.	TTE is recommended for the assessment of myocardial structure and function in patients with suspected HF to establish a diagnosis of HFrEF, HFmrEF, or HFpEF
		TTE is recommended to assess LVEF to identify patients with HF suitable for evidence-based pharamacological treatment and device implantation (e.g. implantable cardioverter defibrillator, cardiac resynchronization therapy) recommended for HFrEF
CPET and Exercise testing	CPET is recommended as part of the evaluation for advanced treatments (heart transplantation and/or mechanical circulatory support)	exercise testing in patients with HF is recommended as part of the evaluation for advanced treatments (heart transplantation and/or mechanical circulatory support)
	CPET or 6-minute walk test should be considered to assess functional capacity in ambulatory HF patients	exercise testing in patients with HF may be considered to assess response before and after treatment (functional capacity assessment with a 6-minute walk test)
	removed	exercise testing in patients with HF should be considered to optimize the prescription of exercise training (preferably cardiopulmonary exercise testing)
	CPET may be considered in select cases to identify the cause of unexplained dyspnea	exercise testing in patients with HF could be considered to identify the cause of unexplained dyspnea (cardiopulmonary exercise testing)
	removed	exercise testing in patients with HF may be considered to detect reversible myocardial ischemia
CMR	CMR is recommended for the assessment of myocardial structure and function in those with poor echocardiogram acoustic windows	CMR with late gadolinium enhancement is recommended for the assessment of all HF patients with cardiomyopathy. CMR should be conducted at an experienced

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Table 2 (continued)

Recommendation	SHA 2022	SHA 2019
		center under the supervision of qualified and well-trained physicians who are familiar with standard methodology and protocols
	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/hemochromatosis	CMR is recommended for the characterization of myocardial tissue in case of suspected myocarditis, amyloidosis, sarcoidosis, Chagas disease, Fabry Disease, noncompaction cardiomyopathy, hemochromatosis, hypertonic cardiomyopathy, stress-induced cardiomyopathy, and ARVC
	CMR with LGE should be considered in DCM to distinguish between ischemic and non-ischemic myocardial damage	
CCTA and others	CTCA should be considered in patients with a low to intermediate probability of CAD or those with equivocal non-invasive stress tests in order to rule out coronary artery stenosis	Non-invasive testing (preferably cardiac computed tomography, but also stress echocardiography, SPECT, PET, myocardial perfusion imaging) may be considered in patients with HF and low to intermediate pretest probability of CAD, to rule out coronary artery stenosis
Invasive tests		
EMB	endomyocardial biopsy may be considered when a specific diagnosis is suspected that would influence therapy but should not be routinely performed.	endomyocardial biopsy should be considered in patients with rapidly progressive HF despite standard therapy
Right heart catheterization	Right heart catheterization is recommended in patients with advanced HF being evaluated for advanced heart therapy (heart transplantation or mechanical circulatory support)	Right heart catheterization is recommended in patients with severe HF being evaluated for heart transplantation or mechanical circulatory support
	removed	Right heart catheterization should be considered in patients with severe mitral regurgitation
genetic testing	Genetic testing is recommended for patient with hypertrophic cardiomyopathy (HCM) and arrhythmogenic right ventricular cardiomyopathy (ARVC)	genetic counseling is recommended for patients with hypertrophic cardiomyopathy, idiopathic dilated cardiomyopathy and ARVC
	Genetic testing should be considered in other suspected cases of familial cardiomyopathy	
	removed	restrictive cardiomyopathy and isolated noncompation cardiomyopathies have a possible genetic origin and should also be considered for genetic testing

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Table 2 (*continued*)

Recommendation	SHA 2022	SHA 2019
		considered depending on the age of disease onset in other family members
Prevention		
	Pimary and secondary prevention of HF	Prevention of HF
primary prevention	Treatment of hypertension is recommended to prevent or delay the onset of HF	Treatment of hypertension is recommended to prevent or delay the onset of HF and prolong life
	treatment with statins is recommended in patients with or at risk of atherosclerotic cardiovascular disease to prevent or delay the onset of HF	treatment with statins is recommended in patients with or at risk of CAD
	SGLT2 inhibitors are recommended in patients with diabetes at high risk of CV disease or with CV disease in order to prevent HF hospitalizations	
	Counseling against risk factors such as sedentary habit, obesity, smoking (all types, including but not exclusive of cigarette, tobacco, khat or sheesha smoking) and alcohol is recommended to prevent or delay the onset of HF.	Counseling and treatment for smoking (all types, including but not exclusive of cigarette, tobacco, khat or sheesha smoking) and alcohol is recommended for people who smoke or who consume excess alcohol, to prevent or delay the onset of HF
		treating other risk factors of HF (e.g. obesity, dysglycemia) should be considered to prevent or delay the onset of HF
secondary prevention	self-management strategies are recommended to reduce the risk of HF hospitalization and mortality	
	influenza and pneumococcal vaccinations should be considered in order to prevent HF hospitalizations	
	a supervised, exercise-based cardiac rehabilitation programme should be considered in patients with more severe disease, frailty or with comorbidities	
pharmacological management		
HFrEF		
RAS inhibition (ACEi/ARB/ARNI)	an ACEi/ARB/ARNI (sacubitril/valsartan) is recommended for patients with HFrEF	an ACE-I, in addition to a beta-blocker is recommended for patients with HFrEF, to reduce the risk of hospitalization and death
		an ARB is recommended to reduce the risk of HF hospitalization and cardiovascular death in symptomatic patients unable to tolerate an ACE-I

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Table 2 (*continued*)

Recommendation	SHA 2022	SHA 2019
Beta-blockers	a beta-blocker is recommended for patients with HFrEF in combination with ACEi/ARB or ARNI	a beta-blocker (extended-release metoprolol, bisoprolol, or carvediol), in addition to ACE-I, is recommended for patients with HFrEF, to reduce hospitalization and death
MRA	An MRA is recommended for patients with HFrEF to reduce the risk of hospitalization and death	An MRA is recommended for patients with HFrEF to who remain symptomatic despite treatment with an ACE-I and a beta blocker, to reduce the risk of hospitalization and death. renal function and potassium levels should be closely monitored in patients prescribed an MRA.
Ivabradine	Ivabradine should be considered in symptomatic LVEF ≤35% who are in sinus rhythm and resting heart rate >70pbm despite maximum tolerated therapy	Ivabradine should be considered to reduce the risk of HF hospitalization in symptomatic patients with LVEF ≤35%, sinus rhythm and who have a resting heart rate ≥70pbm despite treatment with an evidence-based dose of beta-blocker (or maximum tolerated dose below that), in addition to an ACE-I (or ARB) and an MRA
	Removed	Ivabradine should be considered to reduce the risk of HF hospitalization in symptomatic patients with LVEF ≤35%, sinus rhythm and who have a resting heart rate ≥70pbm and are unable to tolerate or have contraindications for beta-blockers. Patients should also receive an ACE-I (orARB) and an MRA
SGLT2 inhibitors	dapagliglozin or empagliflozin are recommended for patients with HFrEF to reduce the risk of HF hospitalization and death	
Soluble guanylate cyclase (sGC) stimulators	vericiguat may be considered in patients in NYHA class II-IV who have had worsening HF despite treatment with an ACEi (or ARNI), a beta-blocker and an MRA to reduce the risk of CV mortality or HF hospitalization	
Other drugs	Potassium binders (sodium zirconium cyclosilicate, patiromer) may be considered in patients who experience hyperkalemia while using a RAASi	

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Table 2 (*continued*)

Recommendation	SHA 2022	SHA 2019
	removed	diltiazem or verapamil are not recommended in patients with HFrEF because they increase the risk of HF worsening and HF hospitalization
	in patients with chronic HFrEF without a specific indication (e.g. venous thromboembolism, AF, a previous thromboembolic event or a cardioembolic source), anticoagulation is not recommended	
	In patients with HFrEF, dihydropyridine and non-dihydropyridine calcium channel-blocking drugs are not recommended treatment for HF	
	In patients with HFrEF, vitamins, nutritional supplements, and hormonal therapy are not recommended other than to correct specific deficiencies	
	In patients with HFrEF, class IC antiarrhythmic medications and dronedarone may increase the risk of mortality	
	In patients with type 2 diabetes and high cardiovascular risk, the dipeptidyl peptidase-4 (DPP-4) inhibitors saxagliptin and alogliptin increase the risk of HF hospitalization and should be avoided in patients with HF	
HFmrEF		
	Diuretics are recommended in patients with congestion and HFmrEF in order to alleviate symptoms and signs	
	SGLT2 inhibitors are recommended in patients with HFmrEF to reduce the risk of hospitalization and death	
	an ACEi/ARB may be considered in patients with HFmrEF to reduce the risk of hospitalization and death	
	a beta-blocker may be considered in patients with HFmrEF to reduce the risk of hospitalization and death	
	an MRA may be considered in patients with HFmrEF to reduce the risk of hospitalization and death	

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Table 2 (*continued*)

Recommendation	SHA 2022	SHA 2019
	sacubitril/valsartan may be considered in patients with HFmrEF to reduce the risk of hospitalization and death	
	In patients with HFmrEF after treatment, GDMT should be continued to prevent relapse of HF and LV dysfunction, even in patients who may become asymptomatic	
HFpEF		
	It is recommended to screen patients with HFpEF for both cardiovascular and non-cardiovascular comorbidities, which, if present, should be treated.	It is recommended to screen patients with HFpEF for both cardiovascular and non-cardiovascular comorbidities, which, if present, should be treated, provided safe and effective interventions exist to improve symptoms, well-being, and/or prognosis
	SGLT2 inhibitors are recommended in patients with HFpEF to reduce the risk of hospitalization and death	
	Treatment of AF should be considered in patients with HFpEF for symptom improvement	
	ARNI may be considered in select patients with HFpEF to reduce the risk of hospitalization and death	
	an MRA may be considered in select patients with HFpEF to reduce the risk of hospitalization and death	
	ARB may be considered in select patients with HFpEF to reduce the risk of hospitalization and death	
	beta blockers may be considered in select patients with HFpEF to reduce the risk of hospitalization and death	
	In patients with HFpEF, routine use of nitrates or phosphodiesterase-5 inhibitors to increase activity or quality of life is not recommended.	
Non-surgical device management of HFrEF		
ICD implantation	an ICD implantation is recommended for secondary prevention in patients with a structurally abnormal heart and documented sustained VT (not within 48 hours after MI) in the absence of a reversible cause	an ICD implantation should be considered for secondary prevention in patients with a structurally abnormal heart and documented sustained VT (not within 48 hours after MI) in the absence of a reversible cause
	an ICD implantation is recommended at least 40 days post-MI in patients with	

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Table 2 (*continued*)

Recommendation	SHA 2022	SHA 2019
	asymptomatic disease with LVEF≤30% despite ≥3 months of optimal medical therapy, provided they are expected to survive substantially longer than 1 year with good functional status	
	An ICD implantation should be considered to reduce risk of sudden cardiac death in selected patients with symptomatic non-ischemic cardiomyopathy and an LVEF ≤35% despite ≥3 months of optimal medical therapy	An ICD implantation may be considered to reduce risk of sudden cardiac death in selected patients with symptomatic non-ischemic cardiomyopathy and an LVEF ≤35% despite ≥3 months of optimal medical therapy
CRT	CRT is recommended for symptomatic patients with HF in sinus rhythm with a QRS duration ≥150ms and LBBB QRS morphology and with an LVEF ≤35% despite optimal medical therapy	CRT is recommended for symptomatic patients with HF in sinus rhythm with a QRS duration ≥130ms and LBBB QRS morphology and with an LVEF ≤35% despite optimal medical therapy, to improve symptoms and reduce morbidity and mortality
	CRT should be considered in patients with LBBB QRS morphology and QRS duration 130-149ms, or non-LBBB QRS morphology and QRS duration ≥150ms, and LVEF ≤35% in NYHA Class III-IV despite optimal medical therapy if they are in AF.	CRT should be considered for patients with LBBB QRS morphology and LVEF ≤35% in NYHA Class III-IV despite optimal medical therapy, to reduce morbidity and mortality, if they are in AF and have a QRS duration ≥ 130ms,provided a strategy to ensure biventricular capture is in place or if the patients is expected to return to sinus rythm. AV nodal ablation may be considered if patients do not have adequate biventricular pacing and continues to be in AF, to optimize response
	Patients with HFrEF who received a conventional pacemaker or an ICD and subsequently develop worsening HF despite optimal medical therapy, and who have a high proportion of RV pacing, should be considered for upgrade to CRT.	Patients with HFrEF who received a conventional pacemaker or an ICD and subsequently develop worsening HF despite optimal medical therapy, and who have a high proportion of RV pacing, may be considered for upgrade to CRT.
Advanced HF		
	Management by an advanced heart failure team is recommended for patients with advanced HF to review HF management and assess suitability for advanced HF therapies (e.g. LVAD, cardiac transplantation, palliative care and palliative inotropes).	
	For patients with advanced HF and hyponatremia, fluid restriction may be considered to reduce congestive symptoms.	

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Table 2 (*continued*)

Recommendation	SHA 2022	SHA 2019
Inotropic support	Continuous intravenous inotropic support should be considered as a bridge therapy in patients with advanced (stage D) HF refractory to optimal medical therapy and device therapy who are eligible and schedule for advanced therapies (MCS or cardiac transplantation)	
	Continuous or intermittent intravenous inotropic support may be considered as palliative therapy for symptomatic relief and functional improvement in select patients with stage D HF despite optimal medical and device therapy who are not eligible for advanced therapies (MCS or cardiac transplantation)	
	Long-term use of either continuous or intermittent intravenous inotropic agents is not recommended except as described above (palliative care or bridge to advanced therapies) due to potential harm.	
Mechanical circulatory support	Durable LVAD implantation is recommended as bridge to transplantation in select cases (advanced HFrEF with NYHA class IV symptoms dependent on continuous intravenous inotropes or temporary MCS).	an LVAD should be considered in patients who have end-stage HFrEF, despite optimal medical and device therapy, and who are eligible for heart transplantation to improve symptoms, reduce the risk of HF hospitalization and the risk of premature death (bridge to decision)
	Durable LVAD implantation should be considered as destination therapy in select cases (advanced HFrEF with NYHA class IV symptoms dependent on continuous intravenous inotropes or temporary MCS).	an LVAD should be considered in patients who have end-stage HFrEF, despite optimal medical and device therapy, and who are not eligible for heart transplantation, to reduce the risk of premature death
	Durable MCS should be considered for symptomatic and functional improvement as well as mortality reduction in select cases (advanced HFrEF who have NYHA class IV symptoms despite optimal medical therapy).	
	Temporary MCS (including percutaneous and extracorporeal ventricular assist devices) should be considered as a "bridge to recovery" or "bridge to decision" in patients with advanced HFrEF and hemodynamic compromise and shock.	

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Table 2 (*continued*)

Recommendation	SHA 2022	SHA 2019
Cardiac transplantation	Cardiac transplantation is recommended to improve survival and quality of life in select cases with advanced HF despite optimal medical therapy	
Cardiovascular comorbidities		
Atrial fibrillation		
	removed	the CHA2DS2-VASC and HAS-BLED scores are recommended tools in patients with HF for the estimation of the risk of thromboembolism and the risk of bleeding associated with oral anticoagulation, respectively
Anticoagulation	Oral anticoagulant is recommended to prevent thromboembolism in all patients with concomitant HF and AF and CHA2DS2-VASc score ≥ 2 in men or ≥ 3 in women	an oral anticoagulant is recommended to prevent thromboembolism for all patients with paroxysmal or persistent/permanent AF and a CHA2DS2-VASC score ≥2, without contraindications, and irrespective of whether a rate of rhythm management strategy is used (including after successful cardioversion)
	DOACs are recommended in preference to VKAs in patients with HF unless contraindicated	for patients with HF and non-valvular AF eligible for an anticoagulant, based on a CHA2DS2-VASC score, NOACs rather than warfarin should be considered as NOACs are associated with a lower risk of stroke, intracranial hemorrhage and mortality which outweigh the increased risk of gastrointestinal hemorrhage
	Oral anticoagulant should be considered to prevent thromboembolism in all patients with concomitant HF and AF and CHA2DS2-VASc score ≥ 1 in men or ≥ 2 in women	an oral anticoagulant may be considered to prevent thromboembolism for all patients with paroxysmal or persistent/permanent AF and a CHA2DS2-VASC score ≥1, without contraindications, and irrespective of whether a rate of rhythm management strategy is used (including after successful cardioversion)
	DOACS are not recommended in preference to VKAs in patients with moderate or severe mitral stenosis or mechanical prosthetic heart valves	NOAC treatment is contraindicated in patients with mechanical valves or at least moderate or severe mitral stenosis
AF catheter ablation	Catheter ablation should be considered for patients with worsening HF symptoms clearly due to paroxysmal or persistent AF despite medical therapy	AV node catheter ablation may be considered to control heart rate and relive symptoms in patients who are unresponsive or intolerant to intensive pharmacological rate

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Table 2 (*continued*)

Recommendation	SHA 2022	SHA 2019
		and rhythm control therapy, accepting that these patients will become pacemaker dependent
		Atrial fibrillation ablation may be considered to restore sinus rhythm in patients with persisting symtptoms and/or signs of HF, despite OMT and adequate control of ventricular rate, to improve clinical/symptomatic status
CCS		
	trimetazidine or ranolazine may be considered in patients with HR<70bpm and/or atrial fibrillation and persistence of CCS symptoms despite beta-blockers	ranolazine may be considered in patients unable to tolerate a beta-blocker to relive angina (effective antianginal treatment, but safety in HF is uncertain)
	nicorandil or a short-acting or long-acting oral or transcutaneous nitrates may be considered may be considered in patients with HR<70bpm and/or atrial fibrillation and persistence of CCS symptoms despite beta-blockers	a short acting oral or transcutaneous nitrate should be considered (effective antianginal treatment, safe in HF)
		a long-acting oral or transcutaneous nitrate should be considered (effective antianginal treatment, not extensively studied in HF)
	felopidine or amlopidine may be considered in patients with HR<70bpm and/or atrial fibrillation and persistence of CCS symptoms despite beta-blockers	
Coronary revascularization	CABG should be considered as the first-choice revascularization strategy if patients are suitable for surgery.	CABG is recommended for patients with significant LAD artery stenosis and multivessel disease to reduce death and hospitalization for cardiovascular causes
	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 anti-anginal drugs.	LV aneurysmectomy during CABG should be considered in patients with a large LV aneurysm if there is a risk of rupture, large thrombus formation, or the aneurysm is the origin or arrhythmias
	Whenever possible, CABG should be avoided in LVAD candidates requiring coronary revascularization.	myocardial revascularization should be considered In the presence of viable myocardium
	Coronary revascularization may be considered to improve outcomes in patients with HFrEF, CCS, and coronary anatomy suitable for revascularization	CABG with surgical restoration may be considered in patients with scarred LAD territory (only at specialized centers), especially if a postoperative LVESV index <70mL/m2 can be predictably achieved.

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Table 2 (*continued*)

Recommendation	SHA 2022	SHA 2019
	PCI may be considered as an alternative to CABG, based on Heart Team evaluation, considering coronary anatomy, comorbidities, and surgical risk.	PCI may be considered if the anatomy is suitable in the presence of viable myocardium and surgery is not indicated
Valvular heart disease		
Aortic stenosis	For patients with HF and severe high gradient aortic stenosis reintervention (TAVI or SAVR) is recommended to reduce mortality and improve symptoms.	in patients with severe aortic regurgitation (in presence of HFrEF), aortic valve repair or replacement is recommended in al symptomatic patients and in asymptomatic patients with resting LVEF ≤50%, who are otherwise fir for surgery
Secondary mitral regurgitation	Percutaneous edge-to-edge mitral valve repair should be considered in carefully selected patients with secondary mitral regurgitation, for whom coronary revascularization is not needed and who are at high risk for surgery and exhibit symptoms despite optimal medical therapy and who would benefit from a reduction of HF hospitalizations after the procedure	
	Combined surgery of secondary mitral regurgitation and CABG should be considered in symptomatic patients with LV systolic dysfunction.	Combined surgery of secondary mitral regurgitation and CABG should be considered in symptomatic patients with LV systolic dysfunction requiring coronary revascularization. Percutaneous mitral clip may be considered if patients are already exausted
	Percutaneous edge-to-edge mitral valve repair may be considered for symptom improvement in medically exhausted patients with secondary mitral regurgitation	
other comorbidities		
Diabetes	SGLT2 inhibitors are recommended in all patients with type-2 diabetes mellitus and HF	
Anemia	Intravenous supplementation with ferric carboxymaltose should be considered in symptomatic patients with EF <50% and iron deficiency (serum ferritin <100ug/L or ferritin between 100 ug/L and 299 ug/L and transferrin saturation <20%, regardless of hemoglobin levels) to alleviate HF symptoms and improve exercise capacity and quality of life.	Intravenous supplementation with ferric carboxymaltose should be considered in symptomatic patients with HFrEF and iron deficiency (serum ferritin <100ug/L or ferritin between 100 ug/L and 299 ug/L and transferrin saturation <20%, regardless of hemoglobin levels) to alleviate HF symptoms and improve exercise capacity and quality of life.
cancer/cardiotoxic treatment	Risk stratification is recommended in patients with cancer scheduled to receive potentially cardiotoxic	

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Table 2 (*continued*)

Recommendation	SHA 2022	SHA 2019
	therapy to assess the likelihood and degree of potential CV toxicity. Such patients should receive medical care aimed at promoting a healthy lifestyle and strict control and management of cardiovascular risk factors according to the current guidelines.	
	Cardiology referral (preferably to a cardio-oncology program or cardiologist with expertise in managing CVD in patients with cancer) and multidisciplinary discussion are recommended before anticancer therapy in high-risk and very high-risk patients and in patients with pre-existing CVD or abnormal findings at baseline CV toxicity risk assessment. Such referral and discussion are also recommended in patients who develop CV toxicity.	
	Clinical assessment and ECG are recommended at baseline in all patients with cancer and echocardiography, cardiac biomarkers, or other cardiac imaging tests in selected patients according to baseline CV toxicity risk and cancer treatment type	
	Baseline comprehensive echocardiography (including 3D LVEF and GLS, if available) is recommended in all patients with cancer at high risk and very high risk of CV toxicity before starting anticancer therapy and periodically during treatment for early detection of cardiac dysfunction.	
	ACEI or ARB, beta-blockers and statins should be considered for primary prevention in high- and very high-risk patients receiving cancer therapies that may cause HF	
	The severity of cancer therapy-related cardiac dysfunction (CTRCD) should be assessed using the combination of new CV symptoms and the change in LVEF, GLS and/or cardiac biomarkers (see the ESC definition/classification)	
	Guideline-directed HF therapy is recommended in patients who	

(*continued on next page*)

Table 2 (*continued*)

Recommendation	SHA 2022	SHA 2019
	develop symptomatic CTRCD or asymptomatic moderate to severe CTRCD during anthracycline chemotherapy or HER2-targeted treatment. *** (Asymptomatic severe CTRCD: LVEF < 40%; asymptomatic moderate CTRCD: LVEF 40–49%; asymptomatic mild CTRCD: LVEF > 50%) (see the ESC definition/classification)	
	ACE-I/ARB and/or beta-blockers should be considered in asymptomatic mild CTRCD (patients who have LVEF ≥ 50% and have developed a significant fall in GLS and/or elevation in troponin and/or NP) during anthracycline chemotherapy or HER2-targeted treatment.	
Amyloidosis	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.	
	Tafamidis is recommended in patients with wtTTR-CA and NYHA class I or II symptoms to reduce symptoms, CV hospitalization and mortality.	
Pregnancy		
Counseling and risk assessment	It is recommended that pre-pregnancy counseling on contraception and the risks of cardiovascular deterioration during pregnancy be offered to patients with a history of HF or cardiomyopathy (including peripartum cardiomyopathy)	
	Patients should be counseled to avoid pregnancy if they have severe heart disease (ejection fraction less than 30% or class III/IV heart failure, severe valvular stenosis, Marfan syndrome with aortic diameter more than 45 mm, bicuspid aortic valve with aortic diameter more than 50 mm, or pulmonary arterial hypertension	
	pregnancy termination may be considered after agreement of by a multi-disciplinary heart team for patients with severe heart disease (ejection fraction less than 30% or class III/IV heart failure, severe valvular stenosis, Marfan	

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Table 2 (*continued*)

Recommendation	SHA 2022	SHA 2019
	syndrome with aortic diameter more than 45 mm, bicuspid aortic valve with aortic diameter more than 50 mm, or pulmonary arterial hypertension	
Management during pregnancy	Close maternal and fetal monitoring is recommended for HF signs or symptoms or other cardiovascular instability by cardiology and obstetric and maternal-fetal medicine teams.	
	Screening for any significant changes in HF symptoms or signs during pregnancy is recommended, particularly in the third trimester and if HF medication is changed.	
	hemodynamic monitoring and MCS are recommended as deemed appropriate by a multidisciplinary heart team for patients presenting with decompensatied HF or cardiogenic shock	
	Monitoring-based adjustment of HF treatment is recommended as appropriate to avoid hypotension and placental hypoperfusion.	
	beta-blockers should be continued in pregnancy and switched to beta-1-selective blockers (bisoprolol, metoprolol succinate).	
	Adjustment of diuretic dosing should be considered to minimize the risk of placental hypoperfusion	
	Hydralazine, oral nitrates and methyldopa may be considered if required.	
	ACE-Is, ARBs, ARNI, MRAs, ivabradine, vericiguat and SGLT2 inhibitors are contraindicated due to risk of fetal harm and should be stopped prior to conception	
Peripartum cardiomyopathy	It is recommended that patients with peripartum cardiomyopathy with severe HF and cardiogenic shock requiring inotropic or vasopressor support be transferred to an advanced HF centre, where necessary interventions can be performed as needed (extracorporeal membrane oxygenation, LVAD and/or cardiac transplantation). Urgent delivery by caesarean section should be considered with MCS immediately available.	

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Table 2 (*continued*)

Recommendation	SHA 2022	SHA 2019
	For refractory cardiogenic shock cases, LVAD implantation as a BTT or BTR should be considered.	
	levosimendan or MCS may be considered for hemodynamically unstable patients with peripartum cardiomyopathy	
	Bromocriptine may be considered for treatment of peripartum cardiomyopathy	
anticoagulation	anticoagulation with low-molecular-weight heparin (LMWH) is recommended during the first and last trimesters, and with VKAs for the second trimester, for patients with HF and AF. DOACs should be avoided	
contraception	It is recommended that the most appropriate contraceptive option be determined based on patient preference and critical assessment of disease and the relative risks and benefits of the contraceptive option considered.	
	Intrauterine devices are the recommended nonpermanent contraceptive option for women with high-risk cardiovascular conditions.	
Sleep apnea	In patients with HF and suspicion of sleep-disordered breathing, a formal sleep assessment may be considered to confirm the diagnosis and differentiate between obstructive and central sleep apnea	
II- Acute HF Management		
Vasodilators	Intravenous vasodilators may be considered for symptomatic relief in AHF with SBP >110 mmHg and without symptomatic hypotension. Symptoms and blood pressure should be monitored frequently during the administration of intravenous vasodilators	Intravenous vasodilators should considered for symptomatic relief in AHF with SBP >90 mmHg and without symptomatic hypotension. Symptoms and blood pressure should be monitored frequently during the administration of intravenous vasodilators
Inotropic agents and vasopressors	Inotropic agents may be considered in patients with SBP <110 mmHg and evidence of hypoperfusion who do not respond to standard treatment, including fluid challenge, to improve peripheral perfusion and maintain end-organ function.	short-term intravenous infusion of inotropic agents may be considered in patients with hypotension (SBP<90mmHg) and/or signs/symptoms of hypoperfusion despite adequate filling status to increase cardiac output, increase blood pressure, improve peripheral perfusion and maintain end-organ

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Table 2 (*continued*)

			function
		Inotropic agents are not recommended routinely, due to safety concerns, unless the patient has symptomatic hypotension and evidence of hypoperfusion.	inotropic agents should not be considered in the absence of cardiogenic shock
Thromboembolism prophylaxis		Anticoagulation is recommended in patients with AHF and other indications for anticoagulation (e.g. AF)	

Table 3. Definition and classification of Heart Failure.

Classification	Ejection fraction (%)
Heart failure with reduced ejection fraction (HFrEF)	≤40
Heart failure with mildly reduced ejection fraction (HFmrEF)	41–49
Heart failure with preserved ejection fraction (HFpEF)	≥50

4. Chronic heart failure

4.1. Etiologies

The SHA 2019 HF guidelines offer an overview of the causes of chronic heart failure (please refer to Fig. 1). The scheme divides the etiologies into two broad categories: HF secondary to diseased myocardium and HF secondary to abnormal loading conditions. In the current update, we highlight the relationship between HF and atrial fibrillation, as well as some of the evidence linking COVID-19 and de-novo HF.

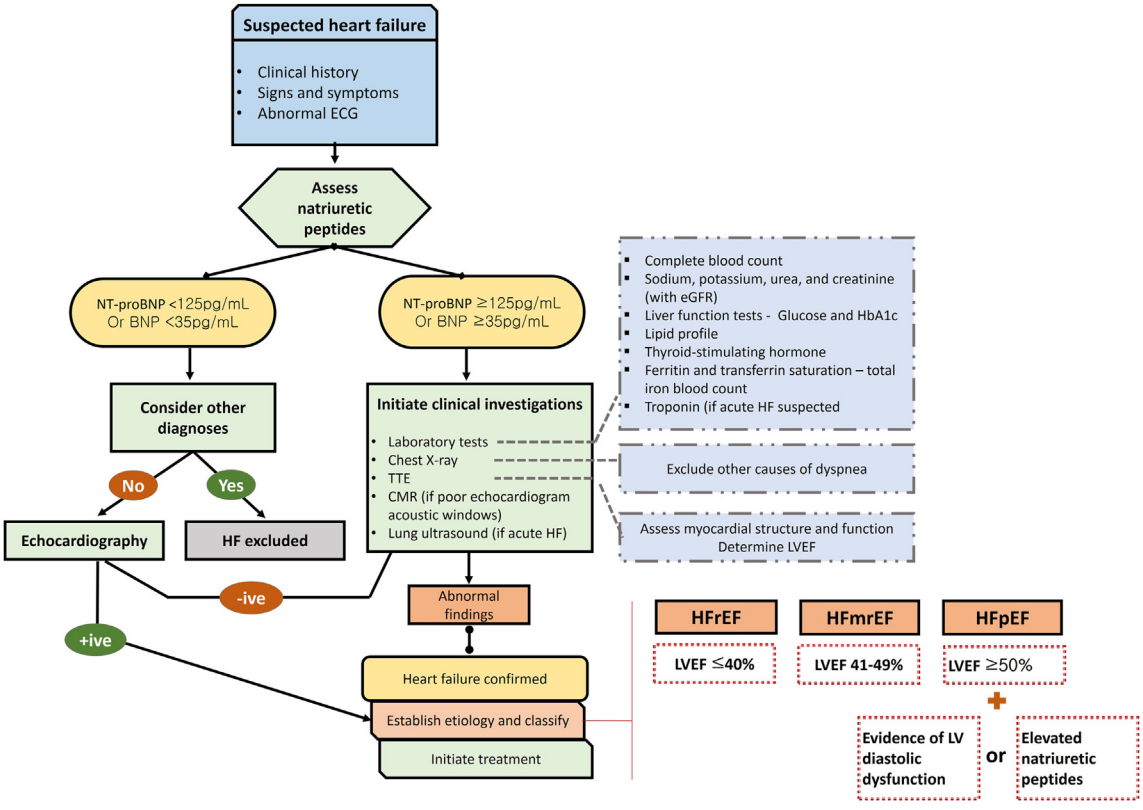

Fig. 1. Algorithm for the diagnosis of HF.

4.1.1. HF and atrial fibrillation

Clinicians should be aware of arrhythmia-induced cardiomyopathy, which leads to a reversible dilated cardiomyopathy [15]. It is therefore important to consider whether atrial fibrillation (AF) is fully or partially responsible for LV dysfunction in patients with concomitant HF and AF. Data from randomized controlled trials suggests that the restoration of sinus rhythm through catheter ablation in patients with concomitant AF and HF can also induce favorable structural remodeling, including early recovery or improvement of LVEF and HF symptoms [16,17]. The efficacy of this approach for LV function improvement is highest when performed early in the natural history of atrial fibrillation and heart failure. Suspicion of arrhythmia-induced cardiomyopathy can be confirmed in case of reversal of cardiomyopathy by elimination of the arrhythmia.

4.1.2. HF and infections

HF can arise as the result of an infection by a virus, bacteria, fungi, etc. The most prominent example is that of COVID-19. A meta-analysis of data from close to 19,000 patients showed that severe COVID-19 was associated with elevated B-type natriuretic peptide (BNP)/N-terminal pro-BNP (NT-proBNP) plasma concentrations and higher mortality [18]. Data also suggests that COVID-19 can cause acute de-novo HF as a result of myocardial injury, with the disease linked to both systolic and diastolic LV dysfunction [19–22]. Immunization against COVID-19 was also associated with an increased risk of myocarditis/pericarditis in large-scale population-wide studies, particularly in younger populations (40 years and younger) [23–25].

4.2. Symptoms and signs

No changes in the symptoms and signs of HF were made to the SHA 2019 HF guidelines. For more information please refer to the appropriate section.

4.3. Diagnosis

When HF is suspected, prior clinical history, physical examination, and resting electrocardiogram will indicate whether a diagnosis of HF is likely. If all results fall within the normal range, HF is highly unlikely and differential diagnoses should be considered. The diagnosis of HF will primarily rely on laboratory tests in addition to non-invasive and invasive imaging and diagnostic modalities (see Table 4). The majority of recommendations for the diagnosis of chronic HF proposed in the 2019 SHA guidelines remain applicable. The 2023 guidelines provide an update to natriuretic peptide cutoff levels to be consistent with current practice, modifies the wording of some recommendations and proposes new recommendations as shown in Table 1 and discussed below. For more information on unchanged recommendations, please refer to the 2019 SHA HF guidelines.

4.3.1. Diagnostic laboratory tests

BNP is an active peptide hormone that results from the cleavage of the precursor pro-BNP into BNP and the inactive N-terminal fragment (NT-proBNP). BNP and NT-proBNP are biomarkers of cardiac hemodynamic stress and are useful for the diagnosis and prognosis of HF regardless of EF [26,27]. BNP and NT-proBNP levels below the cutoff of 125 pg/mL and 35 pg/mL have a high negative predictive value for HF [28–30]. Measuring natriuretic peptides is therefore recommended for the exclusion of HF and subsequently preventing further unnecessary testing. A SHA position statement published in 2022 further discusses the use of biomarkers in the management of HF and acute coronary syndromes [31].

Basic laboratory investigations (serum urea and electrolytes, creatinine, full blood count, liver and thyroid function tests) are also recommended to eliminate other possible conditions that could manifest similarly to HF, for prognostication and for guiding the therapeutic management of patients. Additional diagnostic tests aiming to identify other HF etiologies and comorbidities should be considered in individual patients with HF when there is a clinical suspicion of a particular pathology (see Fig. 1 on HF etiologies in the 2019 SHA HF guidelines).

4.3.1.1. Stress echocardiography and cardiopulmonary exercise testing. Stress echocardiography and Cardiopulmonary Exercise Testing (CPET) can be used for the detection of diastolic dysfunction related to exercise in patients with exertional dyspnea, preserved LVEF, and inconclusive diastolic parameters at rest. Stress echocardiography and CPET can also be effective in the assessment of inducible ischemia, myocardial viability, and in valve disease. Exercise stress echocardiography and cardiopulmonary exercise testing are recommended for the dynamic assessment of HFpEF seeing as the severity of HFpEF is not accurately reflected by resting echocardiography [32]. Stress echocardiography is therefore advisable especially in patients with shortness of breath and no clear resting abnormality; exercise reveals the deterioration of ventricular

Table 4. Recommendations for the diagnosis of HF.

Class	Recommendation
Diagnostic tests	
	The following diagnostic tests are recommended for the initial assessment of a patient with newly diagnosed HF to evaluate the patient's suitability for particular therapies, and to detect reversible/treatable causes of HF and comorbidities interfering with HF: - Complete blood count - Sodium, potassium, urea, and creatinine (with estimated glomerular filtration rate) - Liver function tests (bilirubin, aspartate transaminase, alanine transaminase, gamma-glutamyl transpeptidase, and albumin) - Glucose and HbA1c - Lipid profile - Thyroid-stimulating hormone - Ferritin and transferrin saturation – total iron blood count - Natriuretic peptides (BNP and NT-proBNP) and troponin
	additional diagnostic tests aiming to identify other HF etiologies and comorbidities should be considered in individual patients with HF when there is a clinical suspicion of a particular pathology (see Fig. 2 on HF etiologies in SHA 2019 HF guidelines)
12-lead ECG	
	A 12-lead ECG is recommended in all patients with HF to determine heart rhythm, heart rate, QRS morphology, QRS duration and to detect other relevant abnormalities. This information is needed to plan and monitor treatment.
Non-invasive imaging	
Chest X-ray	
	Chest radiography (X-ray) is recommended in patients with HF to detect/exclude alternative pulmonary or other diseases, which may contribute to dyspnea. It may also identify pulmonary congestion/edema and is more useful in patients with suspected HF in the acute setting.
TTE	
	TTE is recommended for the assessment of myocardial structure and function in patients with suspected HF to establish a diagnosis of HFrEF, HFmrEF, or HFpEF and to identify patients for the most appropriate pharmacological and device therapy.
	TTE is recommended for the assessment of valve disease, right ventricular function and pulmonary arterial pressure in patients with an already established diagnosis of HFrEF, HFmrEF, or HFpEF to identify those suitable for correction of valve disease
	TTE is recommended for the assessment of myocardial structure and function in patients to be exposed to cardiotoxic agents (e.g. Chemotherapy)
	Other techniques (including systolic tissue Doppler velocities, 3D assessment of LVEF and global longitudinal strain) may be considered in a TTE protocol in those at risk of developing HF, to identify myocardial dysfunction at the preclinical stage as well as in patients exposed to cardiotoxic agents
Exercise testing (stress echocardiography and CPET)	
	CPET is recommended as part of the evaluation for advanced treatments (heart transplantation and/or mechanical circulatory support)
	CPET or 6-minute walk test should be considered to assess functional capacity in ambulatory HF patients
	CPET may be considered in select cases to identify the cause of unexplained dyspnea
CMR	
	CMR is recommended for the assessment of myocardial structure and function in those with poor echocardiogram acoustic windows

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Table 4 (continued)

Class	Recommendation
	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/hemochromatosis
	CMR with LGE should be considered in DCM to distinguish between ischemic and non-ischemic myocardial damage
CCTA and others	
	CCTA should be considered in patients with a low to intermediate probability of CAD or those with equivocal non-invasive stress tests in order to rule out coronary artery stenosis
	Other non-invasive imaging (stress echocardiography, SPECT, PET, myocardial perfusion imaging) may be considered in patients with a low to intermediate probability of CAD or those with equivocal non-invasive stress tests in order to rule out coronary artery stenosis
	Noninvasive stress imaging (CMR, stress echocardiography, SPECT, or PET) may be considered for the detection of myocardial viability to help guide revascularization in patients with HF and CAD who are candidates for coronary revascularization
Invasive testing	
ICA	
	Invasive coronary angiography is recommended in patients with HF and angina pectoris recalcitrant to pharmacological therapy, symptomatic ventricular arrhythmias or aborted cardiac arrest (who are considered suitable for potential coronary revascularization) to establish the diagnosis of CAD and its severity
	Invasive coronary angiography should be considered for patients with HFrEF with an intermediate to high pre-test probability of CAD and the presence of ischemia in non-invasive stress test.
EMB	
	Endomyocardial biopsy may be considered when a specific diagnosis is suspected that would influence therapy but should not be routinely performed.
Right heart catheterization	
	Right heart catheterization is recommended in patients with advanced HF being evaluated for advanced heart therapy (heart transplantation or mechanical circulatory support)
	Right heart catheterization should be considered in patients with probable pulmonary hypertension assessed by echocardiography, to confirm pulmonary hypertension and its reversibility before the correction of valve structural heart disease
	Right heart catheterization may be considered to adjust therapy in patients with HF who remain severely symptomatic or require hemodynamic support with parenteral vasoactive agents despite standard therapies and whose hemodynamic status is unclear
	Right heart catheterization is not recommended for routine use to guide treatment selection
Genetic testing	
	Genetic testing is recommended for patient with hypertrophic cardiomyopathy (HCM) and arrhythmogenic right ventricular cardiomyopathy (ARVC)
	Genetic testing should be considered in other suspected cases of familial cardiomyopathy
Lung ultrasound	
	Lung ultrasound should be considered for the confirmation of pulmonary congestion and pleural effusion in patients with AHF
	Lung ultrasound should be performed by a trained physician
	Lung ultrasound may be used to differentiate from respiratory causes of dyspnea, including pulmonary fibrosis and ARDS, and aids in monitoring of response to therapy in patients with cardiogenic pulmonary edema

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Table 4 (*continued*)

Class	Recommendation
	Lung ultrasound is more accurate than portable X-ray in the detection of lung consolidation, and may be used in mechanically ventilated patients
Other considerations	
	reassessment of myocardial structure and function using non-invasive imaging is recommended: - In patients with worsening HF symptoms (including episodes of AHF) or experiencing any other important cardiovascular event - In patients with HF who have received evidence-based pharmacotherapy in maximal tolerated doses, before the decision of device implantation (ICD, CRT) to avoid misuses, overuse, or unjustified use - In patients exposes to therapies that may damage the myocardium (e.g. chemotherapy) , serial assessments or any medications that could lead to cardiotoxicity - In patients receiving CRT for the assessment of change in myocardial function, valvular regurgitation, and diastolic filling pressures
	ultrasound measurement of inferior vena cava diameter may be considered for the assessment of volume status in patients with HF

and peripheral performance in HF patients with no LV dysfunction. Moreover, exercise is an effective way to show chronotropic in HF [33]. CPET or 6-min walk test should be considered to assess functional capacity in ambulatory HF patients [34,35]. CPET is recommended as part of the evaluation for advanced treatments (heart transplantation and/or mechanical circulatory support) considering its prognostic capacity in terms of durable mechanical circulatory support (MCS), transplantation, or survival [36]. CPET may also be considered in select cases to identify the cause of unexplained dyspnea.

4.3.1.2. Cardiac magnetic resonance (CMR). CMR remains the gold standard for measurements of volume, mass, and the EF of both the left and right ventricles. CMR is recommended for the evaluation of myocardial fibrosis and complex congenital heart disease. CMR allows myocardial characterization in myocarditis, amyloidosis, sarcoidosis, Chagas disease, Fabry disease, noncompaction cardiomyopathy, and hemochromatosis [37,38]. CMR with late gadolinium enhancement (LGE) should also be considered in dilated cardiomyopathy (DCM) to differentiate ischemic from non-ischemic myocardial damage; myocardial fibrosis/scarring of the mid-wall typical of DCM can be detected by CMR with LGE, T1 mapping and extracellular volume. It may also be used to guide revascularization by detecting myocardial ischemia in patients with concomitant HF and CAD [39–43].

4.3.1.3. CCTA and other non-invasive modalities. Cardiac computed tomography angiography (CCTA) is a useful noninvasive tool with excellent accuracy for the diagnosis of HF [44]. CCTA can reliably rule-out CAD in patients with low-or-intermediate pretest probability of CAD. CCTA conducted at high spatial and temporal resolution allows fast and convenient non-invasive imaging in addition to exposure to lower doses of ionizing radiation [45]. LV dysfunction can be detected with CCTA with good correlation to echocardiographic assessment [46]. As such, CCTA can be used as a gatekeeper for invasive coronary angiography (ICA) and prevent unnecessary invasive testing. However, it should be noted that compared to CMR, CCTA leads to slight overestimations of end-systolic volume and EF due to its limited temporal resolution, especially in patients with HFrEF. CCTA also has an emerging role in the diagnosis and assessment of HFpEF cases in case of clinical uncertainty [47]; CCTA is useful for the identification of CAD, ischemia, pericardial effusion and constriction. It can also be used for chamber quantification and fibrosis detection. Nuclear imaging techniques such as single photon emission computed tomography (SPECT) and Positron emission tomography (PET) (with or without CT) may be considered for the

assessment of myocardial viability or ischemia [48]. However, the use of nuclear imaging would incur exposure to higher levels of radiation, higher cost and remains limited by restricted availability. Non-invasive imaging techniques other than CCTA (stress echocardiography, SPECT, PET, myocardial perfusion imaging) may be considered in patients with a low to intermediate probability of CAD or those with equivocal non-invasive stress tests in order to rule out coronary artery stenosis. Noninvasive stress imaging (CMR, stress echocardiography, SPECT, or PET) may also be considered for the detection of myocardial viability to help guide revascularization in patients with HF and CAD who are candidates for coronary revascularization [39–43].

4.3.2. Invasive cardiac imaging and diagnostic work-up

Please refer to SHA 2019 HF guidelines for discussion of unchanged recommendations.

4.3.2.1. EMB. Endomyocardial biopsy (EMB) may be considered when a specific diagnosis is suspected that would influence therapy but should not be routinely performed. This includes but is not limited to Suspected fulminant myocarditis or acute myocarditis with acute HF, LV dysfunction and/or rhythm disorders, Suspected myocarditis in hemodynamically stable patients, DCM with recent onset HF, moderate-to-severe LV dysfunction, refractory to standard treatment, and cardiac tumors [49]. The availability of EMB remains limited in Saudi Arabia and it is preferable that patients be referred to experienced centers when EMB is needed.

4.3.2.2. Right heart catheterization. Right heart catheterization is recommended in patients with advanced HF being evaluated for advanced heart therapy (heart transplantation or mechanical circulatory support) [50]. For more information, please refer to SHA 2019.

4.3.3. Genetic testing

Patients with hypertrophic cardiomyopathy (HCM), DCM, and arrhythmogenic right ventricular cardiomyopathy (ARVC) should be provided with genetic counseling. Genetic testing in combination with CMR and cardiac biomarkers allow the diagnosis and risk stratification of HCM as well as the assessment of the need for placement of implantable cardioverter defibrillators (ICDs) for primary prevention of complications [51,52].

ARVC is an inherited disease of the heart muscle associated with potentially life-threatening ventricular arrhythmias, sudden cardiac death, and/or biventricular HF [39]. ARVC is predominantly associated with mutations in desmosomal genes. However, several disease phenotypes have been identified and ARVC has an age-related penetrance [40]. Diagnosis of ARVC remains challenging considering the current limitations of the genetic etiologies of the disease. Genetic testing can reveal pathogenic mutations leading to the diagnosis of ARVC. However, the absence of pathogenic mutations does not necessarily exclude the disease as it could be due to an as-of-yet unidentified mutation. Despite this, genetic testing is a pivotal component in ARVC diagnosis, along with CMR [53,54]. Genetic testing is therefore recommended for patient with HCM and ARVC.

Genetic testing should also be considered in other suspected cases of familial cardiomyopathy, such as DCM. Genetic heterogeneity is characteristic of DCM, with more than 40 genes implicated in the disease [55,56]. Familial disease can occur in up to half of DCM cases and around 20% of patients with an established nongenetic risk factor or a nonfamilial disease were found to carry a pathogenic gene variant [55]. Some genetic mutations are associated with worse clinical outcomes [57]. Screening for DCM may be useful for the early detection and management of the disease, potentially improving prognosis [58]. Moreover, testing for pathogenic mutations would allow the prediction of disease risk for family members before the onset of symptoms.

4.3.4. Diagnosis of heart failure with preserved ejection fraction (HFpEF)

A considerable proportion of HF patients have preserved EF. Yet this patient population continues to pose a significant diagnostic challenge; signs and symptoms of HFpEF are non-specific and markers of diastolic dysfunction are very limited. Natriuretic peptides can be used for screening diagnosis and risk stratification in HF, and have been suggested to predict morbidity and mortality in HFpEF [59]. However, it should be noted that natriuretic peptides are less reliable biomarkers of HF in HFpEF compared to HFrEF and may be more suited to rule out HFpEF rather than diagnose it [60]. Echocardiography provides valuable insights for the diagnosis of HFpEF Scores incorporating echocardiographic findings with other clinical variables have been shown to be promising for the diagnosis of HFpEF [61,62]. HFpEF scoring systems can be considered for the diagnosis of this condition but the choice of which score remains at the treating physician's discretion as none have been developed for or adapted to the local Saudi population. Advanced

Table 5. Echocardiography parameters for the diagnosis of heart failure with preserved ejection fraction.

Parameters
• Left atrial volume index
• Left ventricular mass index
• Left ventricular wall thickness
• Transmitral doppler and tissue doppler indices
• Longitudinal strain patterns
• Tricuspid regurgitation velocity
• Right ventricular systolic function
• Tricuspid annular plane systolic excursion
• Right ventricular systolic pressure

diagnostic modalities might be needed to distinguish between HFpEF and other causes of dyspnea. This includes exercise echocardiography, CMR, invasive haemodynamics and assessment of other conditions that might mimic HFpEF [63,64]. The presence of three key clinical, echocardiographic, and hemodynamic abnormalities are required for the definitive diagnosis of HFpEF (Fig. 1).

Possible echocardiography parameters to aid diagnosis of HFpEF and minimize the need for invasive testing are listed in Table 5. HFpEF has a unique pathophysiology, characterized by severe dysfunction of the diastolic phase of the cardiac cycle that results in elevated ventricular pressures. In addition, impairment of myocardial relaxation and stiffness lead to reduced LV filling, elevated diastolic pressures, and HF symptoms. Hemodynamic measurements reveal prolonged isovolumic pressure decline and upward–leftward shift in the pressure–volume loop, with aberrant myocardial relaxation coupled with high indices of passive stiffness.

4.4. Prevention

Recommendations for the prevention of HF are largely consistent with the SHA 2019 guidelines. In the current 2023 version, we have divided HF prevention into primary and secondary prevention. Primary prevention focuses on the prevention of the onset of HF (see Table 6), while secondary prevention addresses the risk of morbidity and mortality in established HF (see Table 7). For cardiac risk assessment methods, please refer to the Saudi Heart Association Guidelines on Best Practices in the Management of Chronic Coronary Syndromes [65].

4.4.1. Primary prevention

Treatment of hypertension and the use of statins is still recommended to prevent or delay HF onset and is discussed in more details in SHA 2019. A recommendation was added for the use of Sodium-glucose Cotransporter-2 (SGLT2) inhibitors based on emerging clinical evidence of their benefit in diabetes as well as in HF [66–70], discussed in detail in later sections. Pharmacological approaches should also be supplemented with patient counseling regarding risk factors associated with a higher risk of developing HF.

4.4.2. Secondary prevention/Prevention of hospitalization

Self-management can improve outcomes in HF and is recommended to reduce the risk of hospitalization and death with HF [71]. Patient education on self-management strategies address several topics implicated in HF patient management, such as how to adjust diuretics in the case of increasing dyspnoea or oedema or a sudden unexpected weight gain of >2 kg in 3 days, when to alert the healthcare team, lifestyle modifications, importance of treatment adherence, etc. Self-management education methods are flexible; education can be provided in different settings (group session, home visit, telephone/tele-monitoring), by any implicated healthcare provider including the nurse, the physician, or a health educator. Influenza and pneumococcal vaccinations should also be considered based on their association with reduced hospitalizations in HF [72,73]. Moreover, a supervised, exercise-based cardiac rehabilitation program should be

Table 6. Recommendations for the primary prevention of HF.

Class	Recommendation
	Treatment of hypertension is recommended to prevent or delay the onset of HF
	Treatment with statins is recommended in patients with or at risk of atherosclerotic cardiovascular disease to prevent or delay the onset of HF
	SGLT2 inhibitors are recommended in patients with diabetes at high risk of CV disease or with CV disease in order to prevent HF hospitalizations
	Counseling against risk factors such as sedentary habit, obesity, smoking (all types, including but not exclusive of cigarette, tobacco, khat or sheesha smoking) and alcohol is recommended to prevent or delay the onset of HF.

Table 7. Recommendations for the secondary prevention of HF.

Class	Recommendation
	self-management strategies are recommended to reduce the risk of HF hospitalization and mortality
	a beta-blocker is recommended in patients with symptomatic or asymptomatic LV systolic dysfunction, to prevent or delay the onset of HF
	an ICD is recommended in patients with asymptomatic LV systolic dysfunction (LVEF ≤30%) of ischemic origin, who are at least 40 days after acute myocardial infarction or 3 months after revascularization, to prevent sudden death and prolong life
	an ACEi/ARB is recommended in patients with symptomatic or asymptomatic LV systolic dysfunction, to prevent or delay the onset of HF
	an ACEi should be considered in patients with stable CAD even if they do not have LV systolic dysfunction, to prevent or delay the onset of HF
	a supervised, exercise-based cardiac rehabilitation program should be considered in patients with more severe disease, frailty or with comorbidities
	influenza and pneumococcal vaccinations should be considered in order to prevent HF hospitalizations

considered in patients with more severe disease, frailty or with comorbidities [74–78]; in addition to increasing exercise capacity and quality of life, exercise-based rehabilitation can reduce hospitalizations in general and those due to HF specifically. However, while its effect on mortality requires further validation in RCTs, exercise-based cardiac rehabilitation has led to significant reductions in all-cause mortality in several large scale cohort studies [79–83]. Considering its benefit, referral of patients with HF to cardiac rehabilitation programs should be promoted. Recommendations on Angiotensin-converting enzyme inhibitors (ACEi), Angiotensin receptor blockers (ARB), beta-blockers and ICD are discussed in the SHA 2019 HF guidelines.

4.5. Pharmacological management

4.5.1. HFrEF

The algorithm for the pharmacological treatment of HFrEF is shown in Fig. 2. Table 8 shows all recommendations for the pharmacological management of HFrEF; all drugs should be given and doses titrated as needed to achieve intended outcomes as tolerated by the patient. ACEi/ARBs or Angiontensin Receptor Neprilysin Inhibitor (ARNI) (sacubitril/valsartan), SGLT2 inhibitors, MRAs and beta-blockers are recommended for the first line treatment of all patients with HFrEF, unless contraindicated or not tolerated. The ARNI sacubitril/valsartan can be used as first-line therapy, or used to replace ACE-Is in ambulatory HFrEF patients who remain symptomatic despite optimal therapy. Diuretics are also recommended to be used, but only as needed. Digoxin may be considered in patients with AF with symptomatic HFrEF to reduce the risk of hospitalization (both all-cause and HF hospitalizations). Ivabradine should be considered in symptomatic LVEF $\leq$35% who are in sinus rhythm and resting heart rate >70pbm despite maximum tolerated therapy. Hydralazine and isosorbide dinitrate should be considered in symptomatic patients with HFrEF who cannot tolerate an ACEi or an ARB (or for whom they are contraindicated), to reduce the risk of death. Hydralazine and isosorbide dinitrate may also be considered in symptomatic patients with HFrEF despite treatment with an ACEi, ARB, a beta-blocker and a Mineralocorticoid receptor antagonist (MRA) to reduce the risk of HF hospitalization and death. Vericiguat may be considered in patients in NYHA class II-IV who have had worsening HF despite treatment with an ACEi (or ARNI), a beta-blocker and an MRA to reduce the risk of cardiovascular (CV) mortality or HF hospitalization. Potassium binders (patiromer, sodium zirconium cyclosilicate) maybe be considered in patients who experience hyperkalemia while using a Renin–angiotensin–aldosterone system inhibitor (RAASi). More details on the management of hyperkalemia are provided in Section 4.5.5. Evidence in support of the above recommendations is provided in following sections. Recommended target doses of key agents used for managing patients with HF are outlined in Table 9.

The PARADIGM-HF trial consistently demonstrated the benefit of the ARNI sacubitril/valsartan on the level of risk of death and hospitalization in patients with HFrEF and worsening HF [84] (see Tables 10–12).

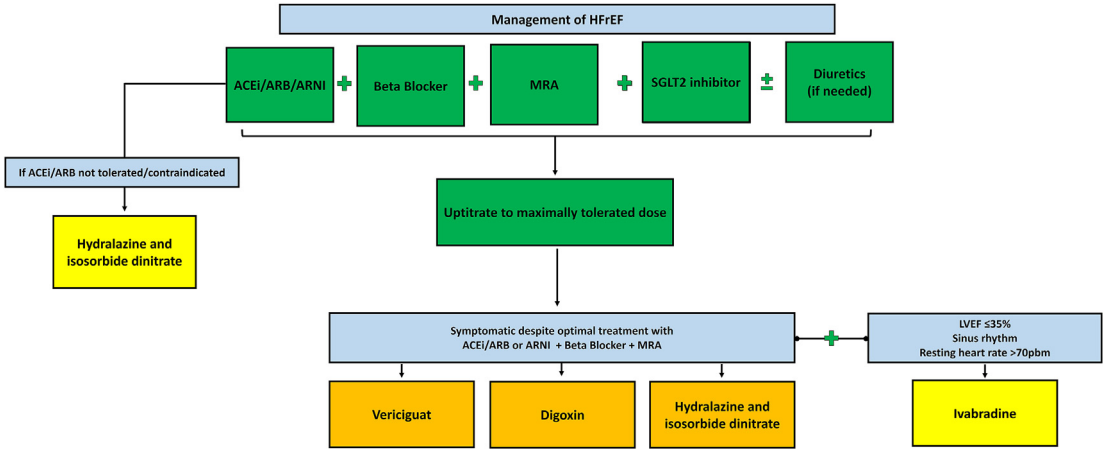

Fig. 2. Algorithm for the pharmacological management of HFrEF.

Sacubitril/valsartan was also shown to be beneficial for the symptomatic improvement of HF, improvement of quality of life, reduction of diabetes requiring insulin treatment, reduction in estimated glomerular filtration rate (eGFR) decline, reduction of loop diuretic requirement and reduction of hyperkalemia rates [84–88]. Additional benefits of sacubitril/valsartan include the reduction of loop diuretic requirement. That being said, sacubitril/valsartan was associated with higher rates of symptomatic hypertension compared to enalapril, albeit with no restriction of its clinical benefits [87,89]. The PIONEER-HF trial also demonstrated the benefit of sacubitril/valsartan in acute decompensated heart failure, leading to more reduction in compared to enalapril therapy with comparable rates of worsening renal function, hyperkalemia, symptomatic hypotension, and angioedema [90]. Current evidence suggests the superior effect of sacubitril/valsartan on cardiac remodeling compared to ACEi/ARB and the potential value of early ARNI initiation for HFrEF [91,92]. Regardless, this needs to be confirmed in larger trials. Moreover, ACEis and ARBs have a well-established efficacy in HFrEF, ensuring reductions in mortality and symptom improvement [93–96].

The benefits of ACEi/ARBs are also relatively comparable to ARNI. A network meta-analysis of 48 randomized controlled trials (RCTs) conducted in patients with HFrEF including monotherapies or combinations of ACEI, ARB, ARNI, Beta blockers, MRA, SGLT2 inhibitor, and ivabradine reported significant reductions in the risk of all-cause death, cardiovascular mortality and hospitalization for HF [97]. This risk reduction was highest with the combination of ARNI, Beta blockers and MRA (60% reduction of all-cause mortality), and the combination of SGLT2i, ACEi, Beta blocker and MRA (58% reduction of all-cause mortality) [97]. Another recent meta-analysis showed that the combination of ARNi, Beta Blocker, MRA, and SGLT2 inhibitor conferred the highest reduction in all-cause mortality among patients with HFrEF (61% reduction) [98]. However, this was closely followed by the combination of ARNi, beta blocker, and MRA, with or without vericiguat (59% reduction with vericiguat, 56% reduction without verciguat) [98]. It is therefore recommended that all patients with HFrEF be treated with ACEi or ARB or ARNI in the first line setting. The choice of drug must be made based on treatment tolerability, possible contraindications as well as treatment accessibility. Patients who cannot tolerate ACEi/ARB or who remain symptomatic despite optimal therapy should be switched to ARNI.

4.5.1.1. Beta blockers. Beta-blockers are a mainstay of HF treatment considering the reversal of the neurohumoral effects of the sympathetic nervous system associated with their use (with or without ACEi/ARB), in addition to their improvement of HF symptoms and prognosis [99–105]. Beta blockers were associated with mortality risk reduction compared to placebo or standard treatment in a meta-analysis of 21 clinical trials including 23,122 patients treated with beta-blockers (focusing on atenolol, bisoprolol, bucindolol, carvedilol, metoprolol, and nebivolol). all beta-blockers were comparable in terms of LVEF improvement, risk of death, sudden cardiac death, death due to pump failure, or drug discontinuation [106]. A more recent meta-analysis of 11 trials including 13,833 patients (aged 40–85 years, of whom 24% were women) confirmed that beta-blockers effectively reduce

Table 8. Recommendations for the pharmacological management of HFrEF.

Class	Recommendation
RAS inhibition (ACEi/ARB/ARNI)	
	an ACEi/ARB/ARNI (sacubitril/valsartan) is recommended for patients with HFrEF
	ARNI (sacubitril/valsartan) is recommended as a replacement for an ACEi (or ARB) to further reduce the risk of hospitalization and death in patients with HFrEF who remain symptomatic despite optimal treatment with an ACEi/ARB and a beta-blocker
Beta-blockers	
	a beta-blocker is recommended for patients with HFrEF in combination with ACEi/ARB or ARNI
Diuretics	
	diuretics are recommended to improve symptoms and exercise capacity in patients with signs and/or symptoms of congestion
	diuretics should be considered to reduce the risk of HF hospitalization in patients with signs and/or symptoms of congestion
MRA	
	An MRA is recommended for patients with HFrEF to reduce the risk of hospitalization and death
Ivabradine	
	Ivabradine should be considered in symptomatic LVEF ≤35% who are in sinus rhythm and resting heart rate >70pbm despite maximum tolerated therapy
hydralazine and isosorbide dinitrate	
	hydralazine and isosorbide dinitrate should be considered in symptomatic patients with HFrEF who cannot tolerate an ACEi or an ARB (or for whom they are contraindicated), to reduce the risk of death
	hydralazine and isosorbide dinitrate may be considered in symptomatic patients with HFrEF despite treatment with an ACEi, ARB, a beta-blocker and an MRA. To reduce the risk of HF hospitalization and death
SGLT2 inhibitors	
	dapagliglozin or empagliflozin are recommended for patients with HFrEF to reduce the risk of HF hospitalization and death
Soluble guanylate cyclase (sGC) stimulators	
	vericiguat may be considered in patients in NYHA class II-IV who have had worsening HF despite treatment with an ACEi (or ARNI), a beta-blocker and an MRA to reduce the risk of CV mortality or HF hospitalization
Other drugs	
	Digoxin may be considered in patients who are symptomatic despite treatment with an ACEi (or ARB), ARB, a beta-blocker and an MRA to reduce the risk of hospitalization. For therapeutic benefit, maintain low digoxin serum concentrations (0.5-0.9 ng/mL)
	Potassium binders (sodium zirconium cyclosilicate, patiromer) may be considered in patients who experience hyperkalemia while using a RAASi
	thiazolidinediones (glitazones) are not recommended in patients with HF because they increase the risk of HF worsening and HF hospitalization
	NSAIDS or COX-2 inhibitors are not recommended in patients with HF because they increase the risk of HF worsening and HF hospitalization
	The addition of an ARB (or renin inhibitor) to the combination of an ACEi and an MRA is not recommended because of increased risk of renal dysfunction and hyperkalemia
	in patients with chronic HFrEF without a specific indication (e.g. venous thromboembolism, AF, a previous thromboembolic event or a cardioembolic source), anticoagulation is not recommended
	In patients with HFrEF, dihydropyridine and non-dihydropyridine calcium channel-blocking drugs are not recommended treatment for HF
	In patients with HFrEF, vitamins, nutritional supplements, and hormonal therapy are not recommended other than to correct specific deficiencies
	In patients with HFrEF, class IC antiarrhythmic medications and dronedarone
	may increase the risk of mortality
	In patients with type 2 diabetes and high cardiovascular risk, the dipeptidyl peptidase-4 (DPP-4) inhibitors saxagliptin and alogliptin increase the risk of HF hospitalization and should be avoided in patients with HF

Table 9. Recommended target doses of disease-modifying agents and diuretics for HFRenin–angiotensin–aldosterone system inhibitors (ACEi, ARB, ARNI).

Disease-modifying agents	Target doses (mg)
ACE inhibitors	
Captopril	50 t/i.d.
Enalapril	20 b.i.d.
Lisinopril	20-40 o.d.
Ramipril	10 o.d.
Beta blockers	
Bisoprolol	10 o.d.
Carvedilol	25 b.i.d.
Metoprolol succinate	200 o.d.
Nebivolol	10 o.d.
ARBs	
Candesartan	32 o.d.
Valsartan	160 b.i.d.
Losartan	150 o.d.
MRA	
Eplerenone	50 o.d.
Spironolactone	50 o.d.
ARNI	
sacubitril/valsartan	97/103 b.i.d.
SGLT2i	
dapagliflozin	10 o.d.
empagliflozin	10 o.d.
I_f channel blocker	
Ivabradine	7.5 b.i.d
Carbonic anhydrase inhibitors	
Acetazolamide	3.5–4 mg/kg
Diuretic	**usual daily doses (mg)**
Loop diuretics	
Furosemide	40–240
Bumetanide	1–5
Torasemide	10–20
Thiazides	
Hydrochlorothiazide	12.5–100
Metolazone	2.5–10
Indapamide	2.5–5
Potassium-sparing diuretics + ACEi/ARB	
Spironolactone/eplerenone	50
Amiloride	5–10
Triamterene	100
Potassium-sparing diuretics - ACEi/ARB	
Spironolactone-eplerenone	100–200
Amiloride	10–20
Triamterene	200

ACEi: angiotensin-converting enzyme inhibitor; ARB: angiotensin II receptor blocker; HF: heart failure; b.i.d,: twice daily; mg: milligrams; o.d.: once daily; t.i.d.: thrice daily.

mortality across all ages [107]. Beta-blockers are therefore recommended for all patients with HFrEF, in combination with ACEi/ARB or ARNI.

4.5.1.2. SGLT2 inhibitors. The DAPA-HF trial demonstrated that dapagliflozin, an SGLT2 inhibitor, led to significant improvements (26%) in the composite endpoint of worsening HF (hospitalization or an urgent visit resulting in i.v. therapy for HF) or CV death compared to standard of care in patients with HFrEF despite optimal medical therapy. Reduction in all-cause mortality, HF symptoms and improvement in physical function as well as quality of life were also reported with dapagliflozin. The survival benefits of this SGLT2 inhibitor were not restricted to patients with diabetes and were observed to have an early onset [108,109]. The EMPEROR-Reduced trial conducted in a similar patient population also reported a similar reduction in the primary endpoint of CV death or HF hospitalization with the SGLT2 inhibitor empagliflozin. Empagliflozin was also associated with significant improvements in quality of life, and reduction in eGFR decline but no significant reduction of CV mortality [110,111]. This benefit was confirmed by several meta-analyses of RCTs, which reported that SGLT2 inhibitors lead to a reduction in the risk of both HF hospitalizations and cardiovascular mortality, in addition to symptomatic improved among patients irrespective of ejection fraction [112–114]. SGLT2 inhibitors are therefore recommended for all patients with HF along with standard therapy.

4.5.1.3. Mineralocorticoid receptor antagonists (MRAs). MRAs are recommended for the first-line management of all patients with HFrEF in addition to an ACEi/ARB or ARNI, beta blocker and SGLT2 inhibitor. Both selective and non-selective MRAs are associated with a reduction in mortality and morbidity in patients with HFrEF [115]. However, caution is advised with the use of MRAs in patients with impaired renal function and serum potassium concentrations >5.0 mmol/L seeing as MRAs have been known to cause hyperkalemia [116]. The risk of hyperkalemia increases along with the dose of MRA. To note that it is hypothesized that hyperkalemia would not modify the efficacy of these drugs [116]. Epleronone was reported to be efficacious and safe when carefully monitored in patients with chronic HFrEF, in NYHA functional Class II and an estimated glomerular filtration rate >30 mL/min/1.73 m2 and potassium <5.0 mmol/L [117].

4.5.1.4. Diuretics. See SHA 2019.

4.5.1.5. I_f-channel inhibitor ivabradine. Ivabradine was demonstrated to significantly reduce the risk of a composite primary endpoint (cardiovascular death or hospital admission for worsening HF) compared to placebo. Ivabradine led to a 21% reduction in

Table 10. Recommendations for the pharmacological management of HFmrEF.

Class	Recommendation
	Diuretics are recommended in patients with congestion and HFmrEF in order to alleviate symptoms and signs
	SGLT2 inhibitors are recommended in patients with HFmrEF to reduce the risk of hospitalization and death
	In patients with HFmrEF after treatment, GDMT should be continued to prevent relapse of HF and LV dysfunction, even in patients who may become asymptomatic
	an ACEi/ARB may be considered in patients with HFmrEF to reduce the risk of hospitalization and death
	a beta-blocker may be considered in patients with HFmrEF to reduce the risk of hospitalization and death
	an MRA may be considered in patients with HFmrEF to reduce the risk of hospitalization and death
	sacubitril/valsartan may be considered in patients with HFmrEF to reduce the risk of hospitalization and death

hospital admission for worsening HF and 5% reduction in deaths due to HF [118]. The INTENSIFY study confirmed the benefit of ivabradine in reducing resting heart rate, relieving signs of decompensation, reducing BNP levels and improving quality of life [119]. Ivabradine should therefore be considered in symptomatic LVEF ≤35% who are in sinus rhythm and resting heart rate >70pbm despite maximum tolerated therapy.

4.5.1.6. Hydralazine and isosorbide dinitrate. See SHA 2019 HF guidelines.

4.5.1.7. Digoxin. The effect of digoxin in patients with HF is conflicting, with no RCTs available on its use in this patient population. Digoxin may be considered in patients who are symptomatic despite treatment with an ACEi (or ARB), ARB, a beta-blocker and an MRA to reduce the risk of hospitalization [120,121]. Serum concentration of digoxin is strongly associated with its safety and efficacy. For therapeutic benefit, it is therefore necessary maintain low digoxin serum concentrations (0.5–0.9 ng/mL) [122]. Some evidence suggests that the use of digoxin might increase mortality (all-cause and cardiovascular) and sudden cardiac death in patients with HF, regardless of concomitant HF [123]. By contrast, a previous meta-analysis detected no deleterious effects of the use of digoxin on mortality in patients with concomitant AF and HF [124].

4.5.1.8. Vericiguat. The VICTORIA trial reported the efficacy and safety of the oral soluble guanylate cyclase stimulator, vericiguat, in patients with a

Table 11. Recommendations for the pharmacological management of HFpEF.

Class	Recommendation
	It is recommended to screen patients with HFpEF for both cardiovascular and non-cardiovascular comorbidities, which, if present, should be treated.
	Diuretics are recommended in congested patients with HFpEF to alleviate symptoms and signs
	SGLT2 inhibitors are recommended in patients with HFpEF to reduce the risk of hospitalization and death
	Treatment of AF should be considered in patients with HFpEF for symptom improvement
	ARNI may be considered in select patients with HFpEF to reduce the risk of hospitalization and death
	an MRA may be considered in select patients with HFpEF to reduce the risk of hospitalization and death
	ARB may be considered in select patients with HFpEF to reduce the risk of hospitalization and death
	beta blockers may be considered in select patients with HFpEF to reduce the risk of hospitalization and death
	In patients with HFpEF, routine use of nitrates or phosphodiesterase-5 inhibitors to increase activity or quality of life is not recommended.

Table 12. Recommendations for ICD implantation.

Class	Recommendation
Secondary prevention	
	an ICD implantation is recommended in patients who have recovered from VT/VF arrest, in the absence of a reversible cause
	an ICD implantation is recommended for secondary prevention in patients with a structurally abnormal heart and documented sustained VT (not within 48 hours after MI) in the absence of a reversible cause
Primary prevention	
	an ICD implantation is recommended to reduce the risk of sudden cardiac death in patients with symptomatic ischemic disease and an LVEF ≤35% despite ≥3 months of optimal medical therapy, provided they are expected to survive substantially longer than 1 year with good functional status
	an ICD implantation is recommended at least 40 days post-MI in patients with asymptomatic disease with LVEF≤30% despite ≥3 months of optimal medical therapy, provided they are expected to survive substantially longer than 1 year with good functional status
	An ICD implantation should be considered to reduce risk of sudden cardiac death in selected patients with symptomatic non-ischemic cardiomyopathy and an LVEF ≤35% despite ≥3 months of optimal medical therapy
	A wearable cardioverter-defibrillator may be considered for patients with HF who are at risk of sudden cardiac death for a limited period of as a bridge to a final device decision
	Primary prevention ICD implantation is not recommended within 40 days of an MI as implantation at this time does not improve prognosis
	ICD therapy is not recommended in patients with NYHA Class IV with severe symptoms refractory to pharmacological therapy unless they are candidates for CRT, a ventricular assist device or cardiac transplantation

reduced EF and recently decompensated chronic HF. Patients who received vericiguat has significantly lower incidence of the primary endpoint of death from CV causes or hospitalization for HF compared to placebo, albeit with no significant reduction in all-cause or cardiovascular mortality [125]. Vericiguat may be considered in patients in NYHA class II-IV who have had worsening HF despite treatment with an ACEi (or ARNI), a beta-blocker and an MRA to reduce the risk of CV mortality or HF hospitalization.

4.5.1.9. Potassium binders. The potassium binder sodium zirconium cyclosilicate (ZS-9) has a demonstrated efficacy for the management of hyperkalemia and maintenance of normokalemia [126]. Another Phase II trial supported the use of sodium zirconium cyclosilicate for the maintenance of normokalemia in HF patients specifically, without need for RAASi therapy adjustment [127]. Patiromer is another potassium binder with recently proven efficacy in the reduction of recurrent hyperkalemia in combination with MRAs when used in patients with HFrEF [128]. A meta-analysis showed that while both potassium binders are safe for the management of hyperkalemia, sodium zirconium silicate might have an advantage in the setting of acute hyperkalemia due to its more rapid reduction of serum potassium levels [129]. Potassium binders (sodium zirconium cyclosilicate, patiromer) may be considered in patients who experience hyperkalemia while using a RAASi.

4.5.2. HFmrEF

4.5.2.1. Therapeutic options. Diuretics are recommended for all patients with HFmrEF to alleviate symptoms and signs in case of congestion. The recently published results of the EMPEROR-Preserved and DELIVER-Preserved RCTs confirmed the efficacy of SGLT2 inhibitors in patients with mildly reduced and preserved ejection fraction (EF>40%) [130,131]. Both trials demonstrated that SGLT2-inhibitors reduce the combined risk of worsening heart failure or cardiovascular death, regardless of the presence of diabetes [130,131]. The benefit of SGLT2 inhibitors was also reported by several meta-analyses to be irrespective of EF [112–114]. SGLT2 inhibitors are therefore recommended for all patients with HFmrEF. A recent meta-analysis of studies on the management of HF with mildly reduced or preserved ejection fraction (EF>40%) confirmed that SGLT2 inhibitors are currently the optimal drug class for these patients

[132]. Overall evidence suggests a potential accumulative improvement in HF hospitalization rather than all-cause death with the combination of SGLT2 inhibitors with an ACEi/ARB/ARNI, an MRA or a beta blocker [132,133]. However, RAASi through ACEi, ARB or ARNI has not yet been specifically investigated among patients with HFmrEF in a RCT and current evidence for their use remains limited. the same applies to MRAs and beta blockers. As a result, these drugs may be considered in patients with HFmrEF to reduce the risk of hospitalization and death. It is important that guideline-directed medical therapy be continued in patients with HFmrEF after treatment to prevent relapse of HF and LV dysfunction, even in patients who may have become asymptomatic [14].

4.5.3. HFpEF

The diagnosis and treatment of HFpEF remains challenging despite its high prevalence among all HF cases. HFpEF is characterized by a heterogeneous population often with multiple comorbidities, as well as different race, age, and etiology. It is therefore recommended to screen HFpEF patients for cardiovascular and noncardiovascular comorbidities, which if present, should be treated. As with HFrEF and HFmrEF, diuretics are recommended for the relief of symptoms in congested patients. Currently, SGLT2-inhibitors is the only drug class with significant benefit in terms of mortality and HF worsening in HFpEF patients [112–114,130,131]. The DELIVER trial is the largest (6263 patients enrolled) and broadest global trial to date in patients with LVEF >40%. 190 patients were enrolled from Saudi Arabia [130]. The results of the DELIVER trial confirmed the reduction of the combined risk of worsening heart failure or cardiovascular death with the use of Dapagliflozin among patients with HFmrEF or HFpEF [130]. Moreover, a patient-level pooled meta-analysis of two RCTs investigating dapagliflozin and another of two RCTs investigating empagliflozin showed that the benefit of these SGLT2 inhibitors is preserved across the spectrum of LVEF [134,135]. SGLT2 inhibitors are therefore recommended for all patients with HFpEF.

Other therapeutic options may be considered, although none of the large RCTs conducted in HFpEF were able to meet their primary endpoints (PEP-CHF trial of perindopril [136], CHARM-Preserved trial of candesartan [137], I-PRESERVE trial of irbesartan [138], TOPCAT trial of spironolactone [139], DIG-Preserved trial of digoxin [140], and PARAGON-HF of sacubitril/valsartan [141]. However, available evidence suggests a potential benefit on the level of HF hospitalization with the combination of SGLT2 inhibitors with other drugs such as ACEi, ARBs, ARNI, MRA and β-blockers [132]. The improvement of mortality with the use of these drugs is less established among patients with HFpEF [132]. That being said, health-related quality of life is an important treatment target in patients with HFpEF that can be improved with these drugs. The management of HFpEF should be individualized rather than follow a one-size-fits-all approach. Based on this, ACEi, ARBs, ARNI, MRA and beta-blockers may be considered in select patients with HFpEF to reduce the risk of hospitalization and death. In patients with HFpEF, nitrates or phosphodiesterase-5 inhibitors did not prove beneficial for the increase of activity or quality of life levels in the NEAT-HFpEF and RELAX trials [142,143]. Their routine use in HFpEF is therefore not recommended.

4.5.4. Management of diuretic resistance

In case of insufficient diureticresponse/diuretic resistance, it is important to check patient adherence and fluid/salt intake. Diuretic dose should be increased as needed and switching from furosemide to bumetanide or torasemide should be considered. The addition of an MRA or the increase of an existing MRA's dose can also help resolve diuretic resistance. The combination of a loop diuretic and thiazide/metolazone could produce diuretic synergy via “sequential nephron blockade”, although this approach was not studied in randomized clinical trials. diuretic resistance might also be resolved by increasing the administration frequency of a loop diuretic to at least two times daily, or administering it on an empty stomach. If needed, short-term intravenous infusion of loop diuretic might be considered. Ultrafiltration could help resolve fluid overload and has been described for the management of diuretic resistance in HF.

4.5.5. Management of hyperkalemia

HF patients frequently experience electrolyte disturbances [144]. A U-shaped relationship with mortality is observed with serum potassium levels; both hypokalemia and hyperkalemia are associated with an increased risk of death and require adequate correction [116,145–149]. Loop and thiazide diuretic administration can often induce hypokalemia. Treatment options include RAAS inhibitors, potassium-sparing diuretics, and prescription of oral potassium supplements (i.e. potassium chloride tablets) or intravenous infusions of potassium-rich solutions.

Hyperkalemia can be caused by RAAS inhibitors, chronic kidney disease (CKD) and increased

absorption. The lowest risk of severe hyperkalemia was observed with sacubitril/valsartan in PARADIGM-HF, compared to enalapril [87]. Immediate treatment is recommended for life-threatening hyperkalemia; a combination of calcium carbonate and/or sodium bicarbonate, insulin, with or without glucose, and beta adrenoceptor agonists should be used to favor potassium entry into the cells without increasing potassium secretion. Once hyperkalemia is addressed, loop diuretics can be administered to ensure potassium levels return to normal values. Another option is potassium binders, which can be used for acute and chronic potassium lowering as discussed in section 4.5.1.

4.6. Non-surgical device management of HFrEF

4.6.1. ICD

ICDs are effective for the prevention of sudden cardiac death [150], leading to a 35% reduction of death primarily in NYHA class II patients [151]. This is important considering the high risk of arrythmia recurrence and death in survivors of cardiac arrest or symptomatic sustained ventricular tachycardia. The benefit of ICD was significantly more prominent in patients with LVEF $\leq$35% compared to patients with higher EF [152]. To note that the AVID study showed that 64% of patients experience recurrence of arrhythmia 3 years after ICD implantation [152]. ICD implantation significantly reduces overall mortality in patients with chronic HFrEF (LVEF$\leq$35%) [152,153], with decreasing benefit as comorbidity increases [150]. Increasing age could also reduce the benefit of ICD implantation, with the least benefit observed in patients older than 75 years [154]. This association could be related to a higher burden of comorbidities with increasing age, other causes of death or limited data. In a meta-analysis, it was demonstrated that an improvement of arrhythmic mortality and all-cause mortality can be achieved with ICD-only therapy in patients with ischemic or non-ischemic heart disease, with an LVEF $\leq$35%, 40 days from MI, and at least 3 months before Cardiac resynchronization therapy (CRT) [155]. The MADIT-II trial reported significant reductions in mortality with ICD implantation in patients with previous MI and LVEF <30%, 37% of whom had congestive heart failure [156]. ICDs are effective for the primary and secondary prevention of sudden cardiac death and their cost may be justified by their cost-effectiveness compared to conventional treatments [157]. In particular, ICD is cost-effective for all non-NYHA IV patients with QRS duration <120 ms and for NYHA I/II non- Left bundle branch block (LBBB) morphology patients with QRS duration between 120 ms and 149 ms [158].

4.6.2. CRT

CRT can reduce morbidity and mortality when used in appropriate clinical settings, and can lead to improvements in cardiac function as well as quality of life [159–161]. Five RCTs comparing CRT with no active device or CRT with a defibrillator were included in a meta-analysis which demonstrated that the effect of CRT on morbidity and mortality is significantly predicted by QRS duration; Survival benefit can be expected in QRS duration exceeding 140 ms [160]. The MADIT-CRT trial demonstrated a 41% reduction in the risk of HF events with CRT in patients with a QRS duration >150 ms [162]. Evidence suggests that CRT prevents the progression of disease in patients with asymptomatic or mildly symptomatic LV dysfunction [163]. The reduction of LV end-systolic volume index and LV mass after CRT was significant in patients with an LVEF>30% [164]. Significant mortality reductions (68%) were associated with LV end-systolic volume index following CRT [165]. Another maker of reverse modeling and clinical improvement with CRT in patients with mild HF was LBBB [165,166]. Patients with LBBB benefited from a lower risk of first and subsequent HF events after CRT. This persists on the long-term, where patients with mild HF symptoms, LV dysfunction, and LBBB were found to have long-term survival benefit from early intervention with a CRT-D [94]. Patients with LBBB with a history of intermittent atrial tachyarrhythmias or by development of in-trial atrial tachyarrhythmias also benefit from CRT-D [95]. Patients with non-LBBB morphology generally do not show the same survival benefit with CRT as that observed with LBBB morphology [167,168]. That being said, individual-patient data meta-analyses have shown that QRS morphology or etiology do not influence the survival and morbidity improvement with CRT after accounting for QRS duration [160,169]. Moreover, QRS morphology or ischemic etiology were not used for patient selection in any of the landmark trials. That being said, the long-term follow-up of the MADIT CRT study demonstrated the role of prolonged PR interval in predicting favorable response in patients with non-LBBB morphology [170].

Overall, evidence supports the long-term benefit of CRT concomitantly with medical therapy [171]. CRT with biventricular pacing can also be beneficial to reduce hospitalization in patients with NYHA Class III–IV symptoms, an EF <35%, and

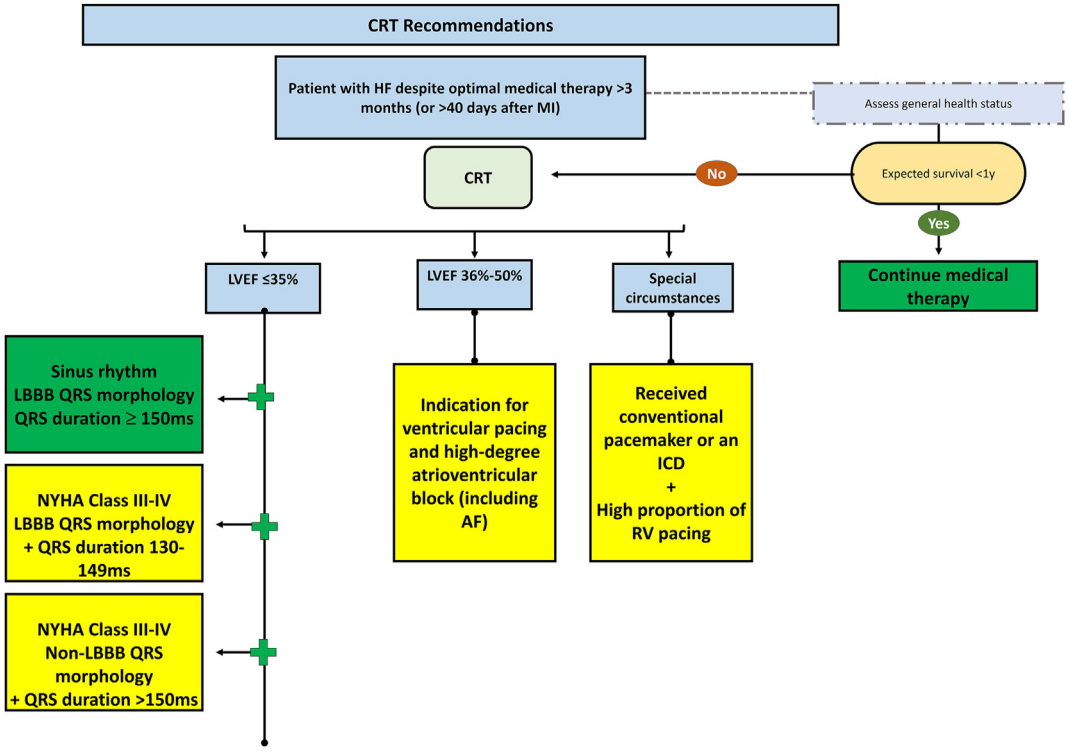

Fig. 3. Algorithm for CRT in HF patients.

intraventricular conduction delay of >120 ms [162]. In an analysis of 19 studies, patients with ischemic cardiomyopathy seemed to have better survival after CRT compared with non-ischemic cardiomyopathy [172]. An algorithm for the use of CRT in HF patients is provided in Fig. 3 (see Table 13).

4.7. Advanced HF

4.7.1. Definition

Clinical indicators of advanced HF based on the ESC 2018 and ACC 2022 guidelines are shown in Table 14. Patients with advanced HF can also be stratified based on the 7 profiles of the INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support) (Table 15). The INTERMACS classification is also useful for the prognostication in the setting of urgent heart transplantation [173], LV assist device (LVAD) implantation [174], and ambulatory advanced HF [175].

4.7.2. Management

4.7.2.1. General considerations. Patients who exhibit clinical indicators of advanced heart failure should be referred to specialty HF care in order to review

Table 13. Recommendations for CRT.

Class	Recommendation
	CRT is recommended for symptomatic patients with HF in sinus rhythm with a QRS duration ≥150ms and LBBB QRS morphology and with an LVEF ≤35% despite optimal medical therapy
	CRT rather than RV pacing is recommended for patients with an EF <50%, regardless of NYHA class, who have an indication for ventricular pacing and high-degree atrioventricular block. This includes patients with AF
	CRT should be considered in patients with LBBB QRS morphology and QRS duration 130-149ms, or non-LBBB QRS morphology and QRS duration ≥150ms, and LVEF ≤35% in NYHA Class III-IV despite optimal medical therapy if they are in AF.
	Patients with HFrEF who received a conventional pacemaker or an ICD and subsequently develop worsening HF despite optimal medical therapy, and who have a high proportion of RV pacing, should be considered for upgrade to CRT.

Table 14. Criteria of advanced HF.

Repeated hospitalizations or emergency department visits for HF in the past 12 mo.
Need for intravenous inotropic therapy.
Persistent NYHA functional class III to IV symptoms despite therapy.
Severely reduced exercise capacity (peak VO2, <12 mL/kg/min or <50% predicted, 6-min walk test distance <300 m, or inability to walk 1 block on level ground because of dyspnea or fatigue).
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 (according to the definitions of HFpEF).
Intolerance to RAASi because of hypotension or worsening renal function.
Intolerance to beta blockers as a result of worsening HF or hypotension.
Recent need to escalate diuretics to maintain volume status, often reaching daily furosemide equivalent dose >160 mg/d or use of supplemental metolazone therapy.
Refractory clinical congestion.
Progressive deterioration in renal or hepatic function.
Worsening right HF or secondary pulmonary hypertension.
Frequent SBP ≤90 mm Hg.
Cardiac cachexia.
Persistent hyponatremia (serum sodium, <134 mEq/L)
Refractory or recurrent ventricular arrhythmias; frequent ICD shocks.

HF indicates heart failure; ICD, implantable cardioverter-defibrillator; MAGGIC,Meta-analysis Global Group in Chronic Heart Failure; NYHA, New York.
Heart Association; RAASi, renin-angiotensin-aldosterone system inhibitors; SBP, systolic blood pressure; SHFM, Seattle Heart Failure model; and VO2, oxygen consumption/oxygen uptake.

current management and assess suitability for advanced HF therapies (e.g. LVAD, cardiac transplantation, palliative care and palliative inotropes). Timely referral has been associated with improved patient outcomes [176–178], and decisions related to advanced HF therapies should take into consideration clinical variables as well as patient values, goals and preferences (see Table 16).

Evidence regarding the benefit of fluid restriction for the symptomatic relief of acute decompensated HF remains uncertain. A registry study reported marginal improvement in hyponatremia with fluid restriction [179]. A pilot RCT also reported the benefit of fluid restriction in terms of quality of life among patients with HFrEF (NYHA class I to IV) [180]. That being said, fluid restriction might not have any influence on hospitalization or mortality as well as other clinical variables, as shown in a meta-analysis [181]. For patients with advanced HF and hyponatremia, fluid restriction may be considered to reduce congestive symptoms.

4.7.2.2. Inotropic support. Positive inotropic agents do not improve survival in HF patients but improve hemodynamic compromise [182]. Continuous intravenous inotropic support can help maintain systemic perfusion and preserve end-organ performance [183–185]. The use of inotropes should therefore be considered as a bridge to advanced therapies (heart transplantation or MCS) considering the possible reduction of pulmonary hypertension and maintenance of end-organ perfusion [186–189]. However, inotropes are associated with a risk of arrythmia and catheter-related infections when used palliatively. While this risk could be reduced with the presence of an ICD, patients should be counseled about these risks and the use of inotropes as palliative therapy should be carefully considered and monitored. It is currently not recommended to maintain long-term use of either continuous or intermittent intravenous inotropic agents unless needed due to the risks of currently available inotropic agents.

4.7.2.3. Mechanical circulatory support. Durable LVADs are associated with improved survival in patients with advanced HFrEF with NYHA class IV symptoms deemed dependent on continuous intravenous inotropes or temporary MCS [190,191]. The improvement in patient survival was higher when LVADs were used as bridge to transplant compared to destination therapy (>5 years vs > 4 years, respectively). In addition to their survival benefit, LVADs lead to functional and quality of life improvement [192,193]. Durable LVAD implantation is therefore recommended as bridge to transplantation and should be considered as destination therapy in select cases (advanced HFrEF with NYHA class IV symptoms dependent on continuous intravenous inotropes or temporary MCS).

Durable MCS should be considered in select cases (advanced HFrEF who have NYHA class IV symptoms despite optimal medical therapy) based on its association with improved survival, as well as symptomatic and functional improvement [194–198]. To note that poor clinical outcomes after MCS were reported in certain cases, such as elevated central venous pressure, pulmonary hypertension, coagulopathy, and INTERMACS profile of 1 [199–202].

Temporary MCS (including percutaneous and extracorporeal ventricular assist devices) should be

Table 15. INTERMACS profiles.

Profile[a]	Profile Description	Features
1	Critical cardiogenic shock	Life-threatening hypotension and rapidly escalating inotropic/pressor support, with critical organ hypoperfusion often confirmed by worsening acidosis and lactate levels.
2	Progressive decline	"Dependent" on inotropic support but nonetheless shows signs of continuing deterioration in nutrition, renal function, fluid retention, or other major status indicator. Can also apply to a patient with refractory volume overload, perhaps with evidence of impaired perfusion, in whom inotropic infusions cannot be maintained because of tachyarrhythmias, clinical ischemia, or other intolerance.
3	Stable but inotrope dependent	Clinically stable on mild-moderate doses of intravenous inotropes (or has a temporary circulatory support device) after repeated documentation of failure to wean without symptomatic hypotension, worsening symptoms, or progressive organ dysfunction (usually renal).
4	Resting symptoms on oral therapy at home	Patient who is at home on oral therapy but frequently has symptoms of congestion at rest or with activities of daily living (dressing or bathing). He or she may have orthopnea, shortness of breath during dressing or bathing, gastrointestinal symptoms (abdominal discomfort, nausea, poor appetite), disabling ascites, or severe lower extremity edema.
5	Exertion intolerant	Patient who is comfortable at rest but unable to engage in any activity, living predominantly within the house or housebound.
6	Exertion limited	Patient who is comfortable at rest without evidence of fluid overload but who is able to do some mild activity. Activities of daily living are comfortable, and minor activities outside the home such as visiting friends or going to a restaurant can be performed, but fatigue results within a few minutes or with any meaningful physical exertion.
7	Advanced NYHA class III	Patient who is clinically stable with a reasonable level of comfortable activity, despite a history of previous decompensation that is not recent. This patient is usually able to walk more than a block. Any decompensation requiring intravenous diuretics or hospitalization within the previous month should make this person a Patient Profile 6 or lower.

ICD indicates implantable cardioverter-defibrillator; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; and NYHA, New York Heart Association.

Adapted from Stevenson et al. [305] with permission from the International Society for Heart and Lung Transplantation.

[a] Modifier options: Profiles 3 to 6 can be modified for patients with recurrent decompensations leading to frequent (generally at least 2 in past 3 mo or 3 in past 6 mo) emergency department visits or hospitalizations for intravenous diuretics, ultrafiltration, or brief inotropic therapy. Profile 3 can be modified in this manner if the patient is usually at home. If a Profile 7 patient meets the modification of frequent hospitalizations, the patient should be moved to Profile 6 or worse. Other modifier options include arrhythmia, which should be used in the presence of recurrent ventricular tachyarrhythmias contributing to the overall clinical course (eg, frequent ICD shocks or requirement of external defibrillation, usually more than twice weekly); or temporary circulatory support for hospitalized patients Profiles 1 to 3.

considered as a "bridge to recovery" or "bridge to decision" in patients with advanced HFrEF and hemodynamic compromise and shock [192,203]. Temporary MCS is valuable for clinical stabilization of patients until decisions on durable MCS, heart transplantation or device removal can be made.

4.7.2.4. Cardiac transplantation. Observational studies have reported the improvement of patient survival from less than 2 years without advanced therapies to more than 12 years in adult heart transplant recipients [204,205]. Heart transplant patients also have better health-related quality of life compared to patients with advanced HF [206,207]. Cardiac transplantation is therefore recommended to improve survival and quality of life in select cases with advanced HF despite optimal medical therapy.

4.8. Cardiovascular comorbidities

4.8.1. Atrial fibrillation (see Table 17)

4.8.1.1. Anticoagulation. For the prevention of embolic events, an oral anticoagulant is recommended in all patients with concomitant HF and paroxysmal, persistent or permanent AF and CHA2DS2-VASc score $\geq$2 in men or $\geq$3 in women (unless contraindicated) [208]. In patients with concomitant HF and AF and lower CHA2DS2-VASc score ($\geq$1 in men or $\geq$ 2 in women), oral anticoagulation should be considered [208,209].

Table 16. Recommendations for the management of advanced HF.

Class	Recommendation
	Management by an advanced heart failure team is recommended for patients with advanced HF to review HF management and assess suitability for advanced HF therapies (e.g. LVAD, cardiac transplantation, palliative care and palliative inotropes).
	For patients with advanced HF and hyponatremia, fluid restriction may be considered to reduce congestive symptoms.
Inotropic support	
	Continuous intravenous inotropic support should be considered as a bridge therapy in patients with advanced (stage D) HF refractory to optimal medical therapy and device therapy who are eligible and schedule for advanced therapies (MCS or cardiac transplantation)
	Continuous or intermittent intravenous inotropic support may be considered as palliative therapy for symptomatic relief and functional improvement in select patients with stage D HF despite optimal medical and device therapy who are not eligible for advanced therapies (MCS or cardiac transplantation)
	Long-term use of either continuous or intermittent intravenous inotropic agents is not recommended except as described above (palliative care or bridge to advanced therapies) due to potential harm.
Mechanical circulatory support	
	Durable LVAD implantation is recommended as bridge to transplantation in select cases (advanced HFrEF with NYHA class IV symptoms dependent on continuous intravenous inotropes or temporary MCS).
	Durable LVAD implantation should be considered as destination therapy in select cases (advanced HFrEF with NYHA class IV symptoms dependent on continuous intravenous inotropes or temporary MCS).
	Durable MCS should be considered for symptomatic and functional improvement as well as mortality reduction in select cases (advanced HFrEF who have NYHA class IV symptoms despite optimal medical therapy).
	Temporary MCS (including percutaneous and extracorporeal ventricular assist devices) should be considered as a “bridge to recovery” or “bridge to decision” in patients with advanced HFrEF and hemodynamic compromise and shock.
Cardiac transplantation	
	Cardiac transplantation is recommended to improve survival and quality of life in select cases with advanced HF despite optimal medical therapy

Registry data revealed increased risk of ischemic stroke, thromboembolism, and death with high CHA2DS2-VASc scores. Direct oral anticoagulants (DOACs) are recommended in preference to vitamin K antagonists (VKAs) in patients with HF seeing as they have similar efficacy but a lower risk of intracranial hemorrhage. A meta-analysis of four RCTs [RELY (dabigatran), ROCKET-AF (rivaroxaban), ARISTOTLE (apixaban), and ENGAGE-TM (edoxaban)] with a total of 19,122 AF patients with HF showed that DOACS are associated with a significantly lower risk of stroke/systemic embolic events and major bleeding compared to VKAs [210]. To note that DOACS are not recommended in preference to VKAs in patients with moderate or severe mitral stenosis or mechanical prosthetic heart valves [210,211]. Oral anticoagulation therapy for the prevention of embolic events is a lifelong treatment. Dosage adjustment should be made according to the recommendation of each drug and relevant anticoagulation guidelines.

4.8.1.2. AF catheter ablation. Catheter ablation was demonstrated to be superior to antiarrhythmic drug therapy in the maintenance of sinus rhythm in drug naïve, resistant, and intolerant patients with AF [212]. Moreover, another meta-analysis including more than 21 thousand patients reported an increased risk of adverse events and in some cases, mortality, with the use of antiarrhythmic drugs. The latter were moderately effective in maintaining sinus rhythm after conversion of AF [213].

A detailed discussion is provided in the SHA 2019 HF guidelines on:

- Rate control and Cardioversion
- The initial management of HF and AF in the acute or chronic setting

Table 17. Recommendations for the management of HF with concomitant atrial fibrillation.

Class	Recommendation
Anticoagulation	
	Oral anticoagulant is recommended to prevent thromboembolism in all patients with concomitant HF and AF and CHA2DS2-VASc score ≥ 2 in men or ≥ 3 in women
	DOACs are recommended in preference to VKAs in patients with HF unless contraindicated
	in patients with AF≥48h duration, or when the duration of AF is unknown, an oral anticoagulant is recommended at a therapeutic dose for ≥3 weeks prior to electrical or pharmacological cardioversion
	intravenous heparin or LMWH and TOE-guided strategy is recommended for patients who have not been treated with an anticoagulant dose for ≥3weeks and require urgent electrical or pharmacological cardioversion for a life-threatening arrhythmia
	Oral anticoagulant should be considered to prevent thromboembolism in all patients with concomitant HF and AF and CHA2DS2-VASc score ≥ 1 in men or ≥ 2 in women
	DOACS are not recommended in preference to VKAs in patients with moderate or severe mitral stenosis or mechanical prosthetic heart valves
Rate control	
	for patients in NYHA Class I-III, a beta-blocker, usually given orally, is safe and therefore recommended as first-line treatment to control ventricular rate, provided the patient is euvolemic
	Treatment with a beta-blocker, MRA, and sacubitril/valsartan reduces the risk of sudden death and is recommended for patients with HFrEF and ventricular arrhythmias
	for patients in NYHA Class I-III, digoxin should be considered when ventricular rate remains high despite beta-blockers or when beta-blockers are not tolerated or contraindicated
	for patients with rapid AF in NYHA class IV, in addition to treatment for AHF, an intravenous bolus of amiodarone or in digoxin-naïve patients, an intravenous bolus of digoxin should be considered to reduce the ventricular rate
	treatment with dronedarone to improve ventricular rate control is not recommended due to safety concerns
Rhythm control management in patients with AF, symptomatic HF, LV systolic dysfunction and no evidence of acute decompensation	
	amiodarone may be considered prior to and following successful electrical cardioversion to maintain sinus rhythm
	dronedarone is not recommended because of an increased risk of hospital admissions for cardiovascular causes and an increased risk of premature death in NYHA Class III-IV patients
	class I antiarrhythmic agents are not recommended because of an increased risk of sudden death
ventricular tachycardia (VT)	
	implantation of an ICD or CRT-D device is recommended for selected patients with HFrEF
	potential aggravating/precipitating factors (e.g. low serum potassium/magnesium, ongoing ischemia) should be sought and corrected in patients with ventricular arrhythmias
	several strategies should be considered to reduce recurrent symptomatic arrhythmias in patients with an ICD (or in those who are not eligible for an ICD), including attention to risk factors and optimal pharmacological treatment of HF, amiodarone, catheter ablation and CRT
	routine use of antiarrhythmic agents (except beta-blockers) is not recommended in patients with HF and asymptomatic non-ventricular arrhythmias because of safety concerns (worsening HF, proarrhythmia, and death)

(continued on next page)

Table 17 (continued)

Bradyarrhythmias	
	in patients with HFrEF who require patient and who have high-degree AV block, CRT rather than RV pacing is recommended
	in patients with HFrEF who require patient and who do not have high-degree AV block, pacing modes that avoid inducing or exacerbating ventricular dyssynchrony should be considered
	when pauses >3 seconds are identified on the ECG, or if the bradycardia is symptomatic and the resting ventricular rate is <50bpm in sinus rhythm or <60bpm in AF, it should be considered whether there is need for any rate-limiting medications prescribed ; for patients in sinus rhythm, beta-blockers should be reduced in dose or withdrawn only as a last resort
	for patients with symptomatic, prolonged or frequent pauses despite adjustment of rate-limiting medication, either beta-blocker withdrawal or pacing may be considered as the next step
	pacing solely to permit initiation or titration of beta-blocker therapy in the absence of a conventional pacing indication is not recommended
Cardioversion	
	urgent electrical cardioversion is recommended if AF is thought to be contributing to the patient's hemodynamic compromise to improve the patient's clinical condition
	electrical cardioversion or pharmacological cardioversion may be considered in patients with persisting symptoms and/or signs of HF despite OMT and adequate control of ventricular rate, to improve clinical/symptomatic status
AF catheter ablation	
	Catheter ablation should be considered for patients with worsening HF symptoms clearly due to paroxysmal or persistent AF despite medical therapy

- Rhythm control management in patients with AF, symptomatic HF, LV systolic dysfunction and no evidence of acute decompensation
- VT
- Bradyarrhythmias

Please refer to the appropriate sections for more information.

4.8.2. CCS

For the diagnosis and management of chronic coronary syndrome (CCS), please refer to the SHA 2022 guidelines on best practices in the management of CCS [65].

4.8.2.1. Medical therapy (see Table 18). A beta-blocker (in an evidence-based dose or maximum tolerated) is recommended as the preferred first-line treatment to relieve angina because of the associated benefits of this treatment (reducing the risk of HF hospitalization and the risk of premature death) [101–104,214,215]. While there is evidence that ivabradine can be considered as an alternative to beta-blockers when they are contraindicated or addition anti-angina therapy is needed, ivabradine was excluded from recommendations for patients with HF and CCS in Saudi Arabia seeing as its indication by the Saudi Food and Drug Administration (SFDA) is restricted to HF and does not include angina. Other drugs (1: trimetazidine or ranolazine; 2: nicorandil or a short-acting/long-acting oral/transcutaneous nitrates; 3: felopidine or amlopidine) may be considered in patients with HR < 70 bpm and/or atrial fibrillation and persistence of CCS symptoms despite beta-blockers [100,216].

To note that ranolazine is not widely used in Saudi Arabia. The following are not recommended:

Ivabradine for stable CAD and patients who had acute coronary syndrome 0 for the last 2 months; Combination of any of ivabradine, ranolazine, and nicorandil because of unknown safety; Combination of nicorandil and a nitrate (because of lack of additional efficacy); Dilitazem and verapamil because of their negative inotropic action and risk of worsening HF.

4.8.2.2. Myocardial revascularization. Evidence on myocardial revascularization in patients with HF remains limited. The STITCH trial failed to show a significant difference between Coronary artery bypass graft surgery (CABG) and medical therapy on the level of all-cause death in its initial analysis in patients with CAD and reduced LV function [217]. A

Table 18. Recommendations for the management of HF with concomitant CCS.

Class	Recommendation
Angina relief	
	a beta-blocker (in an evidence-based dose or maximum tolerated) is recommended as the preferred first-line treatment to relieve angina because of the associated benefits of this treatment (reducing the risk of HF hospitalization and the risk of premature death)
	trimetazidine or ranolazine may be considered in patients with HR<70bpm and/or atrial fibrillation and persistence of CCS symptoms despite beta-blockers
	nicorandil or a short-acting or long-acting oral or transcutaneous nitrates may be considered may be considered in patients with HR<70bpm and/or atrial fibrillation and persistence of CCS symptoms despite beta-blockers
	felopidine or amlopidine may be considered in patients with HR<70bpm and/or atrial fibrillation and persistence of CCS symptoms despite beta-blockers
Coronary revascularization	
	CABG should be considered as the first-choice revascularization strategy if patients are suitable for surgery.
	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 anti-anginal drugs.
	Whenever possible, CABG should be avoided in LVAD candidates requiring coronary revascularization.
	Coronary revascularization may be considered to improve outcomes in patients with HFrEF, CCS, and coronary anatomy suitable for revascularization
	PCI may be considered as an alternative to CABG, based on Heart Team evaluation, considering coronary anatomy, comorbidities, and surgical risk.
	The following are not recommended: - Ivabradine for stable CAD and patients who had ACS for the last 2 months - Combination of any of ivabradine, ranolazine, and nicorandil because of unknown safety - Combination of nicorandil and a nitrate (because of lack of additional efficacy)
	Dilitazem and verapamil are not recommended because of their negative inotropic action and risk of worsening HF

survival advantage as well as a reduction in the combined endpoint of all-cause death or hospitalization for CV causes became clear in the CABG group in the extended 10-year follow-up of the trial [218]. The HEART trial also failed to demonstrate significant differences between CABG and medical therapy, although the trial was underpowered due to low patient enrollment [219]. Little to no RCTs are currently available on Percutaneous coronary intervention (PCI) vs medical therapy or vs CABG in HF. The recently published results of the REVIVED-BCIS2 trial showed that PCI did not lead to lower all-cause mortality or hospitalization for HF in patients with severe ischemic left ventricular systolic dysfunction compared to medical therapy [220]. Meta-analyses of available non-randomized data confirmed better outcomes with CABG compared with PCI and/or medical therapy on the level of mortality, MI and repeat revascularization [221,222].

4.8.3. Valvular heart disease (see Table 19)

4.8.3.1. Aortic stenosis. The selection of an appropriate treatment depends on the accurate assessment of aortic stenosis grade [223]. Aortic valve area can be evaluated using dobutamine stress echocardiography, which can also be used to differentiate between fix severe aortic stenosis and pseudo-severe aortic stenosis [223]. In symptomatic patients with reduced LVEF and "low-flow, low-gradient" aortic stenosis (Valve area <1 cm^2, LVEF <40%, mean pressure gradient <40 mmHg), low-dose dobutamine stress echocardiography should be considered to identify those with severe aortic

Table 19. Recommendations for the management of HF with concomitant valvular heart disease.

Class	Recommendation
Aortic stenosis	
	For patients with HF and severe high gradient aortic stenosis reintervention (TAVI or SAVR) is recommended to reduce mortality and improve symptoms.
	In symptomatic patients with reduced LVEF and "low-flow, low-gradient" aortic stenosis (Valve area <1 cm^2, LVEF <40%, mean pressure gradient <40 mmHg), low-dose dobutamine stress echocardiography should be considered to identify those with severe aortic stenosis suitable for valve replacement
Secondary mitral regurgitation	
	evidence-based medical and device therapy in patients with HFrEF is recommended to reduce functional mitral regurgitation
	Percutaneous edge-to-edge mitral valve repair should be considered in carefully selected patients with secondary mitral regurgitation, for whom coronary revascularization is not needed and who are at high risk for surgery and exhibit symptoms despite optimal medical therapy and who would benefit from a reduction of HF hospitalizations after the procedure
	Combined surgery of secondary mitral regurgitation and CABG should be considered in symptomatic patients with LV systolic dysfunction.
	Percutaneous edge-to-edge mitral valve repair may be considered for symptom improvement in medically exhausted patients with secondary mitral regurgitation
	isolated surgery of the non-ischemic regurgitant mitral valve in patients with severe functional mitral regurgitation and severe LV systolic dysfunction (LVEF<30%) may be considered in selected cases to avoid or postpone transplantation
indications for surgical management	
	in severe primary MR, surgery is indicated in symptomatic patients with an LVEF >30% and an LVESD <55 mm
	in chronic secondary mitral regurgitation, mitral valve surgery is indicated in patients with severe MR undergoing CABG, and an LVEF>30%
	tricuspid valve surgery is indicated in patients with severe TS undergoing left-sided valve intervention (percutaneous balloon valvuloplasty can be attempted if PMC can be performed on the mitral valve)
	tricuspid valve surgery is indicated in patients with severe primary or secondary TR undergoing left-sided valve surgery
	tricuspid valve surgery should be considered in patients with mild or moderate secondary TR with a dilated annulus (≥ 40 mm or > 21 mm/m^2), undergoing left-sided valve surgery
	tricuspid valve surgery should be considered in symptomatic or mildly symptomatic patients with severe isolated primary TR and progressive right ventricular dilatation or deterioration of their right ventricular function

stenosis suitable for valve replacement. This is necessary considering the implication of HF on operative mortality and long-term survival in patients undergoing aortic valve replacement [224]. For patients with HF and severe high gradient aortic stenosis, medical therapy cannot improve outcomes and aortic valve reintervention (TAVI or SAVR) is recommended to reduce mortality and improve symptoms [225]. The choice between TAVI and SAVR should be made by the Heart Team (including a HF specialist).

4.8.3.2. Secondary mitral regurgitation. The MITRA-FR and COAPT trials both investigated Percutaneous edge-to-edge mitral valve repair with or without optimal medical therapy in symptomatic patients with reduced LVEF and moderate-to-severe or severe secondary mitral regurgitation. The MITRA-FR trial could not demonstrate any benefit from percutaneous edge-to-edge mitral valve repair at the 12 month follow-up on the level of all-cause mortality or HF hospitalization [226]. By contrast, the COAPT trial reported a significant mortality reduction as well as less HF hospitalizations at 24 months with percutaneous edge-to-edge mitral valve repair compared to optimal medical therapy alone [227]. Percutaneous edge-to-edge mitral valve repair should be considered in carefully selected

patients with moderate to severe secondary mitral regurgitation, for whom coronary revascularization is not needed and who are at high risk for surgery and exhibit symptoms despite optimal medical therapy and who would benefit from a reduction of HF hospitalizations after the procedure [227]. Patients should be selected based on the inclusion criteria of the COAPT study (i.e. LVEF 20–50%, LV end-systolic diameter <70 mm, systolic pulmonary pressure <70 mmHg, absence of moderate or severe RV dysfunction, absence of severe TR, absence of hemodynamic instability) [228,229]. Combined surgery of secondary mitral regurgitation and CABG should be considered in symptomatic patients with LV systolic dysfunction. The addition of mitral valve repair to CABG was not found to improve LV reverse remodeling at 1 year in patients with moderate regurgitation [230]. After 2 years of follow-up, indices of left ventricular reverse modeling remained comparable albeit with significantly higher incidence of moderate or greater recurrent MR after mitral valve repair compared with valve replacement [231]. Percutaneous edge-to-edge mitral valve repair may be considered for symptom improvement in medically exhausted patients with secondary mitral regurgitation [232].

An algorithm for the management of secondary mitral regurgitation is provided in Fig. 4. It is important to keep in mind that the optimal medical therapy can ensure improvement of secondary mitral regurgitation and preclude the need for intervention [233–235]. The optimal duration of therapy to decrease mitral regurgitation is no less than 3–6 months. Patients who are not responding to guideline-directed medical therapy after this timeframe should be considered for surgical interventions (percutaneous edge-to-edge mitral valve repair or combined surgery of secondary mitral regurgitation and CABG), as deemed appropriate by the Heart Team. Medical therapy should be judged as optimized by a multidisciplinary team before any surgical decisions are made. Through this, the clinician can ensure that the patient is well medicated before opting for surgery, particularly considering the access and cost issues associated with these procedures.

4.9. Other comorbidities (see Table 20)

4.9.1. Diabetes

SGLT2 inhibitors improve clinical outcomes in patients with established cardiovascular disease or 'cardiovascular risk factors, as shown in several clinical trials (EMPA-REG OUTCOME, VERTIS-CV trials, CANVAS, DECLARE-TIMI 58, SCORED trial [66–70]). Meta-analyses of RCTs confirm that

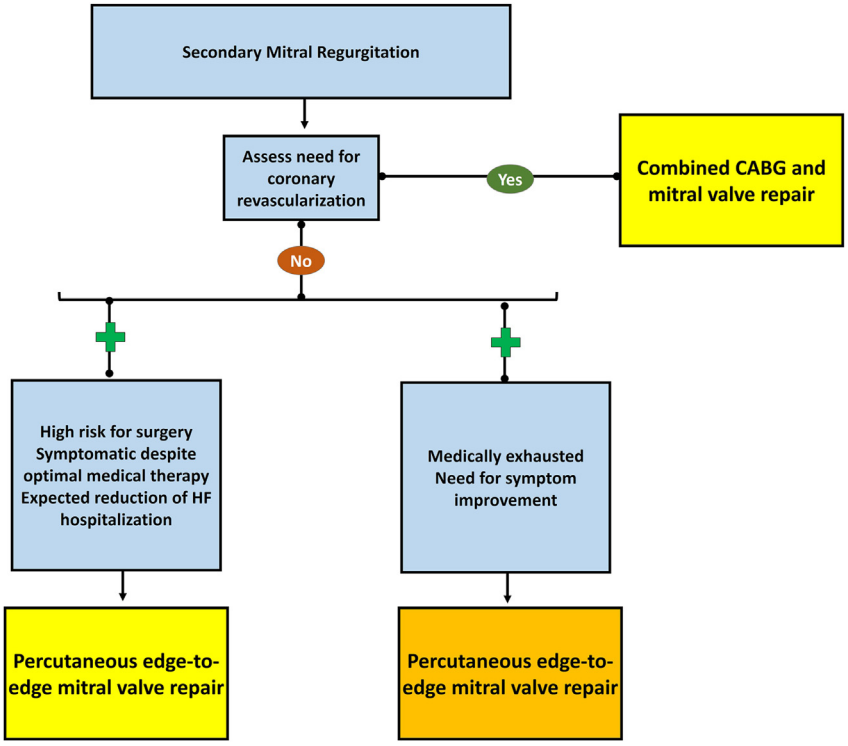

Fig. 4. Management of secondary mitral regurgitation.

Table 20. Recommendations for the management of non-cardiovascular comorbidities in HF patients.

Class	Recommendation
Diabetes	
	SGLT2 inhibitors are recommended in all patients with type-2 diabetes mellitus and HF
	Metformin should be considered as a first-line treatment of glycemic control in patients with diabetes and HF, unless contraindicated
Anemia	
	Intravenous supplementation with ferric carboxymaltose should be considered in symptomatic patients with EF <50% and iron deficiency (serum ferritin <100ug/L or ferritin between 100 ug/L and 299 ug/L and transferrin saturation <20%, regardless of hemoglobin levels) to alleviate HF symptoms and improve exercise capacity and quality of life.
	FCM should be administered via drip infusion (up to a maximum single dose of 1000 mg of iron, but not exceeding 15 mg/kg or the calculated cumulative dose) or bolus injection (at a maximum single dose of up to 200 mg of iron up to three times per week)
cancer/cardiotoxic treatment	
	Risk stratification is recommended in patients with cancer scheduled to receive potentially cardiotoxic therapy to assess the likelihood and degree of potential CV toxicity. Such patients should receive medical care aimed at promoting a healthy lifestyle and strict control and management of cardiovascular risk factors according to the current guidelines.
	Cardiology referral (preferably to a cardio-oncology program or cardiologist with expertise in managing CVD in patients with cancer) and multidisciplinary discussion are recommended before anticancer therapy in high-risk and very high-risk patients and in patients with pre-existing CVD or abnormal findings at baseline CV toxicity risk assessment. Such referral and discussion are also recommended in patients who develop CV toxicity.
	Clinical assessment and ECG are recommended at baseline in all patients with cancer and echocardiography, cardiac biomarkers, or other cardiac imaging tests in selected patients according to baseline CV toxicity risk and cancer treatment type
	Baseline comprehensive echocardiography (including 3D LVEF and GLS, if available) is recommended in all patients with cancer at high risk and very high risk of CV toxicity before starting anticancer therapy and periodically during treatment for early detection of cardiac dysfunction.
	ACEI or ARB, beta-blockers and statins should be considered for primary prevention in high- and very high-risk patients receiving cancer therapies that may cause HF
	The severity of cancer therapy-related cardiac dysfunction (CTRCD) should be assessed using the combination of new CV symptoms and the change in LVEF, GLS and/or cardiac biomarkers (see the ESC definition/classification)
	Guideline-directed HF therapy is recommended in patients who develop symptomatic CTRCD or asymptomatic moderate to severe CTRCD during anthracycline chemotherapy or HER2-targeted treatment. *** (Asymptomatic severe CTRCD: LVEF < 40%; asymptomatic moderate CTRCD: LVEF 40–49%; asymptomatic mild CTRCD: LVEF > 50%) (see the ESC definition/classification)
	ACE-I/ARB and/or beta-blockers should be considered in asymptomatic mild CTRCD (patients who have LVEF ≥ 50% and have developed a significant fall in GLS and/or elevation in troponin and/or NP) during anthracycline chemotherapy or HER2-targeted treatment.

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Table 20 (continued)

Amyloidosis	
	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.
	Tafamidis is recommended in patients with wtTTR-CA and NYHA class I or II symptoms to reduce symptoms, CV hospitalization and mortality.
Hypertension	
	ACEi (or ARB), a beta-blocker, or an MRA is recommended to reduce blood pressure
	A thiazide diuretic (or if the patient is being treated with a thiazide diuretic, switching to a loop diuretic) is recommended to reduce blood pressure when hypertension persists despite treatment with a combination of an ACEi (or alternatively ARB but NOT together with an ACEi), a beta-blocker, and an MRA
	Amlodipine or hydralazine is recommended to reduce blood pressure when hypertension persists despite treatment with a combination of an ACE-I (or altematively an ARB, but not with ACE-I and ARB combined), a beta-blocker, an MRA and a diuretic
	Alpha-adrenoceptor antagonists are not recommended due to lack of effect on survival
	Diltiazem and verapamil are not recommended to reduce blood pressure in patients with HFrEF because their negative inotropic action and risk of worsening HF
Pregnancy	
Counseling and risk assessment	
	It is recommended that pre-pregnancy counseling on contraception and the risks of cardiovascular deterioration during pregnancy be offered to patients with a history of HF or cardiomyopathy (including peripartum cardiomyopathy)
	Patients should be counseled to avoid pregnancy if they have severe heart disease (ejection fraction less than 30% or class III/IV heart failure, severe valvular stenosis, Marfan syndrome with aortic diameter more than 45 mm, bicuspid aortic valve with aortic diameter more than 50 mm, or pulmonary arterial hypertension
	pregnancy termination may be considered after agreement by a multi-disciplinary heart team for patients with severe heart disease (ejection fraction less than 30% or class III/IV heart failure, severe valvular stenosis, Marfan syndrome with aortic diameter more than 45 mm, bicuspid aortic valve with aortic diameter more than 50 mm, or pulmonary arterial hypertension
Management during pregnancy	
	Close maternal and fetal monitoring is recommended for HF signs or symptoms or other cardiovascular instability by cardiology and obstetric and maternal-fetal medicine teams.
	Screening for any significant changes in HF symptoms or signs during pregnancy is recommended, particularly in the third trimester and if HF medication is changed.
	hemodynamic monitoring and MCS are recommended as deemed appropriate by a multidisciplinary heart team for patients presenting with decompensatied HF or cardiogenic shock
	Monitoring-based adjustment of HF treatment is recommended as appropriate to avoid hypotension and placental hypoperfusion.
	beta-blockers should be continued in pregnancy and switched to beta-1-selective blockers (bisoprolol, metoprolol succinate).
	Adjustment of diuretic dosing should be considered to minimize the risk of placental hypoperfusion
	Hydralazine, oral nitrates and methyldopa may be considered if required.
	ACE-Is, ARBs, ARNI, MRAs, ivabradine, vericiguat and SGLT2 inhibitors are contraindicated due to risk of fetal harm and should be stopped prior to conception

(*continued on next page*)

Table 20 (*continued*)

	Peripartum cardiomyopathy
	It is recommended that patients with peripartum cardiomyopathy with severe HF and cardiogenic shock requiring inotropic or vasopressor support be transferred to an advanced HF centre, where necessary interventions can be performed as needed (extracorporeal membrane oxygenation, LVAD and/or
	cardiac transplantation). Urgent delivery by caesarean section should be considered with MCS immediately available.
	For refractory cardiogenic shock cases, LVAD implantation as a BTT or BTR should be considered.
	levosimendan or MCS may be considered for hemodynamically unstable patients with peripartum cardiomyopathy
	Bromocriptine may be considered for treatment of peripartum cardiomyopathy
	Anticoagulation
	anticoagulation with low-molecular-weight heparin (LMWH) is recommended during the first and last trimesters, and with VKAs for the second trimester, for patients with HF and AF. DOACs should be avoided
	Contraception
	It is recommended that the most appropriate contraceptive option be determined based on patient preference and critical assessment of disease and the relative risks and benefits of the contraceptive option considered.
	Intrauterine devices are the recommended nonpermanent contraceptive option for women with high-risk cardiovascular conditions.
Sleep apnea	
	Adaptive seroventilation is not recommended in patients with HFrEF and predominant central sleep apnea because of an increased all-cause and cardiovascular mortality
	In patients with HF and suspicion of sleep-disordered breathing, a formal sleep assessment may be considered to confirm the diagnosis and differentiate between obstructive and central sleep apnea
	Treatment of sleep apnea and obesity hypoventilation syndrome is recommended with non-invasive ventilation as per guidance of sleep experts
	Continuous positive airway pressure may be considered to increase LVEF and improve functional status in patients with HF and sleep apnea
Depression	
	Selective serotonin reuptake inhibitors may be considered as treatment for depression, unless contraindicated
Vaccination	
	Immunization against influenza and pneumococcal disease should be considered

SGLT2 inhibitors lead to a reduction in the risk of both HF hospitalizations and cardiovascular mortality, in addition to symptomatic improvement among patients irrespective of ejection fraction [112–114]. the EMPEROR-Preserved and DELIVER-Preserved RCTs recently confirmed that SGLT2 inhibitors are effective in patients with mildly reduced and preserved ejection fraction (EF>40%), regardless of the presence of diabetes [130,131]. SGLT2 inhibitors are therefore recommended for all patients with HF along with standard therapy.

A review of observational data from 34,000 patients showed a reduction in mortality with the use of metformin in patients with concomitant HF and diabetes [236]. Metformin was also shown to have comparable safety to other glucose-lowering treatments [236]. However, metformin is contraindicated in patients with severe renal or hepatic impairment because of the risk of lactic acidosis [237].

4.9.2. Cancer/cardiotoxic

Risk stratification is recommended in patients with cancer scheduled to receive potentially cardiotoxic therapy to assess the likelihood and degree of potential CV toxicity [238–241]. Such patients should receive medical care aimed at promoting a healthy lifestyle and strict control and management of cardiovascular risk factors according to the current guidelines. Cardiology referral (preferably to a cardio-oncology program or cardiologist with

expertise in managing CVD in patients with cancer) and multidisciplinary discussion are recommended before anticancer therapy in high-risk and very high-risk patients and in patients with pre-existing CVD or abnormal findings at baseline CV toxicity risk assessment. Such referral and discussion are also recommended in patients who develop CV toxicity.

Clinical assessment and ECG are recommended at baseline in all patients with cancer. In addition to this, echocardiography, cardiac biomarkers, or other cardiac imaging tests are also recommended in selected patients according to baseline CV toxicity risk and cancer treatment type [242,243]; cancer therapy-related cardiac dysfunction can be monitored with cardiac biomarkers such as cardiac troponin and natriuretic peptides. Echocardiography remains the preferred modality for the assessment of baseline cardiac function in cancer patients [238].

Baseline comprehensive echocardiography (including 3D LVEF and Global Longitudinal Strain (GLS), if available) is recommended in all patients with cancer at high risk and very high risk of CV toxicity before starting anticancer therapy and periodically during treatment for early detection of cardiac dysfunction [244−254].

ACEI or ARB, beta-blockers and statins should be considered for primary prevention in high- and very high-risk patients receiving cancer therapies that may cause HF. This is based on the significant prevention of LVEF reduction in patients with cancer treated with anthracycline chemotherapy and HER2-targeted therapies with the use of renin−angiotensin−aldosterone system blockers, beta-blockers, and mineralocorticoid receptor antagonists [255−260]. The severity of cancer therapy-related cardiac dysfunction (CTRCD) should be assessed using the combination of new CV symptoms and the change in LVEF, GLS and/or cardiac biomarkers (see the 2022 ESC cardio-oncology guidelines definition/classification) [238]. Guideline-directed HF therapy is recommended in patients who develop symptomatic CTRCD or asymptomatic moderate to severe CTRCD during anthracycline chemotherapy or HER2-targeted treatment (see the 2022 ESC cardio-oncology guidelines definition/classification) [238]. Cardioprotective therapy with ACE-I/ARB and/or beta-blockers should be considered in asymptomatic mild CTRCD (patients who have LVEF $\geq$50% and have developed a significant fall in GLS and/or elevation in troponin and/or NP) during anthracycline chemotherapy or HER2-targeted treatment [261−263].

4.9.3. Amyloidosis

Clinical suspicion of cardiac amyloidosis should be confirmed. Serum free light chains concentration and urine immunofixation electrophoresis are used to rule out amyloid cardiomyopathy [264−268]. Bone scintigraphy can confirm the presence of transthyretin cardiac amyloidosis, but only in case of negative screening for free light chains [269]. Genetic testing should then be done for the differentiation of hereditary and wild-type variants in patients diagnosed with transthyretin cardiac amyloidosis [270].

Light chain immunoglobulin cardiac amyloidosis should be treated by addressing underlying hematological etiologies either with chemotherapy or autologous stem-cell transplant.

Table 21. Recommendations on the diagnosis of AHF.

Class	Recommendation
	At admission, in all patients presenting with suspected AHF, the following diagnostic tests are recommended: a. 12-lead ECG b. Chest X-ray to assess signs of pulmonary congestion and detect other cardiac or non-cardiac diseases that may cause or contribute to the patient's symptoms c. Laboratory assessments in the blood, including cardiac troponins, blood urea nitrogen (or urea), creatinine, electrolytes (sodium and potassium), glucose, complete blood count, liver function tests, and TSH
	Upon presentation, a measurement of plasma natriuretic peptide level is recommended in all patients with acute dyspnea and suspected AHF to help in the differentiation of AHF from noncardiac causes of acute dyspnea
	Echocardiography is recommended immediately in hemodynamically unstable AHF patients and within 48 hours when cardiac structure and function are either not known or may have changed since previous studies

Table 22. Recommendations for the management of acute HF.

Class	Recommendation
oxygen therapy and ventilatory support	
	Monitoring of transcutaneous arterial oxygen saturation (SpO_2) is recommended
	Oxygen therapy is recommended in patients with AHF and SpO2 <90% or partial pressure of atrial oxygen (PaO2) <60 mmHg (8.0 kPa) to correct hypoxemia
	Intubation is recommended during respiratory failure, leading to hypoxemia [PaO_2 <60 mmHg (8.0 kPa)], hypercapnia [$PaCO_2$ >50 mmHg (6.65 kPa)], and acidosis (pH <7.35), if it cannot be managed noninvasively
	Measurement of blood pH and carbon dioxide tension (possibly including lactate) should be considered, especially in patients with acute pulmonary edema or previous history of COPD using venous blood. In patients with cardiogenic shock arterial blood is preferable.
	Noninvasive positive pressure ventilation (CPAP, BiPAP) should be considered in patients with respiratory distress (respiratory rate >25 breaths/min, SpO_2 <90%) and started as soon as possible to decrease respiratory distress and reduce the rate of mechanical endotracheal intubation. Noninvasive positive pressure ventilation can reduce blood pressure and should be used with caution in hypotensive patients. Blood pressure should be monitored regularly when this treatment is used.
Diuretics	
	Intravenous loop diuretics are recommended for all patients with AHF admitted with signs/symptoms of fluid overload to improve symptoms. It is recommended to regularly monitor symptoms, urine output, renal function, and electrolytes during use of intravenous diuretics
	It is recommended to administer IV loop diuretics within 1 hour of first medical contact to reduce the readmission rate
	In patients with new-onset AHF or those with chronic, decompensated HF not receiving oral diuretics the initial recommended dose should be 20- 40-mg intravenous furosemide (or equivalent); for those on chronic diuretic therapy, initial intravenous dose should be at least equivalent to the oral dose or the least effective dose required to reach euvolemia in the shortest time
	It is recommended to give diuretics either as intermittent boluses or as a continuous infusion, and the dose and duration should be adjusted according to patients' symptoms and clinical status
	The combination of a loop diuretic, with either a thiazide-type diuretic or acetazolamide, may be considered in patients with resistant edema or insufficient symptomatic response
Vasodilators	
	Intravenous vasodilators may be considered for symptomatic relief in AHF with SBP >110 mmHg and without symptomatic hypotension. Symptoms and blood pressure should be monitored frequently during the administration of intravenous vasodilators
	In patients with hypertensive AHF, intravenous vasodilators should be considered as the initial therapy to improve symptoms and reduce congestion
Inotropic agents and vasopressors	
	ECG and blood pressure (preferably intra-arterial blood pressure) monitoring is recommended when using inotropic agents and vasopressors, as they can cause arrhythmia, myocardial ischemia, and even hypotension
	Inotropic agents may be considered in patients with SBP <110 mmHg and evidence of hypoperfusion who do not respond to standard treatment, including fluid challenge, to improve peripheral perfusion and maintain end-organ function.
	Inotropic agents are not recommended routinely, due to safety concerns, unless the patient has symptomatic hypotension and evidence of hypoperfusion.
	A vasopressor (norepinephrine preferably) may be considered in patients who have cardiogenic shock, despite treatment with another inotrope, to increase
	blood pressure and vital organ perfusion

(continued on next page)

Table 22 (continued)

Thromboembolism prophylaxis	
	Thromboembolism prophylaxis (c.gw with LMWH) is recommended in patients not already on anticoagulants and with no contraindication to anticoagulation, to reduce the risk of deep venous thrombosis and pulmonary embolism
	Anticoagulation is recommended in patients with AHF and other indications for anticoagulation (e.g. AF)
Other drugs For acute control of the ventricular rate in patients with AF (decompensated patients:	
	Digoxin and/or beta-blockers should be considered as the first-line therapy
	Amiodarone may be considered
	Low-dose opiates may be considered for cautious use to relieve dyspnea and anxiety in patients with severe dyspnea but nausea and hypopnea may occur
Renal replacement therapy	
	Renal replacement therapy should be considered in patients with refractory volume overload and acute kidney injury
	Ultrafiltration may be considered for patients with refractory congestion who failed to respond to diuretic-based strategies.
Cardiogenic shock	
	In all patients with suspected cardiogenic shock, immediate ECG and echocardiography are recommended
	It is recommended that all patients with cardiogenic shock be considered for transfer to a tertiary care center
	In patients with cardiogenic shock complicating ACS, an urgent coronary angiography is recommended with an intent to perform coronary revascularization
	Continuous ECG and blood pressure monitoring are recommended
	Invasive monitoring with an arterial line is recommended
	Fluid challenge should be considered if there is no sign of overt fluid overload or if unsure of the patient's volume status or cause of shock
	Intravenous inotropic agents (dobutamine) may be considered to increase cardiac output
	Vasopressors (norepinephrine preferable over dopamine) may be considered if there is a need to maintain SBP in the presence of persistent hypoperfusion
	intra-aortic balloon pump may be considered in select cases but is not routinely performed
	Short- term mechanical circulatory support may be considered in refractory cardiogenic shock depending on the patient's age, comorbidities, and neurological function
evidence-based disease-modifying therapies	
	in case of worsening of chronic failure with reduced ejection fraction, every attempt should be made to continue evidence-based, disease modifying therapies, in the absence of hemodynamic instability or contraindications

Transthyretin cardiac amyloidosis is treated by reducing or stabilizing the production of Transthyretin. Patients with end-stage familial Transthyretin cardiac amyloidosis can be considered for liver and/or cardiac transplantation. Tafamidis is recommended in patients with genetic testing proven hereditary Transthyretin cardiac amyloidosis or with wild type Transthyretin cardiac amyloidosis and NYHA class I or II symptoms to reduce symptoms, CV hospitalization and mortality [271]. This is based on the reduction of all-cause mortality and cardiovascular hospitalizations, a well as functional improvement associated with tafamidis [271,272].

4.9.4. Pregnancy

4.9.4.1. Pre-pregnancy counseling and risk assessment. It is recommended that pre-pregnancy counseling on contraception and the risks of cardiovascular deterioration during pregnancy be offered to patients with a history of HF or cardiomyopathy (including peripartum cardiomyopathy). A history of peripartum cardiomyopathy is associated with

increased risk in subsequent pregnancies if full recovery of LVEF is not achieved [273,274]. While still associated with transient risks, maternal and neonatal outcomes could be favorable if ejection fraction is recovered prior to subsequent pregnancy in patients who previously suffered from peripartum cardiomyopathy [275]. Moreover, pre-pregnancy counseling ensures patients are well informed of the risks carried by pregnancy in HF, are confident in their health-related decisions and are satisfied with healthcare services [276,277].

Counseling should be informed by pregnancy cardiovascular risk assessment through appropriate tools, and echocardiography for myocardial structure and function assessment. Patients should be counseled to avoid pregnancy if they have severe heart disease (ejection fraction less than 30% or class III/IV heart failure, severe valvular stenosis, Marfan syndrome with aortic diameter more than 45 mm, bicuspid aortic valve with aortic diameter more than 50 mm, or pulmonary arterial hypertension. Pregnancy termination may be considered only after agreement by a multi-disciplinary heart team for patients with severe heart disease.

4.9.4.2. HF management during pregnancy. Close maternal and fetal monitoring is recommended for HF signs or symptoms or other cardiovascular instability by cardiology and obstetric and maternal–fetal medicine teams. Screening for any significant changes in HF symptoms or signs during pregnancy is recommended, particularly in the third trimester and if HF medication is changed [278]. Hemodynamic monitoring and MCS are recommended as deemed appropriate by a multidisciplinary heart team for patients presenting with decompensatied HF or cardiogenic shock. Monitoring-based adjustment of HF treatment is recommended as appropriate to avoid hypotension and placental hypoperfusion. Safe medications in pregnancy include beta-blockers as they are not associated with congenital malformations or cardiac anomalies [279,280]. It is recommended that patients are switched to beta-1-selective blockers (bisoprolol, metoprolol succinate). Hydralazine, oral nitrates and methyldopa are also safe in pregnancy and may be considered if required. Adjustment of diuretic dosing should be considered to minimize the risk of placental hypoperfusion [281,282].

ACE-Is, ARBs, ARNI, MRAs, ivabradine, vericiguat and SGLT2 inhibitors are contraindicated due to risk of fetal harm and should be stopped prior to conception [282]. While no specific information is available for ARNI and ivabradine in pregnancy, significant fetal harm in the second and third trimester (renal and tubular dysplasia, oligohydramnios, fetal growth restriction, ossification disorders of the skull, lung hypoplasia, contractures, large joints, anemia, and intrauterine fetal death) were reported with ACEi and ARB [283–285]. SGLT2 inhibitors are currently contraindicated in pregnancy and breastfeeding due to theoretical toxicity. Similarly, vericiguat is associated with embryo-fetal toxicity and is also contraindicated in pregnancy.

4.9.4.3. Peripartum cardiomyopathy. Peripartum cardiomyopathy is a frequently occurring condition with acute HF that could be accompanies with ventricular arrhythmias or cardiac arrest. It is recommended that pregnant patients with peripartum cardiomyopathy exhibiting signs of both severe HF and cardiogenic shock requiring inotropic or vasopressor support be transferred to tertiary heart centers with the capacity to administer extracorporeal membrane oxygenation, LVAD and/or cardiac transplantation if needed. Regardless of the gestational age, urgent delivery by caesarean section should be considered with MCS immediately available. Considering the possible side effects of adrenergic agents (dobutamine, adrenaline) [286], levosimendan or MCS may be considered for hemodynamically unstable patients. LVAD implantation should be considered in refractory cases of cardiogenic shock as bridge to transplantation or bridge to recovery. Bromocriptine has been associated with LV function recovery and may be considered for treatment of peripartum cardiomyopathy [287,288]. If treatment is initiated, side effects should be considered and include deep venous thrombosis and cessation of lactation. Prophylactic (or therapeutic) anticoagulation should therefore accompany treatment, as detailed below.

4.9.4.4. Anticoagulation. If needed, therapeutic anticoagulation is possible in pregnancy. However, DOACs should be avoided. Low-molecular-weight heparin (LMWH) can be used during the first and last trimesters in patients with concomitant HF and AF who are pregnant. VKAs can be used for the second trimester.

4.9.4.5. Contraception. Considering the risks of pregnancy in patients with HF, contraception counseling should be provided. Patient preference and desires should guide the choice of contraception along with a critical assessment of disease and the relative risks and benefits of the contraceptive option considered. Intrauterine devices are highly effective and reliable long-acting reversible contraception with an annual

failure rate of less than 1% [289]and are therefore the recommended nonpermanent option for women with high-risk cardiovascular conditions [290,291]. Other contraception options, such as progestin-only hormonal contraception and combined hormonal contraception have not been studies in RCTs in HF. Progestin-only hormonal contraceptives seem to be effective and safe for women with valvular heart disease, cardiomyopathy, and well-controlled hypertension [289,290,292]. On the other hand, combined hormonal contraception is associated with significant risks in women with uncontrolled hypertension and cardiovascular diseases such as peripartum cardiomyopathy [293] and are therefore not advisable.

4.9.5. Sleep apnea

In patients with HF and suspicion of sleep-disordered breathing, a formal sleep assessment may be considered to inform clinical decision-making by confirming the diagnosis and differentiating between obstructive and central sleep apnea. This is necessary seeing as the treatment of obstructive sleep apnea and central sleep apnea differs, and these two conditions can co-exist [294–296]. Treatment of sleep apnea and obesity hypoventilation syndrome is recommended with non-invasive ventilation as per guidance of sleep experts. For more information on sleep apnea, please refer to SHA 2019.

4.9.6. Anemia, hypertension, depression and vaccination

Please refer to SHA 2019 HF guidelines (see Table 20).

5. Acute heart failure

For the definition, classification and diagnosis of acute HF (AHF), please refer to Table 21 and the SHA 2019 HF guidelines.

5.1. Management

The management of AHF remains largely unchanged from the SHA 2019 HF guidelines. Please refer to the relevant sections for a detailed discussion of recommendations in Table 22. Two new algorithms are provided in Figs. 5 and 6 on the management of suspected AHF and AHF in general.

5.1.1. Pharmacotherapy

5.1.1.1. Vasodilators. In case response remains less than optimal after IV loop diuretics or a combination of loop diuretics and thiazide-type diuretic or acetazolamide, vasodilators may be considered for

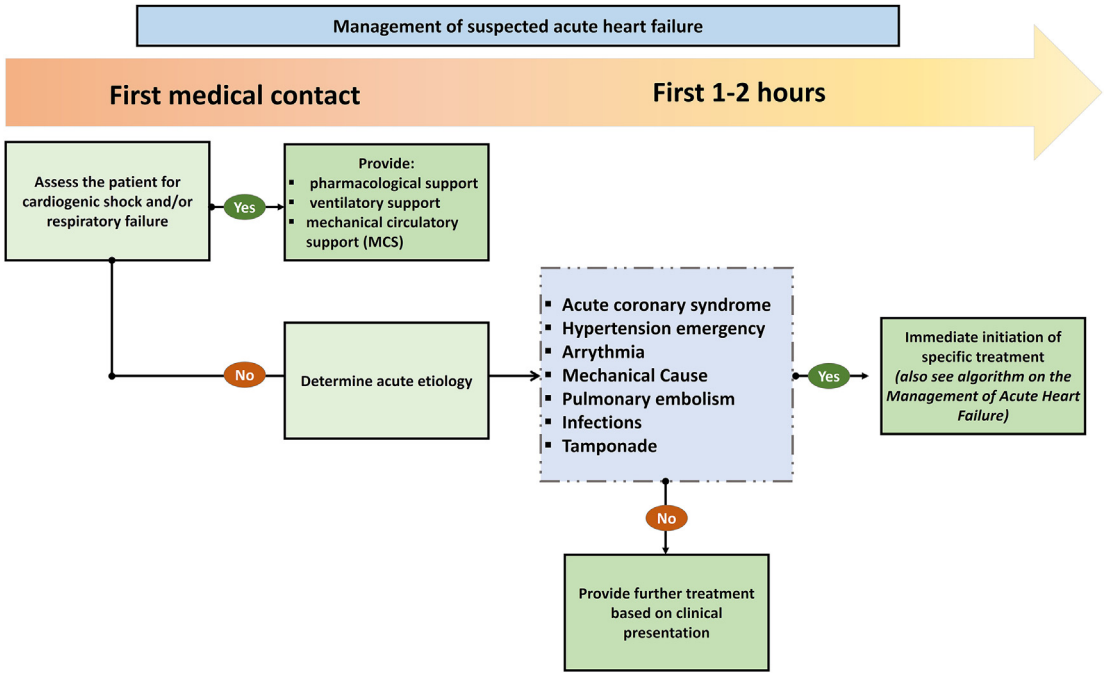

Fig. 5. Algorithm on the management of suspected acute heart failure.

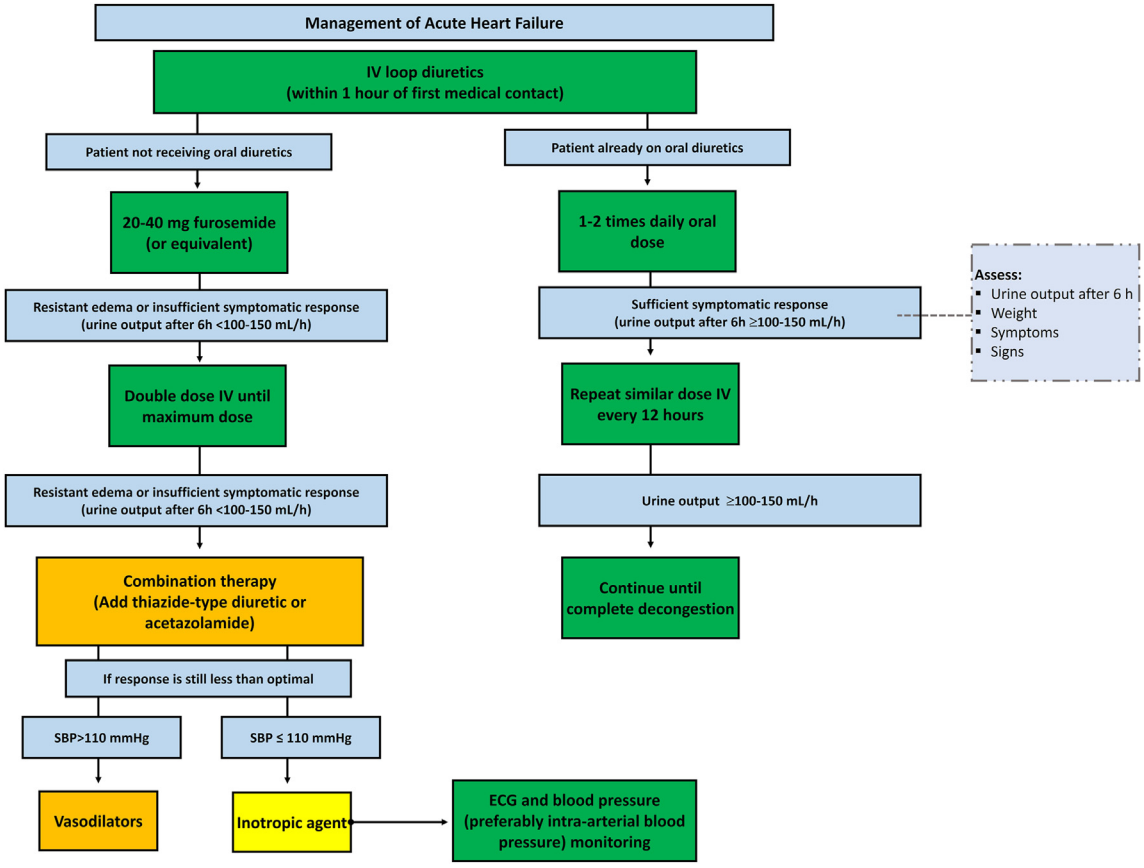

Fig. 6. Management of acute heart failure.

patients with SBP>110 mmHG. To note that two RCTs failed to show significant improvement with early intensive and sustained vasodilation compared to high-dose diuretics [297,298].

5.1.1.2. Inotropic agents and vasopressors. Inotropic agents should be considered for patients with low cardiac output and hypotension (SBP≤ 110mHg). Inotropic agents must be cautiously used starting at low doses and up-titrating as needed [299,300]. ECG and blood pressure monitoring are recommended for all patients receiving an inotropic agent. Inotropic agents are not recommended for routine use due to safety concerns (sinus tachycardia,

Table 23. Recommendations for monitoring and discharge planning.

Class	Recommendation
	Standard noninvasive monitoring of heart rate, rhythm, respiratory rate, oxygen saturation and blood pressure is recommended
	It is recommended that patients should be weighed daily and have an accurate fluid balance chart completed
	it is recommended to evaluate signs and symptoms relevant to heart failure (e.gy dyspnea, pulmonary rales, peripheral edema, and weight) daily to assess the correction of fluid overload pulmonary artery catheter may be considered in patients who, despite pharmacological treatment, present refractory symptoms (particularly with hypotension and hypoperfusion)
	Frequent, often daily, measurement of renal function (blood urea, creatinine) and electrolytes (potassium, sodium) during intravenous therapy and when renin angiotensin-aldosterone system antagonists are initiated is recommended
	An intra- arterial line should be considered in patients with hypotension and persistent symptoms despite treatment
	A pulmonary artery catheter may be considered in patients who, despite pharmacological treatment, present refractory symptoms (particularly with hypotension and hypoperfusion)

Table 24. Recommendations for exercise, multidisciplinary management, and monitoring of patients with HF.

Class	Recommendation
	it is recommended that regular aerobic exercise be encouraged in patients with HF to improve functional capacity and symptoms
	it is recommended that regular aerobic exercise be encouraged in stable patients with HFrEF to reduce the risk of HF hospitalization
	it is recommended that patients with HF are enrolled in a multidisciplinary care management program to reduce the risk of HF hospitalization and mortality
	referral to primary care for long-term follow-up may be considered for stable patients with HF who are on optimal therapy to monitor the effectiveness of the treatment, disease progression and patient adherence
	monitoring of pulmonary artery pressures using a wireless implantable hemodynamic monitoring system (CardioMEMS) may be considered in symptomatic patients with HF with previous HF hospitalization to reduce the risk of recurrent HF hospitalization
	Multiparameter monitoring based on an ICD (IN-TIME approach) may be considered in symptomatic patients with HFrEF (LVEF≤35%) to improve clinical outcomes

Table 25. Recommendations for performance measures in HF.

Class	Recommendation
	oerformance measures based on professionally developed clinical practice guidelines should be used with the goal of improving quality of care for HF
	participating in quality improvement programs and patient registries based on nationally endorsed, clinical practice guideline-based quality and performance measures can be beneficial in improving the quality of HF care.

Table 26. Performance indicators for HF.

performance indicators for HF	
process-related	• Proportion of patients with HFrEF discharged on beta-blocker therapy • Proportion of patients with HFrEF discharged on an ACE-I, ARB or ARNi • Proportion of patients with HFrEF discharged on MRA • Proportion of patients with HFrEF implanted with an ICD • Proportion of patients with LBBB and HFrEF who were implanted with a CRT-D • Time from discharge to first outpatient clinic appointment • Proportion of patients age >18 years with a discharge diagnosis of HF with documentation in the hospital records of an LVEF assessment performed during hospitalization • Proportion of patients counseled on medication, fluid intake, diet, and activity on discharge • Proportion of patients adherent to medication • Proportion of patients satisfied with treatment and overall care • Proportion of HF patients managed by a multidisciplinary team
outcome-related	• Proportion of patients readmitted to hospital within 30 days of discharge • Proportion of patients visiting the emergency department within 30 days of discharge • Proportion of patients readmitted to hospital within 12 months of discharge • In-hospital mortality rate of patients with HF • Mortality rate within 30 days, 60 days, and 1 year of discharge

increased ventricular rate, myocardial ischemia, arrhythmia, mortality).

A vasopressor (norepinephrine preferably) may be considered in patients who have cardiogenic shock, despite treatment with another inotrope, to increase blood pressure and vital organ perfusion [299,301,302].

5.1.1.3. Thromboembolism prophylaxis. Thromboembolism was shown to be effective for the reduction of the incidence of deep vein thrombosis and pulmonary embolism in a meta-analysis involving 19,958 at-risk hospitalized patients [303]. Thromboembolism prophylaxis (e.g. with LMWH) is recommended in patients not already on anticoagulants and with no contraindication to anticoagulation, to reduce the risk of deep venous thrombosis and pulmonary embolism [303,304]. Anticoagulation is recommended in patients with AHF and other indications for anticoagulation (e.g. AF).

5.2. Monitoring and discharge planning

Please refer to the SHA 2019 guidelines for detailed discussion of recommendations on monitoring and discharge planning (Table 23).

6. Multidisciplinary team management

Please refer to the SHA 2019 guidelines for detailed discussion of recommendations provided in Tables 24–26.

7. Conclusions

Cardiovascular diseases carry a significant burden in Saudi Arabia. This focused update of the SHA 2019 HF guidelines provides new and updated recommendations as well as clinical algorithms for the management of HF patients in light of emerging evidence. Clinicians should ensure patients are appropriately diagnosed and treated in order to achieve optimal clinical outcomes. Efforts should also be made to implement both the primary and secondary prevention of HF in Saudi Arabia. Special considerations should be made for the management of special patient populations, such as those with cardiovascular and non-cardiovascular co-morbidities. Overall, the adoption of updated and evidence-based HF management practices by healthcare providers in Saudi Arabia should improve clinical outcomes in patients afflicted by a disease with significant morbidity and mortality.

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