Preamble:

Cardiovascular guidelines are essential to improve patient outcomes, but their implementation remains poor. In addition, they are very "Western-world centric", meaning they do not take into account economic constraints and have very limited diversity in their writing task forces. The iCARDIO Alliance (International CARDIO Alliance to Improve Disease Outcomes) has therefore decided to develop "Global Implementation Guidelines" (iCARDIO Alliance). It is the umbrella organization of a global partnership aimed at making its documents both concise and practical as well as applicable to all cardiovascular care worldwide. In contrast to clinical practice guidelines developed by other medical associations, the evidence-based recommendations given in these guidelines take into account also resource availability on 3 economic levels: 1) "evidence-based" guideline recommendations with no economic consideration, 2) recommendations for when resources are somewhat limited, and 3) recommendations for when resources are severely limited. They are written by a team of world renown experts coming at most 50% from Europe or North America and 50% or more from the rest of the world. The peer review team is also made up of international experts from around the world enriching these documents further. These guidelines also take into consideration patients views as they are also involved in the writing and/or reviewing processes.

In a final phase, which is starting for the Heart Failure 2025 Global Implementation Guidelines right now, we are making the draft document of the guideline available for public review and commentary through an open access publication in the journal Global Cardiology (here) as well as via the website of iCARDIO Alliance (iCARDIO Alliance). All comments should be provided on headed paper (with telephone, address and email of the sender). Please use page, line, table and recommendation numbers for reference in your commentaries as appropriate. Comments received will not be published. Anonymous comments will be disregarded.

The deadline for receiving comments is 19th of January, 2025.
The email address to send comments to is ***guidelines@icardio.org***

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iCARDIO ALLIANCE GLOBAL IMPLEMENTATION GUIDELINES ON HEART FAILURE 2025

ABSTRACT

Despite the availability of several guidelines, inconsistencies in healthcare access, varying infrastructure, resource constraints and diverse local practices restrict their global applicability. This underscores the need for universal recommendations that address the unique challenges faced by patients and healthcare providers worldwide. Our Global Implementation Guidelines emphasize the incorporation of novel therapies, while integrating past directives with the most up-to-date evidence to enable clinicians to optimize heart failure (HF) management. Context-specific recommendations tailored to individual patient needs are highlighted providing a thorough evaluation of the risks, benefits, and overall value of each therapy, aiming to establish a standard of care that improves patient outcomes and reduces the burden of hospitalization in this susceptible population. These guidelines provide evidence based recommendations that represent a group consensus considering the many other published guidelines that have reviewed many of the issues discussed here, but they also make new recommendations where new evidence has recently emerged, and – most importantly – also provide recommendations on a number of issues where resource limitations may put constraints on the care provided to HF patients. Such "economic adjustment" recommendations aim to provide guidance for situations when "Resources are somewhat limited" or when "Resources are severely limited". Hence, this document presents a comprehensive update to HF management guidelines thereby aiming to provide a unified strategy for the pharmacological, non-pharmacological, and invasive management of this significant global health challenge that is tailored to the needs of healthcare around the globe.

INTRODUCTION

Heart failure (HF) is a leading public health challenge, with over 64 million prevalent cases worldwide [1]. Studies from the US have projected a 46% increase in HF cases from 2012 to 2030 due to ageing population, with a significant rise in HF with preserved ejection fraction (HFpEF). In addition, healthcare costs associated with HF are expected to rise by approximately 127% [2]. By 2050, nearly 11 million adults are expected to be affected by HF in the US [3]. To mitigate ths growing public health threat, it is essential to improve the understanding of this condition, promote lifestyle modifications, and implement early detection strategies, and treatment modalities. In 1995, the American Heart Association and the American College of Cardiology published the first clinical guidelines for managing HF [4]. Since then, several countries- and region-specific guidelines have emerged, predominantly from Western countries, which influence decision-making across multiple stakeholders, including patients, clinicians, and healthcare leaders [5-16]. However, uniform implementation of these guidelines across all regions remains a challenge due to variations in infrastructure and local practices [17]. Current evidence suggest that guideline-directed medical therapies (GDMT) significantly decrease mortality and hospitalizations among individuals with HF, particularly HF with reduced ejection fraction (HFrEF), and are therefore recommended as highly cost-effective interventions by the Disease Control Priorities Project [18]. Despite strong evidence supporting GDMT, its utilization remains limited in low- and middle-income countries (LMIC), where barriers at the health system, provider, and patient levels contribute to a 22% to 58% higher 1-year mortality rate compared to high-income countries [1,19,20].

Furthermore, there is a lack of substantial data to ascertain the relevance of current guidelines to diverse populations across the globe. Often, where evidence is strong, the recommendations are unlikely to adjust to accommodate economic constraints and availability [17]. For example, in the Middle East where economic constraints may not play a big role, but a particularly high burden of HF exists, even after accounting for variations in age demographics [21-23,] there remains a huge gap in reaching the guideline-recommended doses for all of the medications. We lack an understanding of the reasons behind this gap in practice [19, 20]. These global disparities underscore the need for new, universally applicable guidelines that can ensure both relevance and effectiveness in HF management.

Thus, this document strives to usher in a new era of practical guidelines that are responsive to unique challenges faced by individual patients and healthcare providers during HF management. By integrating past guidelines with the latest research and evidence, it offers an updated, comprehensive approach, that equips healthcare providers with the tools needed to address the evolving challenges in diagnosis, prevention, and management of acute and chronic HF. Lastly, HF management can be overwhelming due to economic burden, particularly in resource-limited countries with restricted access to advanced therapies. To address this, we have proposed alternative treatment strategies where recommended or strongly recommended grading was given. In cases of suggestive grading, we have not provided economic considerations as these were suggestions, and maybe acceptable to forego in cases of economic limitations. These considerations ensure that the guidelines remain adaptable to diverse healthcare settings while maintaining their efficacy in improving patient outcomes.

GRADING / RECOMMENDATIONS

Based on the available evidence and consensus among the committee members regarding the risks and benefits of interventions, the recommendations were classified as strongly recommend (SR), recommend (R), suggest (Su), and do not do (DND) (*see **Table 1***). To make the document more readable (and particularly to make it shorter), we decided to not reference each recommendation.

Table 1: Grading and Recommendation

No.	DEFINITION	LEVEL OF RECOMMENDATION
1-01	Evidence or consensus that a specific diagnostic test or treatment is effective, beneficial and valuable.	Strongly Recommend (SR)
1-02	Majority of evidence or opinions support the benefits or effectiveness.	Recommend (R)
1-03	Usefulness or effectiveness is less clearly supported by evidence or opinion.	Suggest (Su)
1-04	Evidence or consensus suggests that it is ineffective and, in some cases, may even be harmful.	Do not do (DND)

PREVENTION OF HEART FAILURE

Therapeutic interventions and lifestyle modification in patients at risk of HF have been associated with a decreased incidence of HF and the likelihood of hospitalization due to HF. Considering the available data, the following recommendations have been proposed for the prevention of HF (*see **Figure 1**, **Table 2***).

Table 2: Recommendations for the prevention of heart failure

No.	Guideline Statement	Level of Recommendation
2-01	Request genetic counseling and testing (if available) to facilitiate early diagnosis and prevent or delay the progression of disease in family members of patients with non-ischemic cardiomyopathy.	**R**
2-02	Use GDMT to treat hypertension, and to subsequently prevent HF.	**SR**
2-03	Use evidence-based SGLT2 inhibitors to reduce HF hospitalizations in patients with T2DM and CKD, regardless of diabetes status.	**SR**
Resources severely limited	*Use empagliflozin, dapagliflozin or any regionally approved SGLT2 inhibitor to reduce HF hospitalization in patients with T2DM and CKD regardless of diabetes status.*	
2-04	Use evidence-based GLP-1 RA based therapies to reduce HF hospitalizations in patients with T2DM	**R**
2-05	Use evidence-based SGLT2 inhibitors to reduce HF hospitalization in post-AMI patients with LVEF <45% and/or pulmonary congestion.	**Su**
2-06	Use finerenone in patients with T2DM and CKD to reduce the risk of HF hospitalization.	**SR**
Resources severely limited	*Use any MRA in patients with T2DM and CKD to reduce the risk of hospitalization for HF.*	
2-07	Use optimal therapies (i.e. statins, antihypertensives) in patients with CVD to prevent or delay the onset of HF and reduce the risk of HF hospitalization.	**SR**
2-08	Use ACEi (or ARB if intolerant to ACEi) in patients with/without MI and LVEF ≤40% to decrease the risk of symptomatic HF and mortality	**SR**

2-09	Use HF-specific beta-blockers in patients with recent or remote MI/ACS and LVEF≤40%, to decrease the risk of HF.	**SR**
2-10	Use HF-specific beta-blockers in patients with LVEF≤40% and no prior MI or ACS, to decrease the risk of HF.	**SR**
2-11	Advise at least 5% weight loss in patients with severe obesity (BMI ≥35 kg/m^2) to decrease the risk of HF.	**Su**

SR, Strongly recommend; R, Recommend; Su, Suggest; and DND, Do not do.
ACEi, angiotensin-converting enzyme inhibitors; ACS, acute coronary syndrome; AMI, acute myocardial infarction; ARB, angiotensin receptor blocker; BMI, body-mass index; CVD, cardiovascular disease; CKD, chronic kidney disease; GDMT, guideline-directed medical therapy; GLP-1RA, glucagon-like peptide 1 receptor agonist; HF, heart failure; LVEF, left ventricular ejection fraction; MI, myocardial infarction; MRA, mineralocorticoid receptor antagonist; SGLT2, sodium-glucose cotransporter-2; T2DM, type 2 diabetes mellitus.

DIAGNOSTICS

The diagnosis of HF requires the presence of symptoms and/or signs of HF and objective evidence of cardiac dysfunction. Symptoms and signs lack sufficient accuracy to be used alone to make the diagnosis of HF, thus under- and misdiagnosis of HF can commonly occur. To address this, several diagnostic modalities should be utilized to diagnose or determine the prognosis of HF (*see **Figure 1**, **Table 3***).

Table 3: Recommendations for the diagnostic tests in patients with heart failure

No.	Guideline Statement	Level of Recommendation
3-01	Obtain a 3-generation family history in patients with suspected cardiomyopathy to detect possible inherited conditions.	**Su**
3-02	Inquire regarding family history, previous malignancy, acromegaly, hypo- or hyperthyroidism, exposure to metals or chemicals, alcohol, illicit drug use and exposure to HIV, chemotherapy, immunotherapy or cardiac irradiation in patients with suspected cardiomyopathy.	**SR**
3-03	Measure BNP or NT-proBNP, where available, to make or exclude new diagnosis of HF in patients presenting with dyspnea.	**SR**
Resources severely limited	*In countries where BNP or NT-proBNP is not covered or reimbursed, consider echocardiography if it is covered or reimbursed by third parties.*	
3-04	Perform TTE during the initial assessment (recommendation **a**), and 3-6 months after optimization of therapies for patients with HFrEF (**b**); to evaluate cardiac structure and function, and to guide management.	**(a): SR** **(b): R**
Resources severely limited	*Perform TTE during the initial assessment and diagnosis and then subsequently, only if there are significant changes to the patient's clinical status.*	
3-05	Perform CMR, where available/affordable, to evaluate myocardium in possible cases of inflammatory diseases like myocarditis or sarcoidosis, infiltratative diseases like amyloidosis or Fabry's disease, or iron overload/hemochromatosis, hypertrophic cardiomyopathy, and suspected previous infarction.	**Su**

Resources severely limited	*Consider CMR where the diagnosis remains uncertain following initial clinical evaluation and patient's clinical status changes significantly despite being on GDMT to rule out infiltrative diseases.*	
3-06	Perform PET/CT scan in patients with suspected sarcoidosis.	**R**
3-07	Evaluate patients with HF for possible ischemic heart disease etiology to identify the cause of HF and evaluate the anatomy and functional status. The choice of evaluation method should depend on pre-test probability, and availability of the diagnostic modality.	**SR**
3-08	Perform invasive hemodynamic monitoring to guide the management of selected patients with HF and persistent or worsening NYHA class III/IV symptoms, signs, or diagnostic parameters when hemodynamic status is uncertain.	**Su**
3-09	Perform endomyocardial biopsy in patients with HF, if a specific diagnosis is suspected that could affect the management and prognosis.	**Su**
3-10	Perform non-invasive home tele-monitoring in patients with HF, to decrease hospitalization for HF and risk of CV death.	**Su**
3-11	Perform CPET for selected patients with HF to help determine the cause and severity of exercise intolerance and eligibility for advanced therapies such as MCS and heart transplant.	**SR**
Resources severely limited	*In countries with resource limitations, 6MWT can be considered to evaluate the eligibility for advanced therapies such as MCS and heart transplant.*	
3-12	Perform RHC in patients with persistent right-sided HF to determine PAPI, PASP, PVR, transpulmonary gradient, PCWP, RVSWI and to exclude left-sided HF as underlying cause.	**R**
3-13	Perform genetic counselling and testing in patients with non-ischemic cardiomyopathy, particularly those with family history or those presenting with arrhythmias, to guide diagnosis and management of the patient and possibly affected family members.	**Su**
Resources somewhat limited	*Consider genetic counseling and testing in patients with suspected non-ischemic cardiomyopathy or cardiomyopathy with arrhythmias.*	
3-14	Perform a formal sleep study to determine the presence of CSA in patients being considered for positive pressure mask therapy of sleep apnea with HF.	**Su**

SR, Strongly recommend; R, Recommend; Su, Suggest; and DND, Do not do.
6MWT, 6-minute walk test; BNP, B-type natriuretic peptide; CMR, cardiac magnetic resonance; CSA, central sleep apnea; CPET, cardiopulmonary exercise testing; CV, cardiovascular; HF, heart failure; HFrEF, heart failure with reduced ejection fraction;; MCS, mechanical circulatory support; NT-proBNP, N-terminal prohormone of B-type natriuretic peptide; PAPI, pulmonary artery pulsatility index; PASP, pulmonary artery systolic pressure; PCWP, pulmonary capillary wedge pressure; PET, positron emission tomography; PVR, pulmonary vascular resistance; TTE, transthoracic echocardiography; RHC, right heart catheterization; RVSWI, right ventricular stroke work index.

TREATMENT

(a) Drugs

Pharmacological therapies have been shown to improve symptoms, reduce hospitalizations and reduce mortality in patients with HF by improving cardiac function and slowing the disease progression. Despite strong evidence supporting the benefits of certain medications for HFrEF, several other classes of medications still have either unproven benefits or potential risks of increased fluid retention, drug interactions, HF hospitalization, or mortality. Recommendations regarding the

pharmacological therapies for patients with HF are summarized in ***Figure 2*** *and* ***Figure 3*** *as well as in* ***Table 4*** focusing on drugs commercially available in major parts of the world.

Table 4: Recommendations for pharmacological therapies in patients with heart failure

No.	Guideline Statement	Level of Recommendation
4-01	Use diuretics in patients with HF and signs and symptoms of congestion to alleviate symptoms, improve functional status and decrease the risk of HF hospitalization, irrespective of LVEF.	**SR**
4-02	Use higher dose of IV loop diuretics or addition of a second diuretic (thiazide or acetazolamide) in patients hospitalized/non-hospitalized with HF when diuresis is inadequate to relieve signs and symptoms of congestion.	**R**
4-03	Use ARNI as first-line therapy in patients with HFrEF to reduce mortality and morbidity. If ARNI is contraindicated, use ACEi or ARB.	**SR**
4-04	In patients with HFrEF and NYHA II and III class symptoms who can tolerate ACE or ARB, use ARNI as a replacement therapy to reduce mortality and morbidity.	**SR**
Resources severely limited	*ACE or ARB can be used instead of ARNI among patients with HFrEF and NYHA II and III class symptoms to reduce mortality and morbidity.*	
4-05	Do not use ARNI simultaneously with ACEi or within 36 hours of the last ACEi dose (and vice versa).	**DND**
4-06	Do not use ARNI or ACEi in patients with a history of angioedema.	**DND**
4-07	Use bisoprolol, carvedilol, nebivilol, or sustained-release metoprolol succinate in patients with HFrEF to reduce the risk of cardiovascular mortality and HF hospitalization.	**SR**
4-08	Use MRA in patients with HFrEF, eGFR>30 mL/min/1.73m2 and potassium <5 mEq/L, to reduce morbidity and mortality.	**SR**
4-09	Do not use MRA in patients whose potassium cannot be maintained <5.5 mEq/L while on MRA, to prevent hyperkalemia-related adverse events.	**DND**
4-10	Use eplerenone or finerenone in patients who develop gynecomastia on spironolactone	**SR**
Resources somewhat limited	Use eplerenone in patients who develop gynecomastia on spironolactone	
4-11	Use evidence based SGLT2 inhibitors in patients with HF regardless of EF, to reduce the risk of HF hospitalization and CV death.	**SR**
4-12	Use a combination of hydralazine and isosorbide dinitrate in African-American adults with NYHA class III-IV symptoms, despite receiving optimal therapy, to improve QoL and decrease morbidity and mortality.	**R**
4-13	Use ivabradine in patients with HFrEF (LVEF<35%), NYHA class II to III symptoms, and sinus rhythm with a heart rate≥70 bpm despite being on maximally tolerated GDMT, including beta-blockers, to reduce the risk of HF hospitalization and CV death.	**R**

4-14	Use oral soluble guanylate cyclase stimulator (vericiguat) to reduce HF hospitalization and CV death in high-risk patients with HFrEF and recent worsening of HF despite GDMT.	**R**
4-15	Use oral soluble guanylate cyclase stimulator (vericiguat) to reduce HF hospitalization and CV death in high-risk patients with HFrEFand recent worsening of HF despite GDMT who have a NT-proBNP <5000 pg/ml	**SR**
4-16	Use digoxin in patients with HFrEF who remain symptomatic despite GDMT as tolerated, to decrease HF hospitalization.	**Su**
4-17	Use HF specific beta-blockers, ARNI, ACEi or ARB, SGLT-2 inhibitors and MRA to reduce the risk of HF hospitalization and death in patients with HFmrEF.	**SR**
4-18	Continue GDMT even if patients are asymptomatic after improvement in ejection fraction (HFimpEF), to prevent relapse of HF and LV dysfunction.	**SR**
4-19	Use MRAs in patients with HFpEF, especially those at the lower end of the LVEF spectrum, to decrease HF hospitalization. (**a**) Finerenone; (**b**) spironolactone	**(a): R** **(b): Su**
Resources severely limited	*Use spironolactone in patients with HFpEF especially those at the lower end of the LVEF spectrum, to decrease HF hospitalization*	
4-20	Use ACEI or ARB in patients with HFpEF, especially those at the lower end of the LVEF spectrum to reduce the risk of HF hospitalization.	**Su**
4-21	Use ARNI in patients with HFpEF, especially those at the lower end of the LVEF spectrum. Particularly consider use in patients with LVEF <58% and in women.	**R**
4-22	Use GLP-1 RAs (semaglutide or tirzepatide) in patients with obesity and HFpEF to improve symptoms and QoL.	**SR**
4-23	Use IV nitroglycerin or nitroprusside as an adjuvant therapy to diuretics in patients admitted with decompensated HF or pulmonary congestion, in the absence of systemic hypotension (SBP<90mmHg), to relieve dyspnea.	**Su**
4-24	Reduce digoxin dose or possibly discontinue in patients with acute renal injury or patients with severe renal insufficiency (GFR<30 mL/min/1.73m2), to prevent adverse events.	**SR**
4-25	Use intravenous iron supplementation with ferric carboxymaltose or ferric derisomaltose to improve symptoms, exercise capacity and probably reduce the risk of HF hospitalization in patients with HFrEF/HFmrEF and iron deficiency with or without anemia.	**R**
Resources somewhat limited	*Use iron sucrose,* ferric carboxymaltose *or* ferric derisomaltose (whichever is affordable) instead of the above.	
Resources severely limited	*Use of any non-dextran containing intravenous iron supplementation may be considered, whichever is affordable.*	
4-26	Use potassium binders (patiromer, sodium zirconium cyclosilicate) in patients with HF and hyperkalemia (>5.5mEq/L) who are unable to tolerate any dose of RAASi, (**a**) to enable at least one RAASi initiation and (**b**) MRA dose-up titration.	**(a): R** **(b): Su**
4-27	Initiate all 4 foundational therapies in patients with HFrEF, at low doses once hemodynamically stabilized and then optimize dosages every 1-2 weeks, depending on symptoms, vitals and labs.	**R**

Resources severely limited	*Initiate least expensive combination of quadruple therapy in patients with HFrEF, at low doses once hemodynamically stabilized and then optimize dosages every 1-2 weeks, depending on symptoms, vitals and labs, and then at 3-4 months follow-up.*	
4-28	Do not use thiazolidinediones and non-dihydropyridine calcium channel blockers in patients with HF and LVEF<50%, as they increase the risk of volume overload.	**DND**
4-29	Do not use DPP-4 inhibitors (saxagliptin and alogliptin) in patients with HF, T2DM and high CVD risk, as they increase this risk of HF hospitalization.	**DND**
4-30	Do not use NSAIDs or COX-2 inhibitors in patients with HF, as they increase the risk of worsening HF and HF hospitalization.	**DND**
4-31	Use GDMT before discharge in patients hospitalized with HF to improve outcomes and reduce HF hospitalization.	**SR**
4-32	Continue and optimize pre-existing GDMT in patients hospitalized with HFrEF (with no absolute contraindication) to improve outcomes.	**SR**
4-33	Do not routinely discontinue diuretics and other GDMT in patients experiencing mild decline in GFR or asymptomatic reduction in blood pressure during HF hospitalization.	**SR**
4-34	Consider continuous IV inotropic therapy as "bridge therapy" for patients with advanced HF refractory to GDMT who are eligible and awaiting MCS or cardiac transplantation.	**Su**
4-35	Consider continuous intravenous inotropic therapy as palliative care for patients with advanced HF who are refractory to GDMT and device therapy and ineligible for MCS or heart transplantation.	**Su**

SR, Strongly recommend; R, Recommend; Su, Suggest; and DND, Do not do.
ACEi, angiotensin converting enzyme inhibitors; ACS, acute coronary syndrome; AMI, acute myocardial infarction; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor neprilysin inhibitors; BPM, beats per minute; BNP, B-type natriuretic peptide; COX-2, cyclo-oxygenase-2; CV, cardiovascular; CVD, cardiovascular disease; DPP-4, dipeptidyl peptidase-4; GDMT, guideline-directed medical therapy; GFR, glomerular filtration rate; GLP-1RA, glucagon-like peptide 1 receptor agonist; HF, heart failure; HFimpEF, heart failure with improved ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFmrEF, heart failure with mildly reduced ejection fraction; HFrEF, heart failure with reduced ejection fraction; IV, intravenous; LVAD, left ventricular assist device; LVEF, left ventricular ejection fraction; MCS, mechanical circulatory support; MRA, mineralocorticoid receptor antagonist; NT-proBNP, N-terminal prohormone of B-type natriuretic peptide; NSAIDs, non-steroidal anti-inflammatory drugs; NYHA, New York Heart Association; QoL, quality of life; RAASi, Renin-angiotensin-aldosterone system inhibitors; SGLT2, sodium-glucose cotransporter-2; SBP, systolic blood pressure; T2DM, type 2 diabetes mellitus, and TSAT, transferrin saturation.

(b) Devices

A crucial role has been played by RCTs in shaping decisions regarding cardiac implantable devices such as implantable cardioverter-defibrillators (ICDs), and cardiac resynchronization therapy (CRT) over the past two decades. While subgroup analyses of these trials have provided additional insights, it is important to note that they were not the primary endpoints of these studies and should be interpreted cautiously. Recently, cardiac contractility modulation (CCM) and baroreflex activation therapy (BAT) have shown beneficial effects in patients with HF. Strategies and recommendations regarding device therapies are summarized in ***Table 5*** *and* ***Figure 2***.

Table 5: Recommendations for the device therapies in patients with heart failure

No.	Guideline Statement	Level of Recommendation
5-01	Use maximally tolerated GDMT in patients with HFrEF patients for at least 3 months prior to implementation of a primary prevention ICD and assess LVEF after that, as the LVEF may improve thereby decreasing the need for ICD.	**SR**
5-02	Consider ICD therapy to decrease the risk of SCD and mortality in patients with ischemic/non-ischemic HFrEF; LVEF≤35%; NYHA II or III symptoms on chronic GDMT and prognosis >1yr survival.	**ischemic: SR** **non-ischemic: Su**
Resources severely limited	*Restrict use of ICD therapy to reduce the risk of SCD and total mortality in patients with ischemic/non-ischemic HFrEF; LVEF≤35%; NYHA II or III symptoms on chronic GDMT, survival >1yr among patients who are at highest risk (e.g. arrhythmogenic cardiomyopathy) and most likely to benefit such as those with NYHA Class II symptoms, severely reduced LVEF and frequent NSVT, and who have low likelihood for reverse remodelling.*	
5-03	Use ICD therapy to decrease the risk of SCD and overall mortality in patients who are at least 40 days post-MI, have an LVEF ≤ 30%, and have a prognosis of >1yr survival.	**SR**
Resources severely limited	*Optimize GDMT before considering ICD, in patients who are at least 40 days post-MI, have an LVEF ≤ 30%, and have a prognosis of >1yr survival.*	
5-04	Use a wearable ICD for a limited period or as a bridge to an implanted device in patients with HF who are at high risk of SCD.	**Su**
5-05	Do not use ICD therapy in patients with NYHA class IV and severe symptoms unresponsive to medical therapy, unless they are eligible for CRT, a VAD, or cardiac transplantation.	**DND**
5-06	Use ICD in patients with genetic arrhythmogenic cardiomyopathy and LVEF<45% to decrease the risk of sudden death.	**Su**
5-07	Use CRT to reduce mortality, and HF hospitalization and improve symptoms and QOL in patients with LVEF≤35%; NSR; LBBB with QRS≥150ms; NYHA II-IV symptoms on maximally tolerated GDMT for atleast 3 months.	**SR**
Resources severely limited	*Optimize GDMT maximally in patients with LVEF≤35%; NSR; LBBB with QRS≥150ms; NYHA II-IV symptoms on GDMT, and then consider cheapest available CRT/LBBB pacing device, whenever appropriate.*	
5-08	Use CRT to reduce mortality and HF hospitalization, as well as to improve symptoms and QOL in patients with LVEF≤35%; NSR; non-LBBB pattern with QRS≥150ms; and NYHA II-IV symptoms on maximally tolerated GDMT for atleast 3 months.	**Su**
5-09	Use CRT to reduce mortality and HF hospitalization, as well as improve symptoms and QOL in patients with high-degree or complete atrioventricular block and LVEF <50%.	**Su**
5-10	Use CRT to reduce mortality and HF hospitalization, as well as improve symptoms and QOL, for patients with LVEF ≤ 35%, NSR, LBBB with a QRS duration of 130-149 ms, and NYHA class II-IV symptoms on maximally tolerated GDMT for at least 3 months	**Su**
5-11	Use CRT in patients with LVEF≤35% and have pre-existing RV pacing with symptoms of HF to reduce morbidity.	**R**

5-12	Use CRT to improve symptoms and QoL and reduce mortality and HF hospitalization in patients with AF and LVEF≤ 35% on GDMT if: a) they need RV pacing of more than 20% or otherwise qualify for CRT, or b) AV nodal ablation or pharmacologic control will enable approximately 100% ventricular pacing with CRT.	**Su**
5-13	Use CCM with the Optimizer® Smart system to improve symptoms, QOL and exercise tolerance in patients with HF on GDMT and with LVEF 25-45% in patients in sinus rhythm, and not suitable for CRT.	**Su**
5-14	Use baroreflex stimulation with the Barostim Neo System to improve symptoms, QOL and exercise tolerance in patients with HF and LVEF ≤35% in patients on GDMT in sinus rhythm and not suitable for CRT.	**Su**
5-15	Use phrenic nerve stimulation with the the Remedē System to improve symptoms, sleep quality and QOL in adult patients (including those with HF) with central sleep apnea.	**Su**
5-16	Implant durable LVAD in patients with advanced HFrEF with NYHA class IV symptoms who are deemed to be dependent on continuous IV inotropes or temporary MCS or are either already taking or are intolerant to GDMT.	**SR**
5-17	Use long-term MCS in patients with advanced HFrEF who have NYHA class IV symptoms despite GDMT and not eligible for cardiac transplantation.	**R**
5-18	Use temporary MCS, including percutaneous and extracorporeal ventricular assist devices, as a bridge to recovery or a bridge to decision in patients with advanced HFrEF and hemodynamic compromise and shock.	**Su**
5-19	Use long-term MCS in patients with HFrEF refractory to medical and device therapy and waiting for cardiac transplantation, as a bridge to cardiac transplantation to improve symptoms.	**R**
5-20	Use remote system HF monitoring/telemedicine devices, (**a**) Medical Sensible, Voice Recognition for HF, LAP monitoring) and (**b**) CardioMems [pulmonary sensor]), to guide HF management, if local circumstances allow it.	**(a): Su** **(b): R**

SR, Strongly recommend; R, Recommend; Su, Suggest; and DND, Do not do.
AV, atrioventricular; BAT, baroreflex activation therapy; CCM, cardiac contractility modulation; CRT, cardiac resynchronization therapy; GDMT, guideline-directed medical therapy; GFR, glomerular filtration rate; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; HCM, hypertrophic cardiomyopathy; ICD, implantable cardioverter-defibrillator; IV, intravenous; LAP, left atrial pressure; LBBB, left bundle branch block; LVAD, left ventricular assist device; LVEF, left ventricular ejection fraction; MCS, mechanical circulatory support; MI, myocardial infarction; NSR, normal sinus rhythm; NSVT, non-sustained ventricular tachycardia; NYHA, New York Heart Association; QoL, quality of life; SCD, sudden cardiac death; VAD, ventricular assist device.

(c) Surgery and Trans-Catheter Procedures

Strategies for invasive management and device based therapies for patients with severe valvular diseases or coronary artery diseases are mentioned in ***Table 6*** *and* ***Figure 2***.

Table 6: Recommendations for the invasive management in patients with heart failure

No.	Guideline Statement	Level of Recommendation
6-01	Perform surgical revascularization (CABG) plus GDMT in selected patients with HFrEF (EF≤35%) and suitable coronary anatomy; and if they have diabetes or multivessel disease, to improve symptoms, and reduce hospitalizations, and long-term all-cause mortality.	**R**
6-02	Optimize GDMT and device (CRT in LBBB patients) before intervention in patients with severe secondary MR and symptomatic HFrEF, to improve MR associated LV dysfunction, as it might decrease the need for intervention.	**R**

6-03	Perform M-TEER to improve symptoms and reduce HF hospitalization in patients with NYHA class II-IV symptoms, severe (4+) functional MR, suitable anatomy, LVEF of 20-50%, LVESD<70 mm, PASP<70 mmHg, and who are not eligible for surgery and do not require coronary revascularization	**SR**
Resources severely limited	*Instead of M-TEER, use rigorous GDMT and reassess surgical alternatives.*	
6-04	Perform M-TEER to improve symptoms and reduce HF hospitalization in patients with NYHA class II-IV symptoms, moderate (3+) functional MR, suitable anatomy and LVEF 20-50% who are not eligible for surgery.	**Su**
6-05	Perform mitral valve surgery in patients with secondary MR on GDMT, who are already undergoing CABG to improve symptoms.	**Su**
6-06	Use transcatheter indirect annuloplasty (Carillon device) in patients with moderate or higher functional MR when M-TEER seems not appropriate or feasible to improve symptoms.	**Su**
6-07	Use medical therapy (diuretics, neurohormonal antagonists) in patients with HF and TR to reduce symptoms and severity.	**Su**
6-08	Perform TEER in selected patients with TR to improve QOL.	**Su**
6-09	Perform tricuspid valve surgery in patients with severe TR to reduce symptoms.	**Su**
6-10	Perform TAVI or SAVR in patients with HF and severe AS to improve functional symptoms and decrease the risk of mortality.	**SR**
6-11	Use medical therapy (RAAS inhibitors) in patients with HF symptoms and severe AR to improve symptoms.	**R**
6-12	Perform aortic valve surgery in patients with HF and severe aortic regurgitation regardless of LVEF to reduce mortality and improve symptoms.	**SR**
6-13	Perform heart transplantation for patients with advanced HF that is unresponsive to medical or device therapy (with no absolute contraindications), to improve survival and QoL.	**SR**

SR, Strongly recommend; R, Recommend; Su, Suggest; and DND, Do not do.
AF, atrial fibrillation; AS, aortic stenosis; AR, aortic regurgitation; CABG, coronary artery bypass grafting; GDMT, guideline-directed medical therapy; EF, ejection fraction; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; LBBB, left bundle branch block; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic diameter; MR, mitral regurgitation; M-TEER, mitral transcatheter edge-to-edge repair; NYHA, New York Heart Association; PASP, pulmonary systolic artery pressure; QoL, quality of life; RAASi, Renin-angiotensin-aldosterone system inhibitors; SAVR, surgical aortic valve replacement; TAVI, transcatheter aortic valve implantation; TEER, transcatheter edge-to-edge repair; TR, tricuspid regurgitation.

SPECIAL CONSIDERATIONS

Heart failure management becomes more challenging in the presence of comorbidities, such as amyloidosis, arrhythmia, and pregnancy, due to physiological changes, which can limit treatment options and worsen outcomes. Moreover, certain medications should be avoided due to potential risks to the fetus and other adverse effects. Recommendations about the management of HF in such special conditions are highlighted in ***Table 7*** *and* ***Figure 4***.

Table 7: Recommendations for the special conditions in patients with heart failure

No.	Guideline Statement	Level of Recommendation
	Cardiac Amyloidosis	
7-01	Use serum and urine immunofixation electrophoresis and serum free light chains in patients with clinical suspicion of cardiac amyloidosis for screening.	**SR**
7-02	Use bone scintigraphy to confirm transthyretin amyloidosis in patients with clinical suspicion of amyloidosis without evidence of serum or urine monoclonal light chains.	**SR**
7-03	Perform genetic testing for TTR gene sequencing, in patients with diagnosis of transthyretin cardiac amyloidosis, to differentiate hereditary from wild-type amyloidosis.	**SR**
7-04	Use transthyretin tetramer stabilizer therapy (tafamidis, and acoramidis) to relieve symptoms and improve mortality in patients with wild or variant type cardiac amyloidosis and NYHA class I to III symptoms.	**SR**
Resources severely limited	*Transthyretin tetramer stabilizer therapy (diflunisal) is recommended to relieve symptoms and improve mortality in patients with wild or variant type cardiac amyloidosis and NYHA class I to III HF symptoms.*	
7-05	Use hepatic transthyretin production inhibitor (vutrisiran) in patients with cardiac amyloidosis to improve symptoms, reduce cardiovascular adverse events and all-cause mortality.	**R**
7-06	Use anticoagulation to prevent stroke in patients with cardiac amyloidosis and AF, regardless of CHA_2DS_2-VA score.	**R**
	Hypertrophic Cardiomyopathy	
7-07	Use cardiac myosin inhibitors (mavacamten/aficamten) in patients with symptomatic obstructive HCM despite beta blockers or non-dihydropyridine calcium channel blockers to improve QoL, and decrease the need for septal reduction therapies.	**R**
7-08	Perform invasive therapies (septal reduction therapies) in patients with LVOT≥50 mmHg (at rest or with provocation), and who are moderate to severely symptomatic despite optimal medical therapy to improve symptoms and QoL.	**R**
7-09	Do not use arterial and venous dilators (nitrates and phosphodiesterase type 5 inhibitors), and digoxin in patients with HCM and LVOTO.	**DND**
7-10	Use ICD in patients with family history of sudden death in any one or more first degree relatives under age 40, or sudden death in first degree relative with HCM at any age.	**R**
7-11	Use anticoagulation to prevent stroke in patients with HCM and AF, regardless of CHA_2DS_2-VA score.	**R**
	Other Co-morbidities	
7-12	Request screening for anemia and iron deficiency with complete blood count, serum ferritin concentration and TSAT in all patients with HF.	**SR**

7-13	Use the standard definition of iron deficiency in HF: ferritin <100 µg/L, and if ferritin 100-299 µg/L, then TSAT <20%.	**SR**
7-14	A simplified definition of iron deficiency can be used: TSAT<20%	**R**
Resources severely limited	*TSAT alone may be used for iron deficiency diagnosis in HF.*	
7-15	Request a formal sleep assessment in patients with HF and suspicion of sleep-disordered breathing, to differentiate between obstructive and central sleep apnea.	**R**
7-16	Use CPAP/bi-PAP/adaptive servo-ventilation in patients with HF and obstructive sleep apnea, to improve symptoms, sleep quality and daytime sleepiness.	**Su**
7-17	Use Remede phrenic nerve stimulator in patients with HFrEF and predominant central sleep apnea, to improve symptoms, sleep quality and daytime sleepiness.	**Su**
7-18	Use GLP-1 RAs based therapies (tirzepatide or semaglutide) in patients with moderate-to-severe OSA and obesity, to reduce apnea-hypopnea index, body weight, and improved sleep-related patient-reported outcomes.	**SR**
7-19	Do not use adaptive servo-ventilation in patients with NYHA class II to IV HFrEF and central sleep apnea due to increased risk of all-cause and CV mortality.	**DND**
Resources severely limited	*Lifestyle interventions such as diet and exercise may be considered instead of semaglutide or tirzepatide among patients with morbid obesity to improve QOL and reduce weight.*	
7-20	Use chronic anticoagulation to prevent stroke in patients with HF and permanent-persistent-paroxysmal AF based on CHA_2DS_2-VA score of ≥2, without differences by gender.	**SR**
7-21	Use long-term treatment with an oral anticoagulant in patients with HF and AF with a CHA_2DS_2-VA score of 1, without differences by gender, to decrease the risk of stroke.	**R**
7-22	Use beta-blockers in patients with HFrEF and AF with high ventricular rate (unless congested), to improve symptoms and control ventricular rate.	**R**
7-23	Use digoxin in patients with HF and AF with high ventricular rate despite BB or if BB are contraindicated, to improve the symptoms and control ventricular rate.	**Su**
7-24	Use bolus of amiodarone or digoxin in patients with AF with high ventricular rate in NYHA class IV HF, in addition to treatment for AHF, to reduce the ventricular rate.	**R**
7-25	Perform catheter ablation in patients with HFrEF and symptoms attributable to AF despite medical therapy, to improve symptoms and QoL.	**R**
7-26	Perform AV nodal ablation in patients with HF and LVEF<50%, if rhythm control fails/not desired and ventricular rate remains rapid despite medical therapy, to improve outcomes.	**Su**
7-27	Do not use class IC antiarrhythmic medications and dronedarone in patients with HFrEF and AF due to increased risk of mortality.	**DND**

	Cardio-Oncology	
7-28	Use ACEi or ARB or ARNI, SGLT2 inhibitors and beta-blocker in asymptomatic patients with cancer-therapy-related cardiomyopathy with LVEF<50%, with the aim to decrease the risk of HF and improve cardiac function.	**Su**
7-29	Establish pretherapy baseline cardiac function in patients with CV risk factors or known cardiac disease who are being considered for potentially cardiotoxic anticancer therapies, to help in selection of cancer therapy.	**Su**
7-30	Monitor LV function/ global longitudinal strain, LV mass, and cardiac biomarkers (NT-proBNP, troponin etc) regularly to allow early detection and management of cardiotoxicity in patients with CV risk factors or known cardiac disease being considered for potentially cardiotoxic anticancer therapies.	**Su**
	HF and Pregnancy	
7-31	Counsel related to contraception and risks of cardiovascular deterioration during pregnancy in women with a history of HF or cardiomyopathy, including previous peripartum cardiomyopathy.	**SR**
7-32	Do not use ACEi, ARB, ARNi, MRA, SGLT2 inhibitors, cardiac myosin inhibhitors, Ivabradine and Vericiguat in women with HF or cardiomyopathy, who are pregnant or currently planning for pregnancy because of risk of unclear safety.	**DND**
7-33	Use LMWH in the 1st and 3rd trimester, and VKA or LMWH for the 2nd trimester in pregnant women with HF and AF.	**R**
7-34	Do not use DOACs in pregnant women with HF and AF, due to unclear safety.	**DND**
7-35	Continue beta-blocker, hydralazine and nitrates in women with HF or cardiomyopathy who are pregnant or currently planning for pregnancy.	**R**
7-36	Adjust diuretic dosing in women with HF or cardiomyopathy who are pregnant or currently planning for pregnancy, to minimize the risk of placental hypoperfusion.	**R**
	Miscellaneous	
7-37	Administer pneumococcal and influenza vaccines in patients with HF to reduce the risk of hospitalization for HF.	**SR**
7-38	Use fluid restriction to ~2L/d in patients with HF and fluid retention not easily controlled with diuretics, to reduce symptoms related to congestion.	**R**
7-39	Advise exercise training in patients with HF to improve exercise capacity, QoL and reduce the risk of HF hospitalization, if possible.	**SR**
7-40	Recommend multidisciplinary team care (including a cardiologist, HF nurse, dietitians, and community workers) for high-risk patients with HFduring discharge to optimize care.	**R**

	Goals of Care	
7-41	Use palliative and supportive care focusing on effective communication, conveying prognosis, clarifying goals of care, shared decision-making, symptom management, and caregiver support for HF patients to improve QoL and relieve suffering.	**SR**

SR, Strongly recommend; R, Recommend; Su, Suggest; and DND, Do not do.
ACEi, angiotensin-converting enzyme inhibitors; AHF, acute heart failure; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor neprilysin inhibitors; AF, atrial fibrillation; AS, aortic stenosis; AV, atrioventricular; bi-PAP, bilevel positive airway pressure; CPAP, continuous positive airway pressure; CKD, chronic kidney disease; CV, cardiovascular; DOACs, direct oral anticoagulants; GDMT, guideline-directed medical therapy; GLP-1RA, glucagon-like peptide 1 receptor agonist; HCM, hypertrophic cardiomyopathy; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; ICD, implantable cardioverter defibrillator; LMWH, low molecular weight heparin; LV, left ventricular; LVEF, left ventricular ejection fraction; LVOTO, left ventricular outflow tract obstruction; MRA, mineralocorticoid receptor antagonist; NYHA, New York Heart Association; NSAIDs, non-steroidal anti-inflammatory drugs; OSA, obstructive sleep apnea, QoL, quality of life; SGLT2, sodium-glucose cotransporter-2; T2DM, type 2 diabetes mellitus; TSAT, transferrin saturation; TTR, transthyretin, VKA, vitamin K antagonist.

CONCLUSION

The recommendations provided in this document offer a comprehensive framework for HF management, drawing on the most recent evidence to support physicians in their practice. However, it is pertinent to note that they should not replace clinical judgment. Effective HF management requires adapting these guidelines to the unique circumstances of each patient and the resources available in their region. A comprehensive overview of the recommendations for management of patients with HFpEF and HFrEF / HFmrEF is given in ***Figures 5 to 7***. It is crucial for healthcare providers to offer personalized care tailored to each patient's specific clinical profile, symptoms, comorbidities, and individual preferences. Recognizing potential obstacles to implementing these recommendations, including resource constraints, access to particular interventions and technologies, cultural influences and local standards of care is essential for effective application of these guidelines. By integrating these recommendations with individualized patient care and addressing local healthcare dynamics, clinicians can optimize HF management and improve quality of life for patients.

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This document is now published as a draft document intended for public consultation & review.
Comments and suggestions for revision can be send together with supporting information to: <*guidelines@icardio.org*>.

The deadline for receiving comments is the 19th of January, 2025.

All comments should be provided on headed paper (with telephone, address and email of the sender).
Please use page, line, table and recommendation numbers for reference in your commentaries as appropriate.
Comments received will not be published. Anonymous comments will be disregarded.

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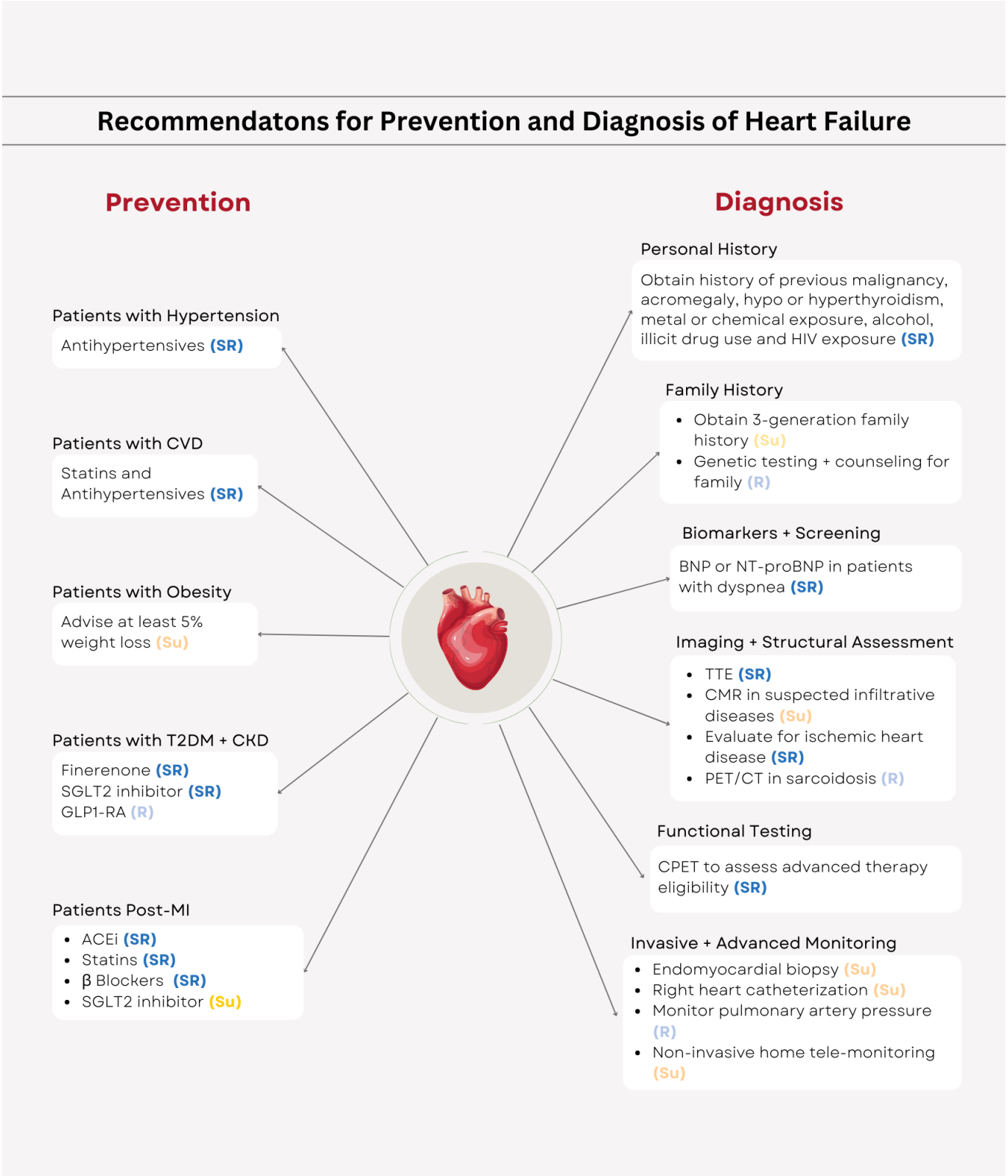
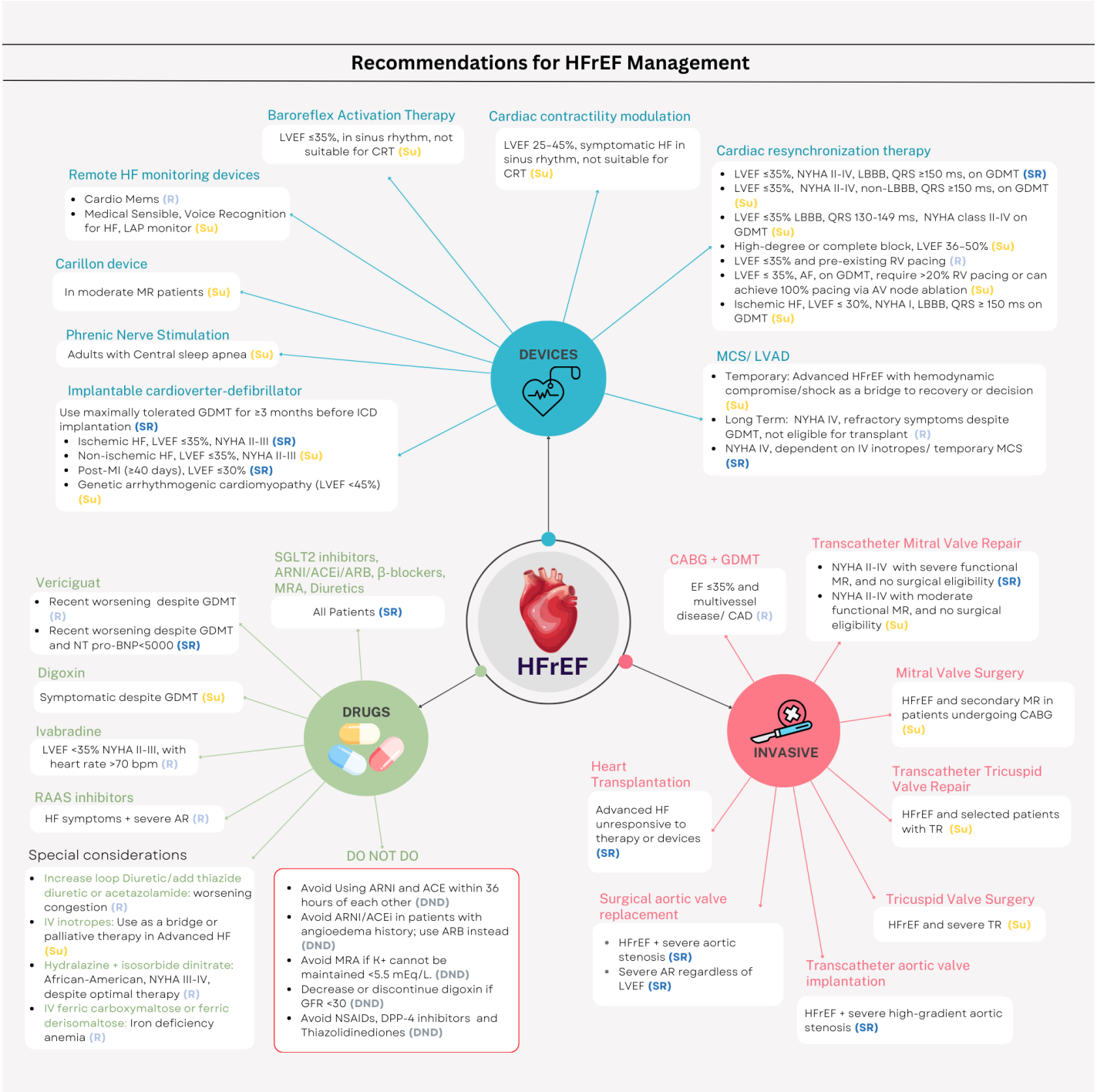
Figure 1: Recommendations for Prevention and Diagnosis of Heart Failure



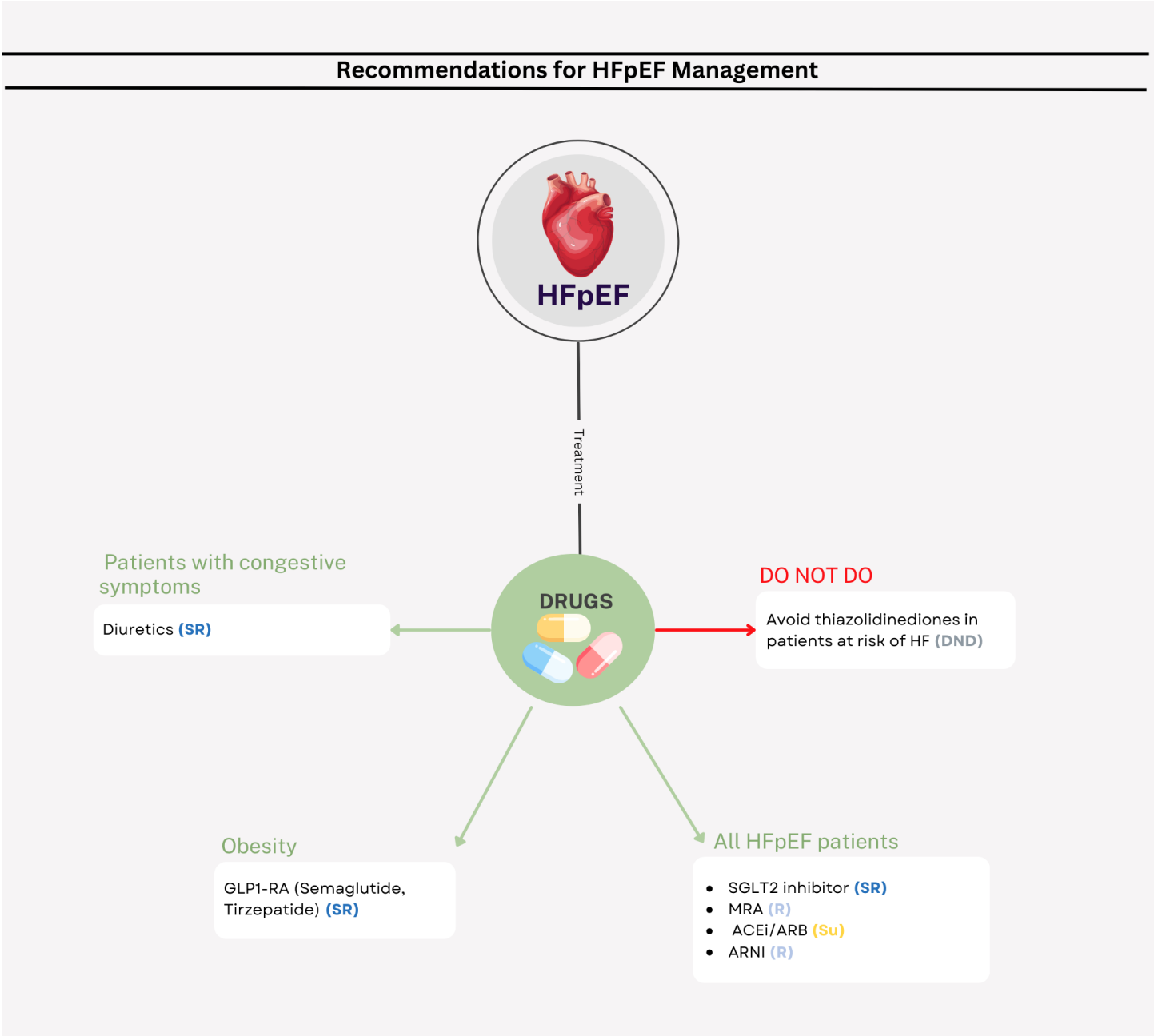
SR, Strongly recommend; R, Recommend; Su, Suggest; and DND, Do not do.
ACEi, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blocker; BNP, brain natriuretic peptide; CMR, cardiac magnetic resonance; CPET, cardiopulmonary exercise training; GDMT, guideline-directed medical therapy; GLP-1RA, glucagon-like peptide 1 receptor agonist; HF, heart failure; NT-proBNP, N-terminal pro-B-type natriuretic peptide; TTE, transthoracic echocardiography; SGLT2, sodium-glucose co-transporter 2

Figure 2: Recommendations for the Management of Heart failure with Reduced Ejection Fraction



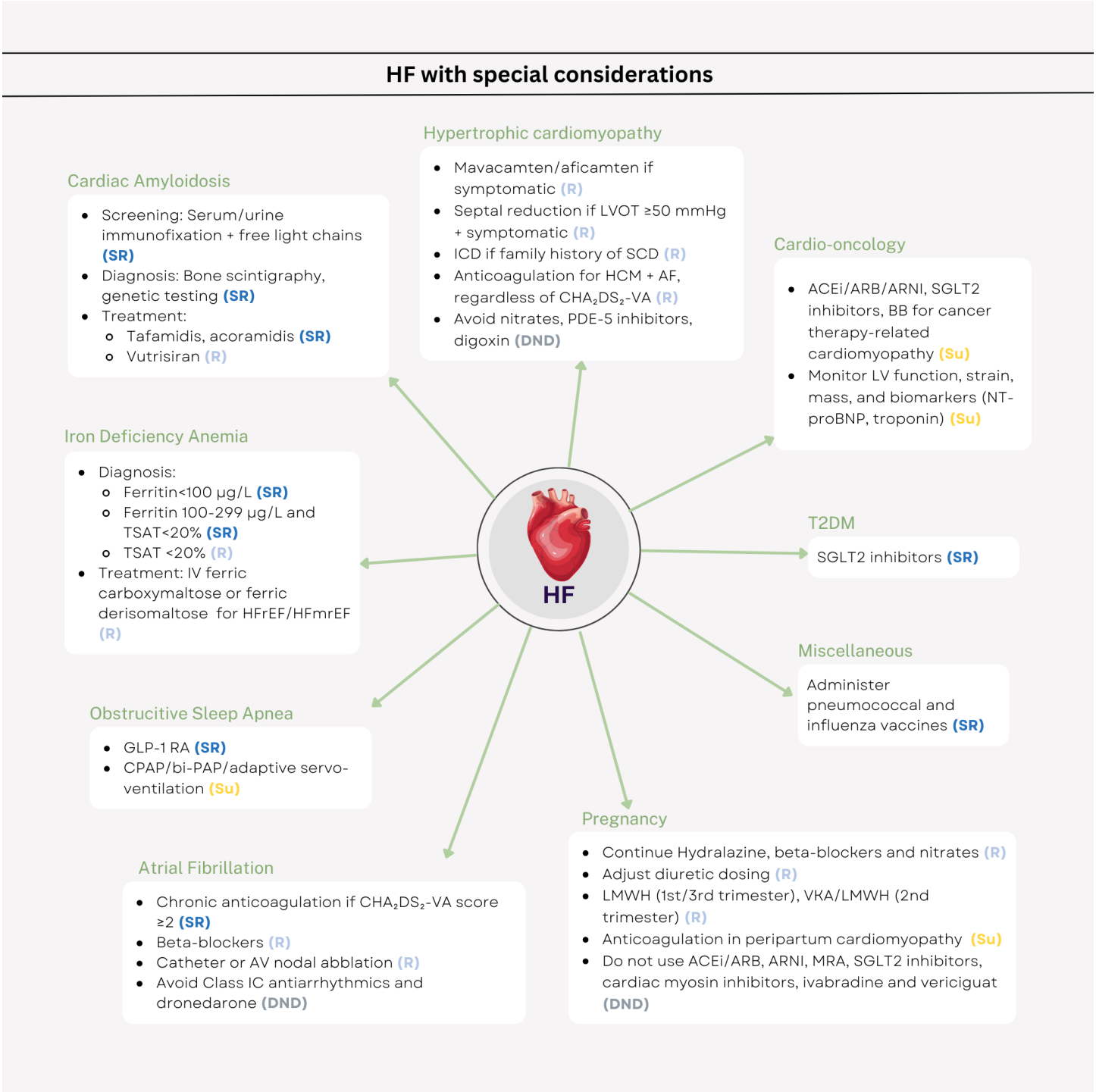
SR, Strongly recommend; R, Recommend; Su, Suggest; and DND, Do not do.
ACEi, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blocker; AHF, acute heart failure; AF, atrial fibrillation; AR, aortic regurgitation; AS, aortic stenosis; AV, atrioventricular; CAD, coronary artery disease; CABG, coronary artery bypass grafting; CRT, cardiac resynchronization therapy, DPP-4, dipeptidyl peptidase-4; GFR, glomerular filtration rate; GDMT, guideline-directed medical therapy; HCM, hypertrophic cardiomyopathy; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; ICD, implantable cardioverter-defibrillator; LBBB, left bundle branch block; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist; MI, myocardial infarction; NSAIDs, non-steroidal anti-inflammatory drugs; NYHA, New York Heart Association; RV, right ventricle; SGLT2i, sodium-glucose co-transporter 2; TSAT, transferrin saturation.

Figure 3: Recommendations for the Management of Heart failure with Preserved Ejection Fraction



SR, Strongly recommend; R, Recommend; Su, Suggest; and DND, Do not do.
ACEi, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blocker; ARNI, Angiotensin receptor neprilysin inhibitor; GDMT, guideline-directed medical therapy; GLP-1RA, glucagon-like peptide 1 receptor agonist; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; MRA, mineralocorticoid receptor antagonist; SGLT2, sodium-glucose co-transporter 2.

Figure 4: Recommendations for the Management of Special Conditions in Patients with Heart Failure



SR, Strongly recommend; R, Recommend; Su, Suggest; and DND, Do not do.
ACEi, angiotensin-converting enzyme inhibitors; AF, atrial fibrillation; ARB, angiotensin receptor blocker; ARNI, Angiotensin receptor neprilysin inhibitor; bi-PAP, bilevel positive airway pressure; CPAP, continuous positive airway pressure; GDMT, guideline-directed medical therapy; GLP-1RA, glucagon-like peptide 1 receptor agonist; HCM, hypertrophic cardiomyopathy; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; HFmrEF, heart failure with mildly reduced ejection fraction; ICD, implantable cardioverter defibrillator; LVOT, Left ventricular outflow tract; LVEF, left ventricular ejection fraction; LMWH, low molecular weight heparin; VKA, vitamin K antagonist; MRA, mineralocorticoid receptor antagonist; PDE-5, phosphodiesterase-5; SCD, sudden cardiac death; SGLT2, sodium-glucose co-transporter 2, TSAT, transferrin saturation.

Figure 5: Overview of Recommendations for Risk Factor & Phenotype Based Management of HFpEF

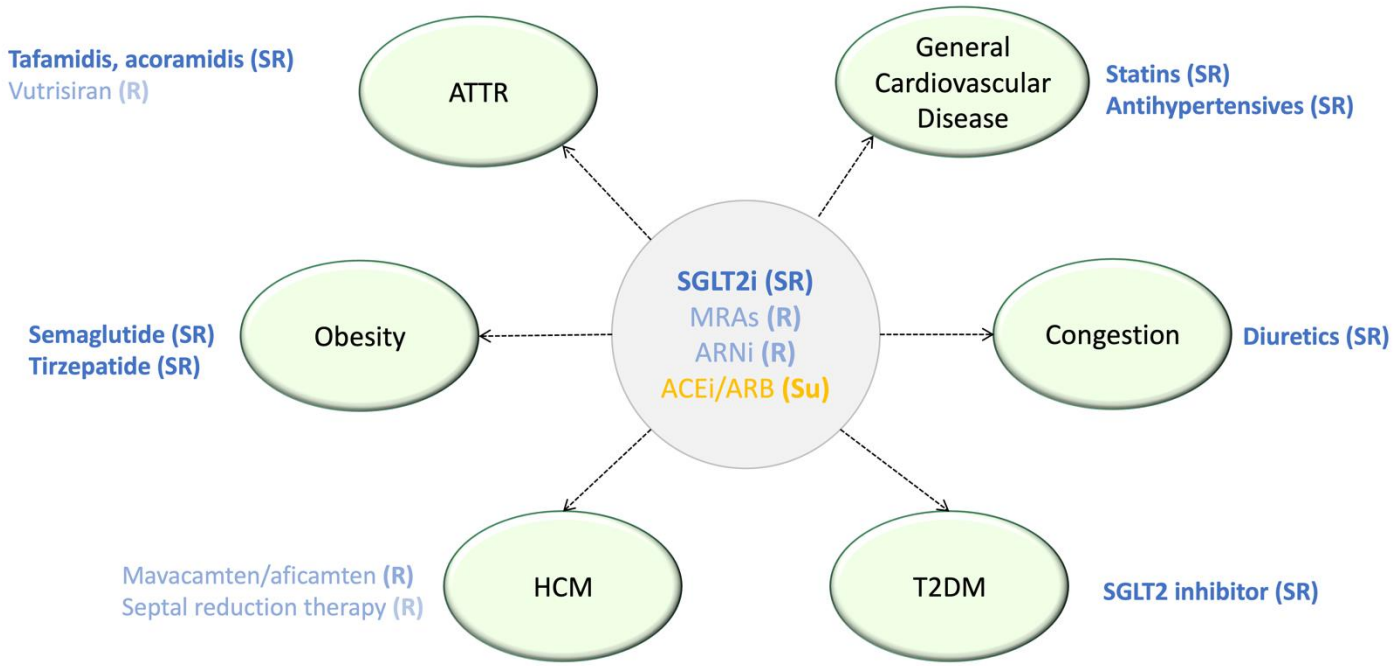


Figure 6: Overview of HFpEF Management

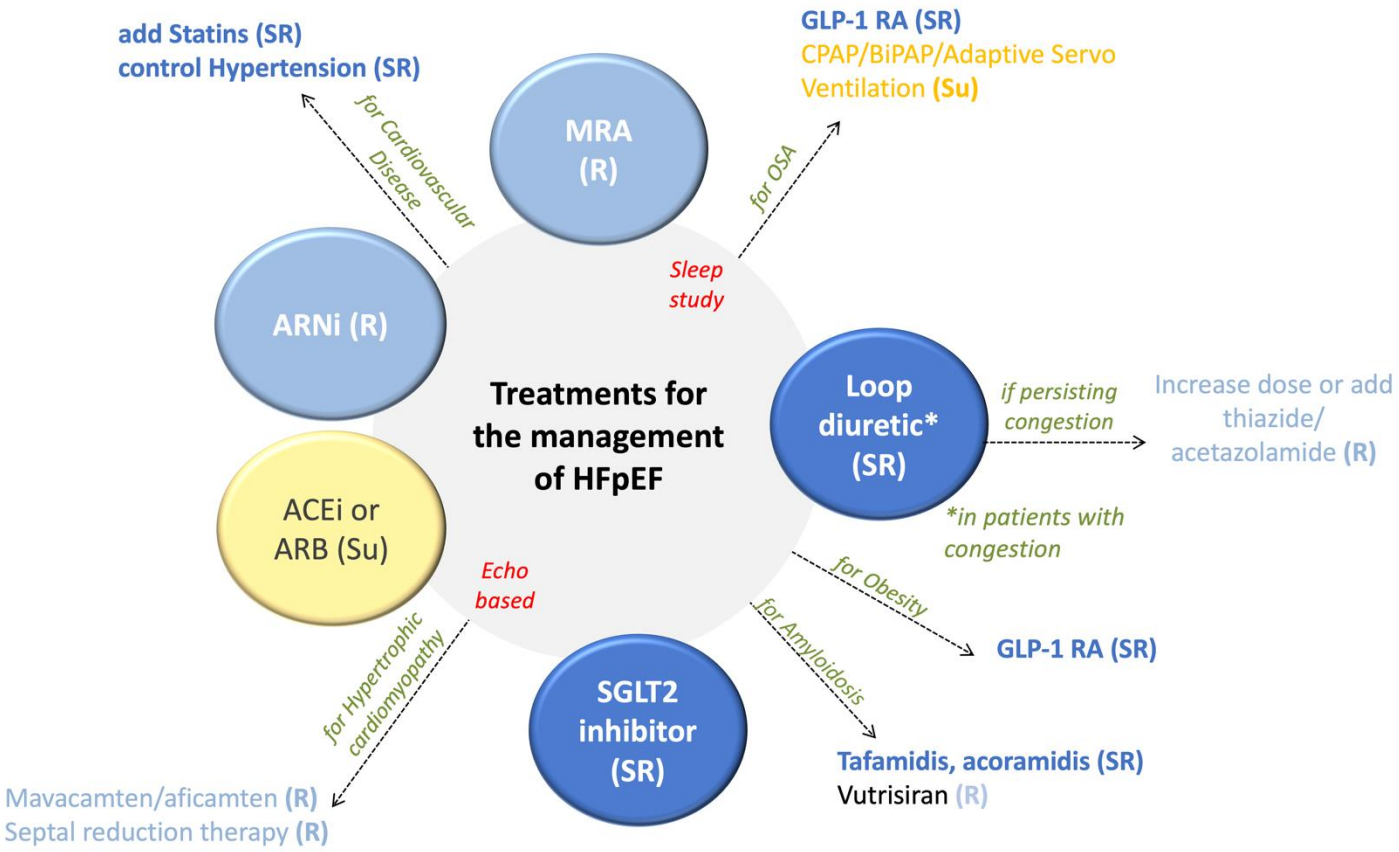


Figure 7: Overview of HFrEF/HFmrEF Management