EDITORIAL

The ten commandments for comprehensive heart failure management

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The South African guidelines for the management of heart failure with a reduced ejection fraction (HFrEF) have been extensively updated and recently published.[1] The guidance is based upon the European Society of Cardiology Guidelines for the treatment of acute and chronic heart failure,[2] and summarises the best current evidence for management of patients with heart failure. It provides information on the definition, diagnosis, and epidemiology of HFrEF in the African context. Best evidence-based therapies for HFrEF are discussed, including established therapies – beta-blockers, angiotensin converting enzyme inhibitors (ACE-i), angiotensin receptor blockers (ARBs), mineralocorticoid receptor antagonists (MRAs), diuretics – that form the cornerstone of heart failure management. These revised guidelines also discuss novel therapies that have recently entered clinical use (angiotensin receptor-neprilysin inhibitor (ARNI), sodium/glucose cotransporter-2 (SGLT2 inhibitors).

The South African guidelines for the management of HFrEF also consider the role of invasive therapies – revascularisation, implantable cardioverter defibrillators (ICDs) and cardiac resynchronisation therapy (CRT) by implantation of a biventricular pacemaker with (CRT-D) or without (CRT-P) an ICD, left ventricular assist device (LVAD) use and orthotopic heart transplantation – with a goal of ensuring efficient utilisation of these expensive therapies in a resource-limited environment. In addition, the role of additional management strategies – digoxin, the combination of hydralazine and nitrates, ivabradine, iron supplementation – is discussed and advice is provided on general preventive strategies (vaccinations).

Importantly, the South African guidelines for the management of HFrEF discuss topics that are of great relevance to the patient with heart failure in sub-Saharan Africa – cardiomyopathy, rheumatic heart disease, HIV-associated cardiovascular disease, peripartum cardiomyopathy and atrial fibrillation – to improve clinical care for these entities that are common causes of heart failure in the region.

TABLE I: Essential principles of comprehensive heart failure management.

1. HFrEF is heart failure with an ejection fraction <40% and diagnosis is suspected clinically followed by confirmatory special investigations with a view to identify an underlying cause.
2. Comprehensive HFrEF management involves numerous treatment modalities.
3. Diuretics provide important symptomatic relief.
4. Beta-blockers, ACE-inhibitors/ARBs and MRAs are the foundation of HFrEF management.
5. Nitrate/hydralazine combination should be considered in black patients.
6. Newer agents add incremental benefit to more established heart failure therapies.
7. There are useful adjunctive agents which improve quality of life for patients who remain symptomatic.
8. Actively look for patients who will benefit from device therapies.
9. Management of atrial fibrillation is needed for many patients with HFrEF.
10. Orthotopic heart transplantation remains an excellent treatment modality for patients with HFrEF refractory to medical therapy.

Historical reports support the view that heart failure therapy is poorly implemented despite good evidence that adherence to clinical practice guidelines improves outcomes in patients with HFrEF.[3] Clinicians are encouraged to implement the recommended interventions to improve both morbidity and mortality in heart failure patients. This requires patient education to promote adherence, overcoming clinical inertia to continue escalation of therapy to achieve comprehensive heart failure care as well as the necessary knowledge base of what treatment a patient can and should be offered.

In this brief article, we discuss 10 key areas of focus in heart failure management – see Table I. While there can be no substitute to read the actual guideline in its entirety, the following essential take-home messages are of relevance:

1. HFrEF is heart failure with an ejection fraction <40% and diagnosis is suspected clinically followed by confirmatory special investigations with a view to identify an underlying cause.

HFrEF is defined as presentation with symptoms and signs of heart failure in the presence of an ejection fraction of 40% or less – see Table II. Most practitioners will, however, implement HFrEF therapy at an ejection fraction cut-off of 50% or less. Further diagnostic modalities are essential to confirm the diagnosis, rule out reversible causes of heart failure (valvular heart disease, pericardial constriction) and reversible causes of left ventricular dysfunction (hypertension, arrhythmia) and to assess the ejection fraction. Investigations helpful in this regard are the electrocardiography (ECG) – a normal ECG makes diagnosis of heart failure unlikely – and echocardiography. NT-pro-BNP, where available is also supportive, and an NT-proBNP <125pg/mL has a negative predictive value of the presence of heart failure of 94%. If there is still doubt after these investigations further imaging by cardiovascular magnetic resonance (CMR) is helpful – Figure 1.

TABLE II: Revised definition and classification of heart failure.

Type of heart failure		
HFrEF	**HFmrEF**	**HFpEF**
Symptoms and signs	**Symptoms and signs**	**Symptoms and signs**
LVEF <40%	LVEF 40% - 49%	LVEF >50%
	Elevated levels of natriuretic peptide (proBNP >125pg/ml or BNP >35pg/ml	Elevated levels of natriuretic peptide (proBNP >125pg/ml or BNP >35pg/ml
	At least 1 additional criterion: • relevant structural heart disease (LVH and/or LAE) • diastolic dysfunction	At least 1 additional criterion: • relevant structural heart disease (LVH and/or LAE) •diastolic dysfunction

HFrEF = heart failure with reduced ejection fraction, HFmrEF = heart failure with mid-range ejection fraction, HFpEF = heart failure with preserved ejection fraction, LVEV = left ventricular ejection fraction, LAE = left atrial enlargement.

Adapted from Ponikowski P, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur Heart J 2016;37(27):2129-2200.

2. Comprehensive HFrEF management involves numerous treatment modalities.

Once the diagnosis of HFrEF is established the patient should be commenced on evidence-based therapies which include lifestyle changes, pharmacological therapies, devices, and surgical interventions – Figure 2.

3. Diuretics provide important symptomatic relief.

Loop diuretics are essential to manage the primary symptoms of heart failure congestion, even though they do not confer survival benefit. The aim is to maintain patients on the lowest possible dose that controls symptoms, and many patients will be able to titrate the dose themselves depending on their symptoms and/or sudden increases in body weight.

4. Beta-blockers, ACE-inhibitors/ARBs and MRAs are the foundation of HFrEF management.

The combination of beta-blockers, ACE-inhibitors/ARBs and MRAs forms the cornerstone of heart failure therapy. Morbidity and mortality benefit of these agents is well-established in large randomised clinical trials (RCTs). It is essential to commence these three agents carefully, at a low dose, with the aim of gradually increasing in a stepwise fashion every 2 - 3 weeks to the maximally tolerated dose. The aim is to achieve the target dose as studied in various RCTs. Issues preventing patients from achieving optimal therapeutic disease include symptomatic hypotension, worsening renal function, worsening symptoms of heart failure or significant bradycardia.

5. Nitrate/hydralazine combination should be considered in black patients.

The most underused therapy for patients with HFrEF in SSA is the combination of hydralazine and nitrates. This vasodilator combination has been shown to have excellent mortality benefit, is well tolerated and has the additional advantage of being relatively safe to prescribe in pregnancy.

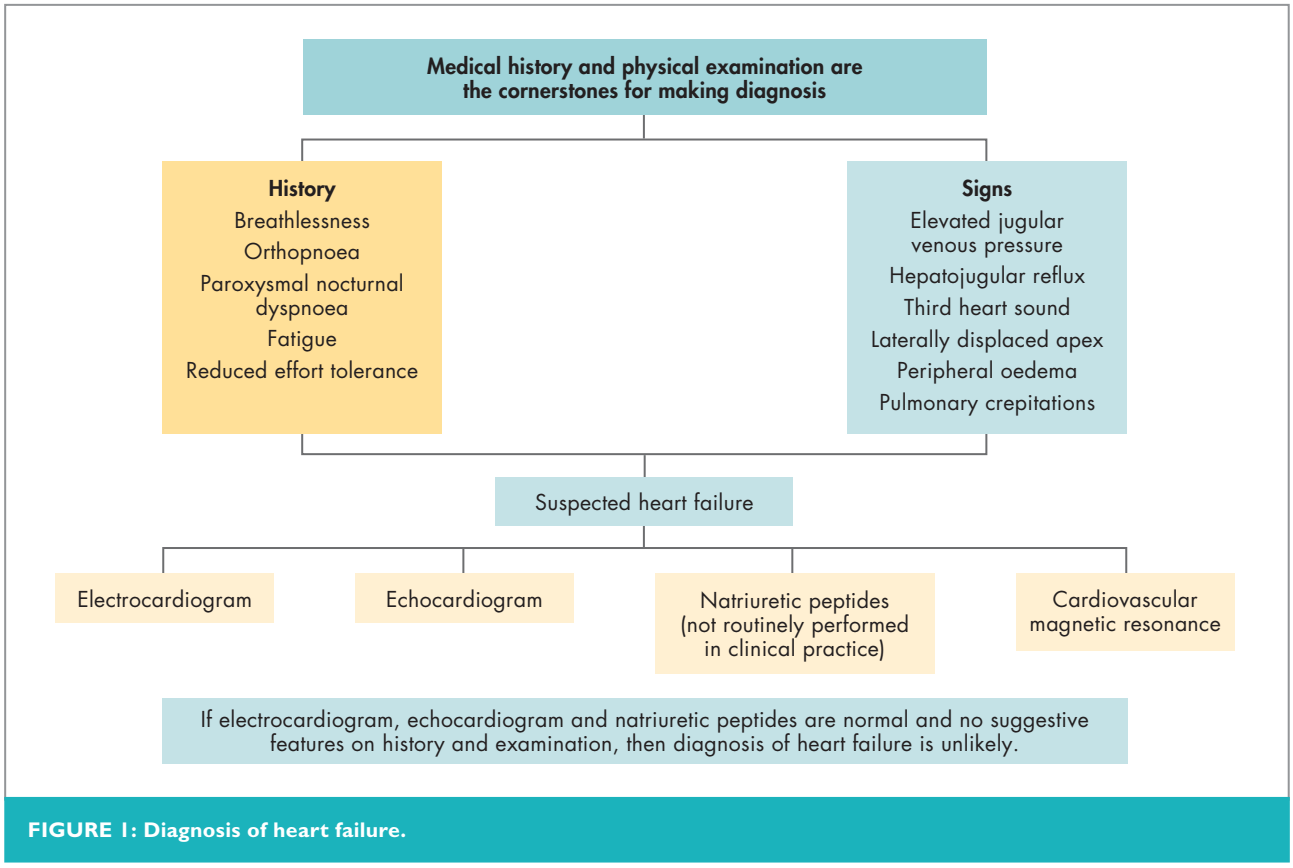

FIGURE 1: Diagnosis of heart failure.

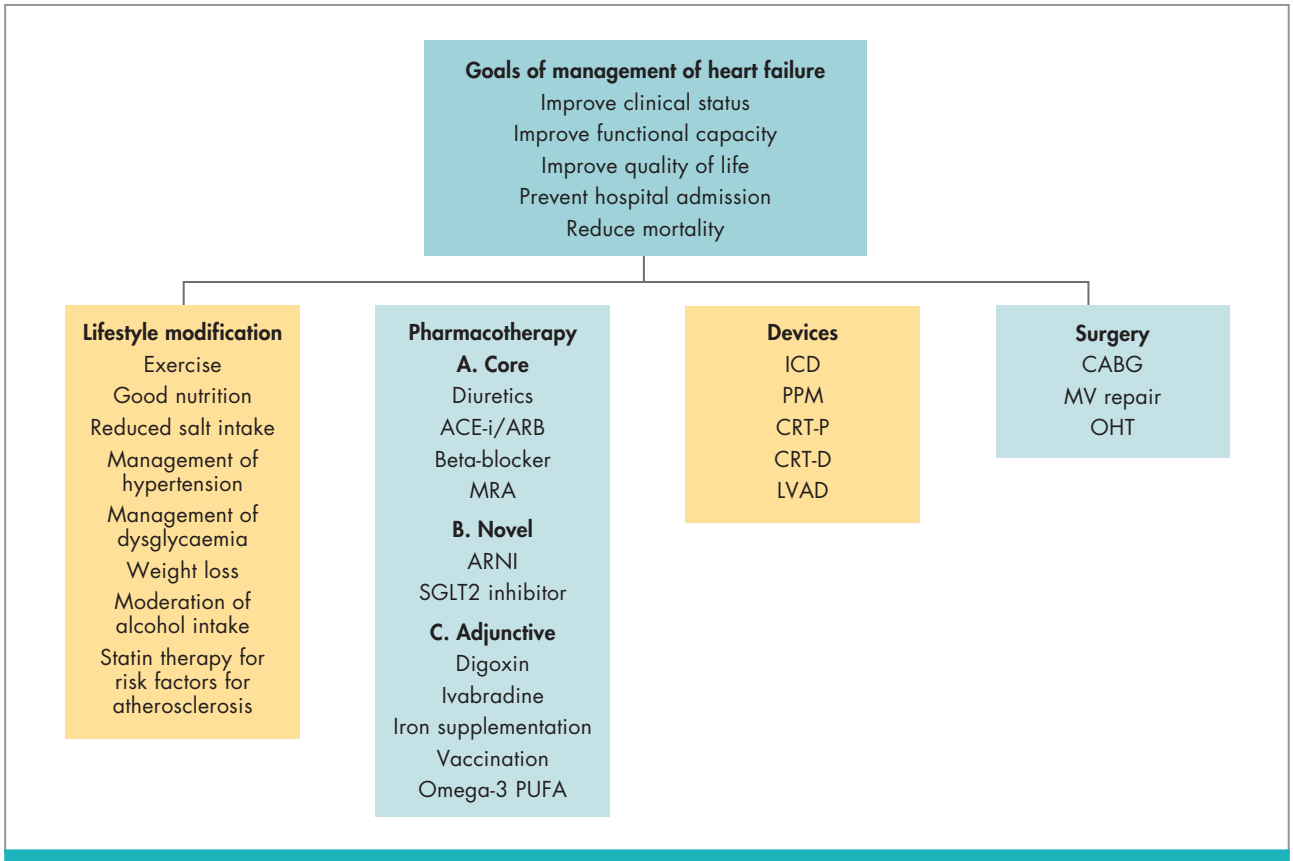

FIGURE 2: Principles of management of heart failure.

It should therefore strongly be considered in black patients with HFrEF in the peripartum period as well as in patients with ongoing symptoms despite beta-blockade, ACE-I/ARBs and MRAs use.

6. Newer agents add incremental benefit to more established heart failure therapies.

SGLT2 inhibitors and ARNI are agents that have recently been introduced in clinical practice in South Africa. These agents reduce cardiovascular death and hospitalisations for heart failure and all patients with HFrEF with ongoing symptoms should be considered candidates for these drugs.

7. There are useful adjunctive agents which improve quality of life for patients who remain symptomatic.

If patients remain symptomatic, the following agents can be added to the drugs already mentioned. Ivabradine, digoxin and intravenous iron (if a patient is iron deficient) are all useful adjunctive therapies that reduce heart failure hospitalisation but have not been shown to reduce mortality.

8. Actively look for patients who will benefit from device therapies.

Cardiac resynchronisation therapy with a biventricular pacemaker should be considered for patients with a QRS width broader than 150ms who remain in refractory heart failure despite maximally tolerated medical therapy. An internal cardioverter-defibrillator is indicated for patients who survive a sudden cardiac death and can be considered for primary prevention, especially if the patient has ischaemic left ventricular dysfunction. Left ventricular assist devices are expensive treatment modalities with a high complication rate – they should be considered in patients who need a bridge to transplantation, though they are increasingly used as destination therapy in many settings.

9. Management of atrial fibrillation is needed for many patients with HFrEF.

Atrial fibrillation is the most common arrhythmia associated with HFrEF, and its presence denotes underlying structural heart disease. Anticoagulation remains by far the most important intervention to reduce the risk of thromboembolic events. Rate control is a reasonable initial strategy but in patients who are young or when the possibility of a tachycardia-induced cardiomyopathy is high, atrial fibrillation ablation may be of value. There should be a low threshold to refer patients with atrial flutter for radiofrequency ablation as the recurrence rate of this arrhythmia is high and rate control can be challenging.

10. Orthotopic heart transplantation remains an excellent treatment modality for patients with HFrEF refractory to medical therapy.

Surgical therapy involves a big spectrum of procedures which include coronary revascularisation (in a select group of patients), percutaneous mitral valve repair and most importantly orthotopic heart transplantation. Heart transplantation has excellent 10-year survival rates and should be considered in patients who deteriorate in terms of functional state despite adequate medical and device therapy.

In summary, there are numerous interventions that improve quality of life and increase survival in patients with HFrEF. The goals of comprehensive HFrEF therapy should be making a correct diagnosis, to ascertain the underlying cause of heart failure, to relieve symptoms, increase survival and to improve quality of life. Therefore, the importance of treating patients with all modalities that offer proven outcome benefit to achieve these goals cannot be overstated. At all times, every effort should be made to achieve guideline directed therapy.[4] However, it is important to remember that while guideline documents summarise the best clinical practice, they remain just what they are – guidelines. Therapy needs to be tailored to a given patient's underlying clinical state, individual preferences, and social circumstances to achieve the best clinical outcome.

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