DILATED CARDIOMYOPATHY AND TREATMENT OF CHRONIC HEART FAILURE

Dilated cardiomyopathy of unknown cause is one of the leading causes of heart failure in Africa.

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For the past 10 years Karen Silwa's research has focused mainly on immune activation in heart failure, and idiopathic and peripartum cardiomyopathy. In recent years she has established research collaborations with various national and international centres. She is a founding member of the new World Heart Failure Society, a working group member of the international campaign to revitalise academic medicine (ICRAM), and on the editorial board of The Lancet.

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EPIDEMIOLOGY

Dilated cardiomyopathy (DCM) of unknown cause vies with rheumatic heart disease and hypertension as one of the leading causes of heart failure in Africa. Whereas the incidence and prevalence of DCM in the USA is reported to be 36.5 per 100 000 individuals, there are no population-based data on the burden of DCM in Africa. The prevalence of idiopathic DCM as a cause of heart failure in hospitalised cases is higher in Africa than in Europe and North America, where cardiomyopathy is rare. This apparent difference in prevalence may be related to a greater preponderance of nutritional and inflammatory heart diseases in Africa.

DCM occurs at any age, but is common in the third and fourth decades of life. Men are affected twice as commonly as women. The majority of patients with DCM, especially those over 55 years of age, die within 5 years of their first symptoms. Chetty and Mitha reported 65% mortality over a 3-year period in a small study of 20 black patients with DCM. About 25% improve spontaneously. The most common causes of death are progression of congestive heart failure or arrhythmias. A persistently low arterial pressure and mitral and/or tricuspid incompetence carry a poor prognosis.

AETIOLOGY

Although the causes of idiopathic DCM are largely unknown, manifestation of the disease probably represents a final common expression of myocardial damage that could be provoked by multiple insults, including haemodynamic, infective, immunological, toxic, nutritional and genetic factors. Possible aetiological factors that have been examined in Africa include burnt-out, untreated hypertension, alcohol, thiamine deficiency, pregnancy and childbirth, viral myocarditis and HIV, iron overload and other metabolic causes, genetic factors, and immune mechanisms.

METHODS FOR DIAGNOSIS OF DCM AND HEART FAILURE IN CLINICAL PRACTICE

Heart failure should never be the only diagnosis! Symptoms and signs are important as they alert the observer to the possibility that heart failure exists. The clinical suspicion of DCM and heart failure must be confirmed by objective tests with the aim of documenting the degree of left ventricular dilatation and dysfunction (Fig. 1 – modified ESC Guidelines, 2005).

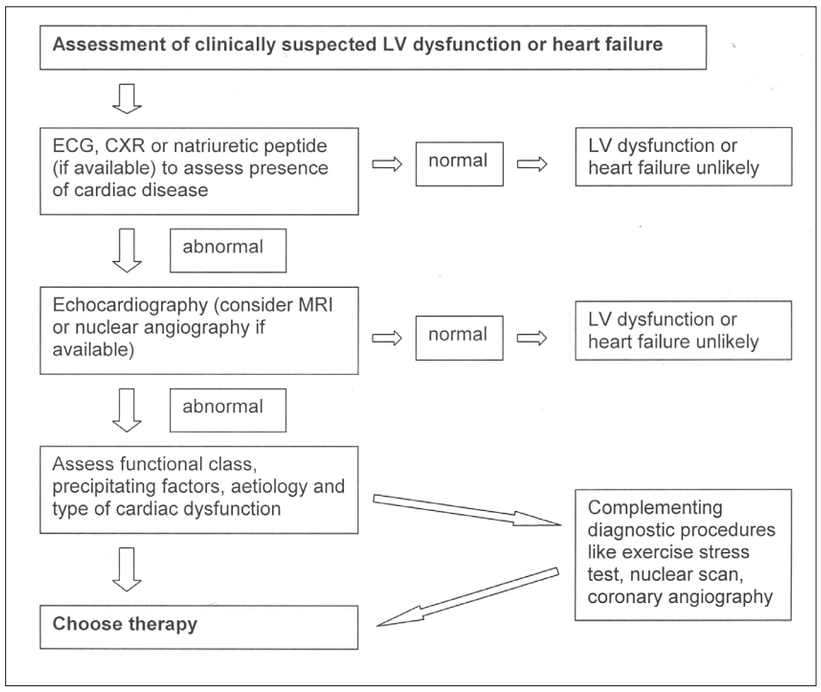

Fig.1. Algorithm for the diagnosis of left ventricular dysfunction or heart failure.

There is poor correlation between the symptoms and the severity of cardiac dysfunction. However, symptoms are related to prognosis, particularly if persistent after therapy.

TREATMENT OF CHRONIC HEART FAILURE

Aims

The aims in treating heart failure are the following:

- prevention
- controlling the diseases leading to cardiac dysfunction
- preventing the progression to heart failure once dysfunction has been diagnosed
- improvement of symptoms
- improving survival.

Prevention of heart failure should always be the primary objective. When left ventricular systolic dysfunction is already present the most important objective is to correct, where possible, the underlying cause of ventricular dysfunction (e.g. alcohol, drugs, ischaemia, thyroid disease) (Table I).

Table I. **Recommendations for patients at high risk of developing heart failure**

Control of systolic and diastolic hypertension
Treatment of lipid disorders in accordance with recommended guidelines
Avoidance of patient behaviours that may increase the risk of heart failure (e.g. smoking, alcohol abuse)
ACE inhibition in patients with a history of atherosclerotic vascular disease, diabetes mellitus, or hypertension and associated cardiovascular risk factors
Control of ventricular rate in patients with supraventricular tachyarrhythmias
Periodic evaluation for signs and symptoms of heart failure

ACC/AHA Guideline for Evaluation and Management of Heart Failure
(*J Am Coll Cardiol* 2001; **38:** 2101-2113).

MANAGEMENT OF CHRONIC HEART FAILURE

Heart failure is a complex syndrome and the stepwise therapeutic approach includes general advice and non-pharmacological measures, pharmacological therapy and insertion of mechanical devices.

Non-pharmacological management

Heart failure patients and their relatives should receive general advice. Patients should weigh themselves regularly at a fixed time (e.g. in the morning) and carefully monitor weight gain. In the case of unexpected weight gain of > 2 kg in 3 days, the patient should alert a doctor or adjust his/her diuretic dose accordingly. Fluid restriction to 1.5 - 2 l/day oral intake is advised in advanced heart failure. The treatment of heart failure includes weight reduction in obese patients. However, 50% of patients with severe heart failure develop clinical or subclinical malnutrition that is called cardiac cachexia, an important predictor of reduced survival.

In acute heart failure physical rest or bed rest is recommended. However, stable patients (New York Heart Association Functional Class (NYHA FC) II - III) should be encouraged to exercise and advised on how to carry out daily physical activities that do not induce symptoms. Standardised recommendations for exercise training in heart failure patients have been published by the European Society of Cardiology Working Group on Cardiac Rehabilitation.

Pharmacological therapy

Surveys of prescribing patterns in both hospital and primary care settings have usually shown delays in translating the evidence from clinical drug trials into routine practice. Patients are thereby denied the benefit of drug therapies proven to improve

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well-being and to prolong life. Less than 50% of patients with heart failure are actually on ACE-inhibitors and even in the highly supervised environment of contemporary heart failure trials, beta-blocker use ranges from 35% to 55%. It is therefore important not to lose sight of our primary goal: the use of ACE-inhibitors and beta-blockers in all patients with heart failure.

Practical recommendations for the use of ACE-inhibitors, beta-blockers, aldosterone antagonists and angiotensin-receptor blockers (ARBs) in heart failure have been published recently.

The current available and recommended types of pharma cological management are outlined in Table II.

Practical recommendations

After establishing the clinical diagnosis of heart failure and possible introduction of a diuretic to treat symptoms and signs of sodium and water retention the first goal should be to assess left ventricular function using echocardiography, radionuclide ventriculography and radiological left ventricular angiography. This first diagnostic step is regarded as representing the minimum standard of care.

The next step requires the initiation of first-line therapy, which, for all patients with heart failure due to left ventricular dysfunction, consists of both an ACE-inhibitor and a beta-blocker, unless there are contraindications.

Recent trials have suggested that a beta-blocker-first strategy is safe and potentially beneficial. A study of black DCM patients from Soweto, Johannesburg, evaluated the therapeutic value of initiating a beta blocker (carvedilol) before an ACE inhibitor in the treatment of heart failure. The carvedilol-first group reached a greater total carvedilol dose, and had a better improvement of ejection fraction and symptoms. The recently published Cardiac Insufficiency Bisoprolol Study (CIBIS III) trial proved both the safety and efficacy of a beta-blocker-first therapy in heart failure. However, it is important to understand that the greatest benefit for our patients is realised when both agents are used.

Step 3 requires the prescription of additional therapy for patients with persistent signs and symptoms of heart failure. Guidelines recommend the addition of spironolactone in patients with severe symptoms (NYHA FC III - IV). There is also new evidence that ARBs should be added in patients with persistent symptoms (NYHA FC III - IV). It is important to note that there is insufficient evidence as to whether both an ARB and spironolactone should be used in addition to an ACE-inhibitor.

The main role of cardiac glycosides (e.g. digoxin) in heart failure is for patients presenting with atrial fibrillation when rapid control of ventricular rate is needed (which cannot be achieved with cautious introduction and up-titration of a beta-blocker).

Table II. **Pharmacological approach to chronic left ventricular systolic dysfunction**

	Asymptomatic LV dysfunction (NYHA I)	**Symptomatic heart failure (NYHA II)**	**Worsening heart failure (NYHA III - IV)**	**End-stage heart failure (NYHA IV)**
ACE-inhibitor	Indicated	Indicated	Indicated	Indicated
Angiotensin receptor blocker	Only indicated if ACE-inhibitor intolerant	Indicated with or without ACE-inhibitor	Indicated with or without ACE-inhibitor	Indicated with or without ACE-inhibitor
Diuretic	Not indicated	Indicated in presence of fluid retention	Indicated, combination of diuretics	Indicated, combination of diuretics
Beta-blocker	Post MI	Indicated	Indicated (under specialist care)	Indicated (under specialist care)
Aldosterone antagonists	Recent MI	Recent MI	Indicated	Indicated
Cardiac glycosides	Atrial fibrillation	Atrial fibrillation or when in sinus rhythm and improved from more severe heart failure	Indicated	Indicated

In the recent African-American Heart Failure Trial (A-Heft), the combination of hydralazine (initiated at a dose of 37.5 mg and titrated to a target dose of 75 mg tds) and isosorbide dinitrate (initiated at a dose of 20 mg and titrated to a dose of 40 mg tds) improved survival and additional outcomes when added to ACE-inhibitors, spironolactone and beta-blockers in African-Americans with NYHA FC III - IV heart failure.

Pacemakers and implantable cardioverter defibrillators (European Society of Cardiology Guidelines)

Pacemakers have been used in patients with heart failure to treat bradycardia when conventional indications exist. Pacing of the right ventricle only in patients with systolic dysfunction will induce ventricular dys-synchrony and may increase symptoms.

Resynchronisation therapy using bi-ventricular pacemakers can be considered in patients with reduced left ventricular ejection fraction, ventricular dys-synchrony (QRS width > 120 ms) and in those who remain symptomatic (NYHA FC III - IV) despite optimal medical therapy to improve symptoms. Recent publications have shown that, in addition to improving symptoms and exercise capacity, bi-ventricular pacing has a significant beneficial effect on mortality.

An implantable cardioverter defibrillator (ICD) in combination with bi-ventricular pacing can be considered in patients who remain symptomatic with severe heart failure (NYHA FC III - IV) with a left ventricular ejection fraction $\leq$ 35% and QRS duration of $\geq$ 120 ms to improve mortality and morbidity.

CONCLUSIONS

Under-prescribing and under-dosing of ACE-inhibitors and beta-blockers – both drugs that reduce mortality in patients with heart failure – is a major problem worldwide. The objective is to treat all patients with both an ACE-inhibitor and a beta-blocker, ideally at the target doses used in large randomised trials. There is now good evidence that this goal can be achieved if a concerted effort is made in hospitals, outpatient clinics and the community.

Further reading

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IN A NUTSHELL

Prevention of heart failure is of the utmost importance in patients at risk.

Heart failure should never be the only diagnosis.

All patients with symptoms of heart failure should be investigated for the presence of left ventricular dysfunction.

Patients should be advised to monitor weight gain.

Patients with severe heart failure often develop malnutrition that is called cardiac cachexia, an important predictor of reduced survival.

In acute heart failure physical rest or bed rest is recommended.

Stable patients should be encouraged to and advised on how to carry out daily physical activities that do not induce symptoms.

All patients with heart failure should be treated with both an ACE-inhibitor and a beta-blocker up-titrated to recommended doses if tolerated.

An implantable cardioverter defibrillator (ICD) in combination with bi-ventricular pacing can be considered in patients who survived cardiac arrest or who have sustained ventricular tachycardia which is associated with severe heart failure (NYHA FC III - IV) with a left ventricular ejection fraction $\leq$ 35% and QRS duration of $\geq$ 120 ms to improve mortality and morbidity.