

Heart failure

Ker JA, MBChB, MMed(Int), MD

Faculty of Health Sciences, University of Pretoria

Correspondence to: Prof James Ker, e-mail: james.ker@up.ac.za

Abstract

Heart failure is a clinical syndrome that can result from any structural or functional cardiac disorder that impairs the performance of the ventricle: either to eject blood (systolic dysfunction) [or reduced ejection function] or to fill with blood (preserved ejection fraction or diastolic heart failure).

SA Fam Pract 2010;52(3): 213-215

What is new?

About half of all clinical heart failure patients have preserved ejection fraction and this condition seems to be increasing in prevalence, especially with increasing age. The most effective therapy for this form of heart failure is currently unknown.

Comorbidities have a large influence on worse outcome in heart failure. Systemic hypertension, ischaemia of the ventricle, diabetes mellitus, chronic obstructive pulmonary disease, sleep apnoea, depression, anaemia and chronic renal disease add considerable complexities to diagnosis and management of heart failure.

Biochemical testing for heart failure

Measurement in plasma of brain natriuretic peptide or its precursor, N terminal proBNP (NT-proBNP) has aided in the diagnosis of heart failure. An elevated NT-proBNP is caused by stretching of cardiac myocytes and therefore the test cannot distinguish between left ventricular failure or right ventricular failure from other causes. A low BNP (or NT-proBNP) has a high negative predictive value, making it a useful rule-out test.

Stages of heart failure

There are four recognisable stages in the progression of heart failure.

Stage A: There are no symptoms or signs of heart failure. The heart has a normal structure and function, but the patient has *risk factors* for heart failure:

hypertension, elevated cholesterol, diabetes, alcohol abuse, cardiotoxic drugs (e.g. chemotherapeutic drugs, cocaine, etc).

Stage B: There are no symptoms or signs but the heart of the patient has a structural abnormality (e.g. left ventricular hypertrophy, myocardial infarction, heart murmur, LV dilatation) or is functionally abnormal e.g. reduced ejection fraction, and diastolic dysfunction.

Stage C: There are now symptoms and signs of heart failure.

Stage D: These patients have progressed and still have marked/resistant symptoms despite maximal medical therapy.

Therapy for heart failure (What works?)

Physical activity is now recommended for all heart failure patients, except for those who are acutely decompensated.

Prevention of heart failure is possible through adequate blood pressure control in hypertensives, control of ischaemic heart disease occurrence and diabetes mellitus [*Stage A*]. Preventative treatment with an angiotensin-converting enzyme inhibitor (ACE-I) or angiotensin-receptor blocker (ARB) are given to individuals with high risk but normal ejection fraction (HOPE study; ONTARGET) or those with asymptomatic left ventricular dysfunction [*Stage B*]. Treatment post myocardial infarction with a beta-blocker [*Stage B*] can also slow progression of heart failure. For *Stage C* heart failure (symptoms and signs of heart failure),

There's no need to treat your patient's risk factors like different patients.



Hypertension and dyslipidaemia are relatively well-diagnosed, but only 9% of patients with both risk factors are controlled ⁽¹⁾

Caduet®:

- Targets 2 modifiable risk factors simultaneously, reducing risk of CV events ⁽²⁾
- The coadministration of Norvasc® and Lipitor® results in significant reductions in non-fatal MI and fatal CHD ⁽³⁾
- Simplifies treatment, which may lead to improved adherence and increased patient satisfaction ⁽⁴⁾



**Hypertension
Dyslipidaemia**



References

1. Wong ND, Lopez V, Franklin S, Tang S, Williams GR. Prevalence, treatment status, and control of concomitant hypertension and dyslipidemia in US adults in 2001-2002. *Circulation* 2005;112(17 suppl 2): 831. Abstract 3840.
2. Mandis AJ. JEWEL Program: Optimizing Treatment for Patients with Hypertension and Additional Cardiovascular Risk Factors. Abstract presented at the European Meeting on Hypertension, June 12-16, 2006, Madrid, Spain.
3. Sever PS, Dahlöf B, Poulter NR, Wedel H, Beavers G, Caulfield M, et al for the ASCOT investigators. Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial-Lipid lowering Arm (ASCOT-LLA): a multicentre randomised controlled trial. *Lancet* 2003;361:1149-1158.
4. Nichol MB, Patel BV, Thiebaud P, Leslie RS, Tang SSK, Solomon H, et al. A single pill combining antihypertensive and statin therapies improves patient adherence compared with multi-drug combinations: results from the Caduet® adherence research program and education (CARPE) – PBM adherence study. Abstract P-526A. *J Clin Hypertension* 2006;8(6):456.

[S] CADUET™ 5 mg/10 mg, 5 mg/20 mg, 5 mg/40 mg, 5 mg/80 mg, 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg film coated tablets (39/7.0/0326, 0327, 0328, 0329, 0330, 0331, 0332, 0333). **COMPOSITION:** Each film coated tablet contains 5 mg/10 mg, 5 mg/20 mg, 5 mg/40 mg, 5 mg/80 mg, 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg amlodipine besylate/atorvastatin calcium dosage strengths respectively. **PHARMACOLOGICAL CLASSIFICATION:** A 7.0 Vascular Medicines & A 7.6 Other **INDICATIONS:** Patients at increased cardiovascular risk due to concomitant hypertension and dyslipidaemia and/or patients with angina and concomitant dyslipidaemia. CADUET may be used either alone or in combination with other anti-hypertensive or anti-anginal drugs. **WARNINGS:** Hepatic effects: Due to the atorvastatin component, CADUET should be administered with caution in patients with impaired liver function. **Skeletal muscle effects:** Patients should be advised to promptly report unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever. CADUET therapy should be discontinued if markedly elevated CPK levels occur or myopathy is diagnosed or suspected. **Before treatment:** CADUET should be prescribed with caution in patients with pre-disposing factors for rhabdomyolysis. **CONTRA-INDICATIONS:** Known hypersensitivity to dihydropyridines, amlodipine, atorvastatin or any component of this medication; Active liver disease or unexplained persistent elevations of serum transaminases exceeding 3 times the upper limit of normal, myopathy or in patients who are pregnant, breast-feeding, or of child-bearing potential not using appropriate contraceptive measures. **DOSAGE AND DIRECTIONS FOR USE: Initial Therapy:** The recommended starting dose of CADUET should be based on the appropriate combination of recommendations for the amlodipine and atorvastatin components considered separately. The maximum dose of the amlodipine component of CADUET is 10 mg once daily. The maximum dose of the atorvastatin component of CADUET is 80 mg once daily. **Substitution Therapy:** CADUET may be substituted for its individually titrated components. Patients may be given the equivalent dose of CADUET or a dose of CADUET with increased amounts of amlodipine, atorvastatin or both for additional antihypertensive effects, blood pressure lowering, or lipid lowering effect. CADUET may be used to provide additional therapy for patients already on one of its components. As initial therapy for one indication and continuation of treatment of the other, the recommended starting dose of amlodipine/atorvastatin should be selected based on continuation of the component being used previously and on the recommended starting dose for the component being added. **SIDE-EFFECTS AND SPECIAL PRECAUTIONS:** Common: Somnolence, dizziness, headache, palpitations, flushing, abdominal pain, nausea, oedema, fatigue, allergic reaction, insomnia, hypoaesthesia, paraesthesia, diarrhoea, dyspnoea, constipation, flatulence, pruritus, rash, myalgia, arthralgia, back pain, asthenia, chest pain. **LICENSE HOLDER:** Pfizer Laboratories (Pty) Ltd, Reg. No.: 1954/000781/07, P.O. Box 783720, Sandton, 2146, South Africa. Tel.: 0860 PFIZER (734397) P1 Ref: 02/2006-4. Please refer to detailed package insert for full prescribing information. 01/CAD/02/2008/JA.



Working for a healthier world™

Pfizer Call Centre: 0860 Pfizer (734 937)
Website: www.Pfizer.co.za

neuro-hormonal inhibitions for patients with reduced ejection fraction has mortality benefits. ACE-inhibitors, ARBs, beta-blockers (bisoprolol, metoprolol), alpha-beta blockers (carvedilol) and aldosterone antagonists all are evidence-based therapies for mortality reduction. Cardiac resynchronisation therapy for heart failure with biventricular pacemakers with or without intracardiac defibrillators are recent additions to mortality reduction therapy. Isobide dinitrate plus hydralazine therapy have mortality benefits especially in African patients, but can be tried in others as well.

What does not reduce mortality? (What does not work?)

Statins given purely for heart failure do not reduce mortality. Digoxin, once the standard treatment, has not reduced mortality compared to placebo, in patients with low ejection fraction and in patients with normal ejection fraction. Digoxin is used to control atrial fibrillation should it occur in heart failure.

Calcium channel blockers also have no mortality benefit.

Inotropic therapy is associated with increased mortality.

What is the problem with treatment?

The majority of the randomised clinical trials in heart failure were done on patients with reduced ejection fraction. These patients have improved mortality on standard anti-neuro-hormonal therapy.

However, the therapy of heart failure patients with preserved ejection fraction has very little evidence. The few trials done in this condition have not shown the same mortality benefit. Much work needs to be done for patients with heart failure and preserved ejection fractions (almost half of all heart failure patients).

Bibliography

- 1 Yan AT, Yan RT, Liu PP. Narrative review: Pharmacotherapy for chronic heart failure: Evidence from recent clinical trials. *Ann Intern med* 2005;142:132–145.
- 2 Aronow WS. Epidemiology, Pathophysiology, Prognosis and treatment of systolic and diastolic heart failure. *Cardiol in Rev* 2006;14:108–124.
- 3 Lee DS, Gona P, et al. Relation of disease pathogenesis and risk factors to heart failure with preserved or reduced ejection fraction. Insights from Framingham. *Circulation* 2009;119:3070–3077.
- 4 Krum H, Abraham WT. Heart failure. *Lancet* 2009;373:941–955.