Heart failure prevention: a priority

Each year the number of heart failure patients rises with an annual increase in new patients of 10 per cent. Prevention of heart failure is therefore an important goal but physicians are currently not doing enough in this regard. Every reasonable opportunity should be utilised to assess left ventricular function in populations at a high risk of heart failure. **Dr Prithwish Banerjee** discusses the conditions that can lead to heart failure and examines the best treatment options.

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The ever increasing burden of heart failure (HF) is a bitter reality worldwide. In the UK between three to 20 per 1000 population are currently suffering from HF[1]. The number increases to more than 80 per 1000 population above the age of 75. Year on year the number of HF patients rises with at least one new case per 1000 population and an annual increase in new patients of 10 per cent[1]. Measures to stem the tide of HF must now be put in place and a priority should be to focus on the prevention of new cases.

Risk factors for HF

A number of risk factors[2] predispose individuals to developing left ventricular (LV) remodelling and subsequent HF due to LV systolic or diastolic dysfunction. The process may take years[3]. Myocardial infarction (MI) carries an eight to 10 fold risk of developing HF and its prevention therefore is of critical importance[4]. Treatment of systemic hypertension, with or without LV hypertrophy, also reduces the incidence of HF, both due to systolic and diastolic dysfunction[5]. Whereas, the incidence and prevalence of HF in type 2 diabetes is 7.7 per cent and 11.8 per cent respectively[6]. The other modifiable risk factors for HF include hyperlipidaemia, obesity, alcohol excess, smoking, valve disease and cardiotoxic drugs[2,7,8]. All of these risk factors need to be treated aggressively[2].

Treatment of risk factors

Diabetes patients with one or more risk factors or those with microalbuminuria or smoking habits should be given an angiotensin converting enzyme (ACE) inhibitor[2]. Hyperlipidaemia should be treated with statins, obesity with weight loss and increase in physical activity, while alcohol excess and smoking should be managed with a change of habit. Cardiotoxic drugs should be used with caution and there should be proper echocardiographic monitoring.

This article will now discuss in further detail some of the various conditions that can lead to HF and review best treatment options.

Asymptomatic LV systolic dysfunction

Studies indicate that the prevalence of asymptomatic LV systolic dysfunction (ALVD) in some populations is from just under eight per cent to 16 per cent[9-12] and this rises with age. Patients with ALVD have approximately half the mortality rate (five per cent annual rate) of those with overt symptoms of HF but their risk of death is five to six times that of a normal age matched population[2].

In the Study of Left Ventricular Dysfunction (SOLVD)[13], patients with untreated ALVD developed overt HF at a 10 per cent annual rate, with a further eight per cent annual risk of death or hospitalisation for HF. An attempt to identify

those that have ALVD is therefore required and would allow us to focus on preventing their progression to overt HF. Adopting a low threshold for assessment of LV function in populations at a high risk of cardiovascular disease is likely to reveal such subjects. A general awareness therefore of the need to assess LV function early and more frequently (during a reasonable clinical opportunity) is required in individuals with diabetes, hypertension, hyperlipidaemia, and in those with previous cardiovascular disease.

Treatment

There is good evidence that in such subjects with a high cardiovascular risk early intervention with ACE inhibitors, angiotensin receptor blockers (ARBs), statins or antiplatelet therapy with clopidogrel significantly reduces the occurrence of HF even when LV systolic function is normal[14-18].

If asymptomatic LVSD develops, an ACE inhibitor is recommended to prevent progression to HF[19]. A beta-blocker should also be added if this has occurred after an MI[19]. Clinical opportunities to assess LV function may include admissions with acute coronary syndromes (ACS); admissions with poorly controlled (or complications of) hypertension, diabetes, gross hyperlipidaemia or alcoholism; and prior to major surgery under a general anaesthetic. Those with a family history of cardiomyopathies may also be considered for early assessment of LV function since relatives of those with idiopathic dilated cardiomyopathy often have asymptomatic LV dilatation and may be at increased risk for developing HF[20]. In addition, those with a history of alcohol excess or cardiotoxic drug therapy are likely to have ALVD.

LV systolic function after MI

With the development of the MINAP (Myocardial Infarction National Audit Project) database[21], recording LV systolic function in all hospitalised ACS patients has become mandatory in the UK. However, there is need to assess LV function early after ACS.

Treatment

Therapies such as the aldosterone antagonist eplerenone have been shown to be effective in such patients post MI. The EPHESUS trial randomised 642 patients three to 14 days after acute MI, if they had signs and symptoms of HF and an LVEF ≤40 per cent, to eplerenone or placebo on top of optimal medical treatment. A significant reduction in overall mortality, death from cardiovascular causes or hospitalisation from CVS causes was seen in the eplerenone group at a mean follow-up of 16 months[22].

Much of the benefits occurred early. At 30 days after randomisation[23], eplerenone reduced the risk of all-cause mortality by 31 per cent (3.2 per cent *versus* 4.6 per cent in eplerenone and placebo-treated patients, respectively; $p = 0.004$) and reduced the risk of CV mortality/CV hospitalisation by 13 per cent (8.6 per cent *versus* 9.9 per cent in eplerenone and placebo-treated patients, respectively; $p = 0.074$). Eplerenone also reduced the risk of CV mortality by 32 per cent ($p=0.003$) and the risk of sudden cardiac death by 37 per cent ($p=0.051$). In order to commence eplerenone early after MI all such patients must have an early assessment of LV function done, preferably by echocardiography.

Valve disease post MI

Cardiac remodeling following MI is accepted as a determinant of the clinical course of HF. Patients with valve disease or congenital heart disease should be assessed by a specialist and considered for early correction to prevent development of HF[18]. In view of frequent instances of missed surveillance of valve disease leading to HF, particularly in aortic stenosis and mitral regurgitation, a case for early elective surgery has been made in these situations well before symptoms or LV dysfunction develop[24] or current criteria for operating are achieved.

Treatment

All patients with a history of MI should be commenced on an ACE inhibitor and a beta-blocker to delay progression to HF[19]. Drug therapy with ACE inhibitors, ARBs, beta-blockers and aldosterone antagonists have all been shown to limit or reverse remodeling if started early in the post infarct stage[25,26]. Healthy lifestyle choices should be encouraged such as abstinence from smoking, regular exercise, weight reduction and avoiding excess alcohol[18].

Other prevention measures

Percutaneous intervention (PCI) for coronary disease has become widely prevalent as a result of advancing technology enabling more complex coronary disease to be tackled. Even the very elderly (eg, >85 year olds) with CHD, who were previously managed with medical treatment, are now being increasingly considered for coronary intervention. The use of techniques that minimise LV systolic dysfunction

References

1. Coronary heart disease: national service framework for coronary heart disease – modern standards and service models. Chapter 6: heart failure. DoH, UK, 2000
2. Comprehensive Heart Failure Practice Guideline. *Journal of Cardiac Failure* 2006; **12**: e1–e122
3. Moser M, Hebert PR. Prevention of disease progression, left ventricular hypertrophy and congestive heart failure in hypertension treatment trials. *J Am Coll Cardiol* 1996; **27**: 1214–8
4. Arnold JM, Yusuf S, Young J, *et al.* Prevention of Heart Failure in Patients in the Heart Outcomes Prevention Evaluation (HOPE) Study. *Circulation* 2003; **107**: 1284–90.
5. Baker DW. Prevention of heart failure. *J Card Fail* 2002; **8**: 333–46
6. Nichols GA, Hillier TA, Erbey JR, Brown JB: Congestive heart failure in type 2 diabetes: prevalence, incidence, and risk factors. *Diabetes Care* 2000; **24**: 1614–19
7. He J, Ogden LG, Bazzano LA, *et al.* Risk factors for congestive heart failure in US men and women: NHANES I epidemiologic follow-up study. *Arch Intern Med* 2001; **161**: 996–1002
8. Seymour L, Bramwell V, Moran LA. Use of dexrazoxane as a cardioprotectant in patients receiving doxorubicin or epirubicin chemotherapy for the treatment of cancer. *Cancer Prev Control* 1999; **3**: 145–59
9. McDonagh TA, Morrison CE, Lawrence A, *et al.* Symptomatic and asymptomatic left-ventricular systolic dysfunction in an urban population. *Lancet* 1997; **350**: 829–33
10. Mosterd A, Hoes AW, de Bruyne MC, *et al.* Prevalence of heart failure and left ventricular dysfunction in the general population; The Rotterdam Study. *Eur Heart J* 1999; **20**: 447–55
11. Rodeheffer RJ, Jacobsen SJ, Gersh BJ, *et al.* The incidence and prevalence of congestive heart failure in Rochester, Minnesota. *Mayo Clin Proc* 1993; **68**: 1143–50
12. Lee ET, Cowan LD, Welty TK, *et al.* All-cause mortality and cardiovascular disease mortality in three American Indian populations, aged 45-74 years, 1984-1988. The Strong Heart Study. *Am J Epidemiol* 1998; **147**: 995–1008
13. Jong P, Yusuf S, Rousseau MF, *et al.* Effect of enalapril on 12-year survival and life expectancy in patients with left ventricular systolic dysfunction: a follow-up study. *Lancet* 2003; **361**: 1843–8
14. The European trial of Reduction of cardiac events with Perindopril in stable coronary artery disease Investigators. Efficacy of perindopril in reduction of cardiovascular events among patients with stable coronary artery disease: randomised, double-blind, placebo controlled, multicentre trial (the EUROPA study). *Lancet* 2003; **362**: 782–88
15. Brenner BM, Cooper ME, de Zeeuw D, *et al.* Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. *N Engl J Med* 2001; **345**: 861–69
16. Khekshus J, Pedersen TR, Olsson AG, *et al.* The effects of simvastatin on the incidence of heart failure in patients with coronary heart disease. *J Cardiac Fail* 1997; **3**: 249–54
17. Yusuf S, Zhao F, Mehta SR, *et al.* Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. *N Eng J Med* 2001; **345**: 494–502
18. Swedberg K, Cleland J, Dargie H, *et al.* Guidelines for the diagnosis and treatment of chronic heart failure: executive summary (update 2005). *Eur Heart J* 2005; **26**(11): 1115–40
19. Hunt SA, Baker DW, Chin MH, *et al.* ACC/AHAGuidelines for the evaluation and management of chronic heart failure in the adult: executive summary of a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (committee to revise the 1995 guidelines for the evaluation and management of heart failure):*Circulation* 2001; **104**: 2996–3007.
20. Vasan RS, Larson MG, Benjamin EJ, *et al.* Left ventricular dilatation and the risk of congestive heart failure in people without myocardial infarction. *N Engl J Med* 1997; **336**: 1350–5
21. Birkhead JS, Walker L, Pearson M, *et al.* Improving care for patients with acute coronary syndromes: initial results from the National Audit of Myocardial Infarction Project (MINAP). *Heart* 2004; **90**: 1004–9
22 Pitt B, Remme W, Zannad F, *et al.* Eplerenone, a selective aldosterone blocker, in patients with left ventricular dysfunction after myocardial infarction *N Engl J Med* 2003; **348**: 1309–21
23. Pitt B, White H, Nicolan J, *et al.* Eplerenone reduces mortality 30 days after randomisation following acute myocardial infarction in patients with left ventricular systolic dysfunction and heart failure. *J Am Coll Cardiol* 2005; **46**: 425–31
24. Frigerio M, Roubina E.Drugs for Left Ventricular Remodeling in Heart Failure. *Am J Cardiol*; **96**: 10–18
25. Enriquez-Sarano M. Is functional assessment of mitral regurgitation using transthoracic echocardiography accurate? *Nature Clinical Practice Cardiovascular Medicine* 2006; **3**: 126–27
26. Cohn JN, Ferrari R, Sharpe N. Cardiac remodeling – concepts and clinical implications: a consensus paper from an international forum on cardiac remodeling. *J Am Coll Cardiol* 2000; **35**(3): 569–82
27. National Institute for Clinical Excellence. Chronic heart failure. Management of chronic heart failure in adults in primary and secondary care. Clinical guideline 5, 2003
28. Krumholz HM, Radford MJ, Wang Y, *et al.* National use and effectiveness of beta-blockers for the treatment of elderly patients after acute myocardial infarction. *JAMA* 1998; **280**: 623–9
29. Soumerai SB, McLaughlin TJ, Spiegelman D, *et al.* Adverse outcomes of underuse of beta-blockers in elderly survivors of acute myocardial infarction. *JAMA* 1997; **277**: 115–21
30. Cabana MD, Rand CS, Powe NR, *et al.* Why don't physicians follow clinical practice guidelines? A framework for improvement. *JAMA* 1999; **282**: 1458–65
31. Veatch RM. Reasons physicians do not follow clinical practice guidelines. *JAMA* 2000; **283**: 1685
32. Weingarten SR, Henning JM, Badamgarav E, *et al.* Interventions used in disease management programmes for patients with chronic illness-which ones work? Meta-analysis of published reports. *BMJ* 2002; **325**: 925
33. Ansari M, Shlipak MG, Heidenreich PA, *et al.* Improving guideline adherence: a randomized trial evaluating strategies to increase beta-blocker use in heart failure. *Circulation* 2003; **107**: 2799–804
34. LaPointe NMA, DeLong ER, Chen A, *et al.* Multifaceted Intervention to Promote Beta-Blocker Use in Heart Failure. *Am Heart J* 2006; **151**(5): 992–98

(such as thrombectomy in primary PCI, distal embolic protection in vein graft intervention) will have a major impact in preventing future HF. Primary PCI intervention for ST elevation MI is already known to prevent and limit LV dysfunction and should be carried out where possible[27], and efforts to reduce the transfer time from symptom onset to PCI should be made to further benefit LV function.

Reducing underuse of standard evidence based therapy for HF, such as beta-blockers and ACE inhibitors will also prevent decompensation of stable HF[28,29]. There is still apathy amidst physicians to use beta-blockers in HF despite clear evidence and guidelines[30,31]. Multifaceted interventions are necessary to improve physicians' adherence to guidelines[32]. Despite the relative lack of major success of studies using such multifaceted intervention[33,34], investigators should continue to explore new types of interventions, physician incentives, and technological advances to try to improve the use of beta-blockers in HF.

Conclusion

Prevention of HF is an important goal. We are currently not doing enough in this regard. Every reasonable opportunity should be utilised to assess LV function in populations at a high risk of HF. This will allow a certain number of asymptomatic LV dysfunction patients to be identified (whether screening for such patients should be performed is a separate debate) and treated with evidence based therapy to prevent progression to overt HF. All risk factors for HF, particularly CAD and hypertension and diabetes should be treated early and aggressively. All post MI patients should be treated with an ACE inhibitor and a beta-blocker to prevent HF. In addition, early assessment of LV function in post MI patients is required to identify those that would benefit from eplerenone therapy.

Conflict of interest: none declared.