

Arrhythmias

- It is essential to recognize and correct precipitating factors for arrhythmias, improve cardiac function and reduce neuro-endocrine activation with beta-blockade, ACE inhibition, and possibly, aldosterone receptor antagonists (Class of recommendation I, level of evidence C).

Ventricular arrhythmias

- In patients with ventricular arrhythmias, the use of anti-arrhythmic agents is only justified in patients with severe, symptomatic, sustained ventricular tachycardias and where amiodarone should be the preferred agent (Class of recommendation IIa, level of evidence B).^{87,89}
- ICD implantation is indicated in patients with heart failure and with life threatening ventricular arrhythmias (i.e. ventricular fibrillation or sustained ventricular tachycardia) and in selected patients at high risk of sudden death (Class of recommendation I, level of evidence A).^{95,96,110–112}

Atrial fibrillation

- For persistent (non-self-terminating) atrial fibrillation, electrical cardioversion could be considered, although its success rate may depend on the duration of atrial fibrillation and left atrial size (Class of recommendation IIa, level of evidence B).
- In patients with atrial fibrillation and heart failure and/or depressed left ventricular function, the use of anti-arrhythmic therapy to maintain sinus rhythm should be restricted to amiodarone (Class of recommendation I, level of evidence C) and, if available, to dofetilide (Class of recommendation IIa, level of evidence B).¹¹³
- In asymptomatic patients beta-blockade, digitalis glycosides or the combination may be considered for control of ventricular rate (Class of recommendation I, level of evidence B). In symptomatic patients with systolic dysfunction digitalis glycosides are the first choice (Class of recommendation IIa, level of evidence C). In PLVEF, verapamil can be considered (Class of recommendation IIa, level of evidence C).
- Anti-coagulation in persistent atrial fibrillation with warfarin should always be considered unless contraindicated (Class of recommendation I, level of evidence C).
- Management of acute atrial fibrillation is not depending on previous heart failure or not. Treatment strategy is depending on symptoms and haemodynamic stability. For options see.¹⁰⁶

Symptomatic systolic left ventricular dysfunction and concomitant angina or hypertension

Specific recommendations in addition to general treatment for heart failure because of systolic left ventricular dysfunction. If angina is present

Table 20 Recommended components of care and following programmes (class level of evidence C)

- Use a multi-disciplinary team approach
- Vigilant follow-up, first follow-up within 10 days of discharge
- Discharge planning
- Increased access to health care
- Optimizing medical therapy with guidelines
- Early attention to signs and symptoms (e.g. telemonitoring)
- Flexible diuretic regimen
- Intense education and counselling
- Inpatient and outpatient (home-based)
- Attention to behavioural strategies
- Address barriers to compliance
- Early attention to signs and symptoms (e.g. telemonitoring)
- Flexible diuretic regimen

- (1) optimize existing therapy, e.g. beta-blockade
- (2) add long-acting nitrates
- (3) if not successful, add amlodipine or felodipine
- (4) consider coronary revascularization.

If hypertension is present

- optimize the dose of ACE-inhibitors, beta-blocking agents, and diuretics.⁴⁰
- add spironolactone or ARBs if not present already
- if not successful, try second generation dihydropyridine derivatives.

Care and follow-up

See also *Table 20*.

- An organized system of specialist heart failure care improves symptoms and reduces hospitalizations (Class of recommendation I, level of evidence A) and mortality (Class of recommendation IIa, level of evidence B) of patients with heart failure.^{71,114–118}
- It is likely that the optimal model will depend on local circumstances and resources and whether the model is designed for specific sub-groups of patients (e.g. severity of heart failure, age, co-morbidity, and left ventricular systolic dysfunction) or the whole heart failure population (Class of recommendation I, level of evidence C).^{119–122}

References

1. The Task Force on Heart Failure of the European Society of Cardiology. Guidelines for the diagnosis of heart failure. *Eur Heart J* 1995;16:741–751.
2. The Task Force of the Working Group on Heart Failure of the European Society of Cardiology. The treatment of heart failure. *Eur Heart J* 1997;18:736–753.
3. Remme WJ, Swedberg K. Guidelines for the diagnosis and treatment of chronic heart failure. *Eur Heart J* 2001;22:1527–1560.
4. How to diagnose diastolic heart failure. European Study Group on Diastolic Heart Failure. *Eur Heart J* 1998;19:990–1003.
5. Mosterd A, Hoes AW, de Bruyne MC *et al*. Prevalence of heart failure and left ventricular dysfunction in the general population. *Eur Heart J* 1999;20:447–455.

6. McDonagh TA, Morrison CE, Lawrence A *et al.* Symptomatic and asymptomatic left-ventricular systolic dysfunction in an urban population. *Lancet* 1997;350:829–833.
7. Cleland JG, Khand A, Clark A. The heart failure epidemic: exactly how big is it? *Eur Heart J* 2001;22:623–626.
8. McMurray J, McDonagh T, Morrison CE *et al.* Trends in hospitalization for heart failure in Scotland 1980–1990. *Eur Heart J* 1993;14:1158–1162.
9. Cleland JG, Gemmell I, Khand A *et al.* Is the prognosis of heart failure improving? *Eur J Heart Fail* 1999;1:229–241.
10. Cleland JG, Swedberg K, Follath F *et al.* The Euro Heart Failure Survey Programme—a survey on the quality of care among patients with heart failure in Europe. Part 1: patient characteristics and diagnosis. *Eur Heart J* 2003;24:442–463.
11. Wheeldon NM, MacDonald TM, Flucker CJ *et al.* Echocardiography in chronic heart failure in the community. *Q J Med* 1993;86:17–23.
12. Remes J, Miettinen H, Reunanen A *et al.* Validity of clinical diagnosis of heart failure in primary health care. *Eur Heart J* 1991;12:315–321.
13. Task Force on Acute Heart Failure. Executive summary of the guidelines on the diagnosis and treatment of acute heart failure: the Task Force on Acute Heart Failure of the European Society of Cardiology. *Eur Heart J* 2005;26:384–416.
14. McMurray J, Swedberg K, Hogg K. Heart failure with preserved left ventricular systolic function. *J Am Coll Cardiol* 2004;43:317–327.
15. Wood P. Heart failure. In: Wood P, ed. *Diseases of the Heart and Circulation*. London: Eyre and Spottiswoode; 1950.
16. Braunwald E. Heart failure: an overview. In: Fishman AP, ed. *Heart Failure*. New York: McGraw-Hill; 1977.
17. Denolin H, Kuhn H, Krayenbuehl HP *et al.* The definition of heart failure. *Eur Heart J* 1983;4:445–448.
18. Poole-Wilson PA. Chronic heart failure causes pathophysiology, prognosis, clinical manifestations, investigation. In: Julian DG, Camm AJ, Fox KM *et al.*, eds. *Diseases of the Heart*. London: Bailliere-Tindall; 1989. p48.
19. Wang TJ, Evans JC, Benjamin EJ *et al.* Natural history of asymptomatic left ventricular systolic dysfunction in the community. *Circulation* 2003;108:977–982.
20. Lipkin DP, Canepa-Anson R, Stephens MR *et al.* Factors determining symptoms in heart failure: comparison of fast and slow exercise tests. *Br Heart J* 1986;55:439–445.
21. Puri S, Baker BL, Oakley CM *et al.* Increased alveolar/capillary membrane resistance to gas transfer in patients with chronic heart failure. *Br Heart J* 1994;72:140–144.
22. Butman SM, Ewy GA, Standen JR *et al.* Bedside cardiovascular examination in patients with severe chronic heart failure: importance of rest or inducible jugular venous distension. *J Am Coll Cardiol* 1993;22:968–974.
23. Stevenson LW, Perloff JK. The limited reliability of physical signs for estimating hemodynamics in chronic heart failure. *JAMA* 1989;10:884–888.
24. Marantz PR TJW-SSS, Budner N, Lense L *et al.* The relationship between left ventricular systolic function and congestive heart failure diagnosed by clinical criteria. *Circulation* 1988;77:607–612.
25. Adams KF, Zannad F. Clinical definition and epidemiology of advanced heart failure. *Am Heart J* 1998;135:S204–S215.
26. Killip T, Kimball JT. Treatment of myocardial infarction in a coronary care unit. A two year experience with 250 patients. *Am J Cardiol* 1967;20:457–464.
27. Khot UN, Jia G, Moliterno DJ *et al.* Prognostic importance of physical examination for heart failure in non-ST-elevation acute coronary syndromes: the enduring value of Killip classification. *JAMA* 2003;290:2174–2181.
28. McMurray J, Ostergren J, Pfeffer M *et al.* Clinical features and contemporary management of patients with low and preserved ejection fraction heart failure: baseline characteristics of patients in the Candesartan in Heart failure-Assessment of Reduction in Mortality and morbidity (CHARM) programme. *Eur J Heart Fail* 2003;5:261–270.
29. Luchner A, Burnett JC, Jougasaki M *et al.* Evaluation of brain natriuretic peptide as marker of left ventricular dysfunction and hypertrophy in the population. *J Hypertens* 2000;18:1121–1128.
30. Clerico A, Del Ry S, Maffei S *et al.* The circulating levels of cardiac natriuretic hormones in healthy adults: effects of age and sex. *Clin Chem Lab Med* 2002;40:371–377.
31. Tsutomoto T, Wada A, Maeda K *et al.* Attenuation of compensation of endogenous cardiac natriuretic peptide system in chronic heart failure: prognostic role of plasma brain natriuretic peptide concentration in patients with chronic symptomatic left ventricular dysfunction. *Circulation* 1997;96:509–516.
32. Krüger S, Graf J, Merx MW *et al.* Brain natriuretic peptide predicts right heart failure in patients with acute pulmonary embolism. *Am Heart J* 2004;147:60–65.
33. Maisel AS, Krishnaswamy P, Nowak RM *et al.* Rapid measurement of B-type natriuretic peptide in the emergency diagnosis of heart failure. *N Engl J Med* 2002;347:161–167.
34. Working Group Report. How to diagnose diastolic heart failure? European Study Group on Diastolic Heart Failure. *Eur Heart J* 1998;19:990–1003.
35. Caruana L, Petrie MC, Davie AP *et al.* Do patients with suspected heart failure and preserved left ventricular systolic function suffer from “diastolic heart failure” or from misdiagnosis? A prospective descriptive study. *BMJ* 2000;321:215–218.
36. Thomas JD, Choong CY, Flachskampf FA *et al.* Analysis of the early transmitral Doppler velocity curve: effect of primary physiologic changes and compensatory preload adjustment. *J Am Coll Cardiol* 1990;16:644–655.
37. Sohn DW, Chai IH, Lee DJ *et al.* Assessment of mitral annulus velocity by Doppler tissue imaging in the evaluation of left ventricular diastolic function. *J Am Coll Cardiol* 1997;30:474–480.
38. Bellenger NG, Davies LC, Francis JM *et al.* Reduction in sample size for studies of remodeling in heart failure by the use of cardiovascular magnetic resonance. *J Cardiovasc Magn Reson* 2000;2:271–278.
39. Grothues F, Moon JC, Bellenger NG *et al.* Interstudy reproducibility of right ventricular volumes, function, and mass with cardiovascular magnetic resonance. *Am Heart J* 2004;147:218–223.
40. Turnbull F. Effects of different blood-pressure-lowering regimens on major cardiovascular events: results of prospectively-designed overviews of randomised trials. *Lancet* 2003;362:1527–1535.
41. Anker SD, Ponikowski P, Varney S *et al.* Wasting as independent risk factor for mortality in chronic heart failure. *Lancet* 1997;349:1050–1053.
42. Working Group on Cardiac Rehabilitation and Exercise Physiology and Working group on Heart Failure of the European Society of Cardiology. Recommendations for exercise testing in chronic heart failure patients. *Eur Heart J* 2001;22:37–45.
43. The SOLVD Investigators. Effect of enalapril on mortality and the development of heart failure in asymptomatic patients with reduced left ventricular ejection fractions. *N Engl J Med* 1992;327:685–691.
44. Pfeffer MA, Braunwald E, Moye LA *et al.* Effect of captopril on mortality and morbidity in patients with left ventricular dysfunction after myocardial infarction. Results of the survival and ventricular enlargement trial. The SAVE Investigators. *N Engl J Med* 1992;327:669–677.
45. Kober L, Torp-Pedersen C, Carlsen JE *et al.* Effects on mortality by trandolapril after myocardial infarction. *N Engl J Med* 1995;333:1670–1676.
46. 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;361:1843–1848.
47. Flather M, Yusuf S, Kober L *et al.* Long-term ACE-inhibitor therapy in patients with heart failure or left-ventricular dysfunction: a systematic overview of data from individual patients. ACE-Inhibitor Myocardial Infarction Collaborative Group. *Lancet* 2000;355:1575–1581.
48. The CONSENSUS Trial Study Group. Effects of enalapril on mortality in severe congestive heart failure. Results of the Cooperative North Scandinavian Enalapril Survival Study (CONSENSUS). *N Engl J Med* 1987;316:1429–1435.
49. The acute infarction ramipril efficacy. Effect of ramipril on mortality and morbidity of survivors of acute myocardial infarction with clinical evidence of heart failure. *Lancet* 1993;342:821–828.
50. Kaddoura S, Patel D, Parameshwar J *et al.* Objective assessment of the response to treatment of severe heart failure using a 9-minute

- walk test on a patient-powered treadmill. *J Card Fail* 1996; 2: 133–139.
51. Bayliss J, Norell M, Canepa-Anson R *et al*. Untreated heart failure: clinical and neuroendocrine effects of introducing diuretics. *Br Heart J* 1987;57:17–22.
 52. Packer M, Bristow MR, Cohn JN *et al*. The effect of carvedilol on morbidity and mortality in patients with chronic heart failure. US Carvedilol Heart Failure Study Group. *N Engl J Med* 1996; 334: 1349–1355.
 53. Australia/New Zealand Heart Failure Research Collaborative Group. Randomised, placebo-controlled trial of carvedilol in patients with congestive heart failure due to ischaemic heart disease. *Lancet* 1997;349:375–380.
 54. Packer M, Coats AJ, Fowler MB *et al*. Effect of carvedilol on survival in severe chronic heart failure. *N Engl J Med* 2001;344:1651–1658.
 55. CIBIS-II Investigators and Committees. The cardiac insufficiency bisoprolol study II (CIBIS-II): a randomised trial. *Lancet* 1999; 353:9–13.
 56. MERIT-HF Study Group. Effect of metoprolol CR/XL in chronic heart failure. Metoprolol CR/XL randomised intervention trial in congestive heart failure (MERIT-HF). *Lancet* 1999;353:2001–2007.
 57. The RESOLVD Investigators. Effects of metoprolol CR in patients with ischemic and dilated cardiomyopathy. *Circulation* 2000;101: 378–384.
 58. Flather MD, Shibata MC, Coats AJ *et al*. Randomized trial to determine the effect of nebivolol on mortality and cardiovascular hospital admission in elderly patients with heart failure (SENIORS). *Eur Heart J* 2005;26:215–225.
 59. The Capricorn Investigators. Effect of carvedilol on outcome after myocardial infarction in patients with left-ventricular dysfunction: the CAPRICORN randomised trial. *Lancet* 2001; 357:1385–1390.
 60. The Beta-Blocker Evaluation of Survival Trial Investigators. A trial of the beta-blocker bucindolol in patients with advanced chronic heart failure. *N Engl J Med* 2001;344:1659–1667.
 61. Poole-Wilson PA, Swedberg K, Cleland JG *et al*. Comparison of carvedilol and metoprolol on clinical outcomes in patients with chronic heart failure in the Carvedilol Or Metoprolol European Trial (COMET): randomised controlled trial. *Lancet* 2003;362:7–13.
 62. Pitt B, Zannad F, Remme WJ *et al*. The effect of spironolactone on morbidity and mortality in patients with severe heart failure. Randomized Aldactone Evaluation Study Investigators. *N Engl J Med* 1999;341:709–717.
 63. 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;348:1309–1321.
 64. Granger CB, McMurray JJ, Yusuf S *et al*. Effects of candesartan in patients with chronic heart failure and reduced left-ventricular systolic function intolerant to angiotensin-converting-enzyme inhibitors: the CHARM-Alternative trial. *Lancet* 2003; 362:772–776.
 65. Pfeffer MA, Swedberg K, Granger CB *et al*. Effects of candesartan on mortality and morbidity in patients with chronic heart failure: the CHARM-Overall programme. *Lancet* 2003;362:759–766.
 66. Maggioni AP, Anand I, Gottlieb SO *et al*. Effects of valsartan on morbidity and mortality in patients with heart failure not receiving angiotensin-converting enzyme inhibitors. *J Am Coll Cardiol* 2002; 40:1414–1421.
 67. Cohn JN, Tognoni G. A randomized trial of the angiotensin-receptor blocker valsartan in chronic heart failure. *N Engl J Med* 2001; 345:1667–1675.
 68. Pfeffer MA, McMurray JJ, Velazquez EJ *et al*. Valsartan, captopril, or both in myocardial infarction complicated by heart failure, left ventricular dysfunction, or both. *N Engl J Med* 2003;349: 1893–1906.
 69. McMurray JJ, Ostergren J, Swedberg K *et al*. Effects of candesartan in patients with chronic heart failure and reduced left-ventricular systolic function taking angiotensin-converting-enzyme inhibitors: the CHARM-Added trial. *Lancet* 2003;362:767–771.
 70. Jong P, Demers C, McKelvie RS *et al*. Angiotensin receptor blockers in heart failure: meta-analysis of randomized controlled trials. *J Am Coll Cardiol* 2002;39:463–470.
 71. Coletta AP, Cleland JG, Freemantle N *et al*. Clinical trials update from the European Society of Cardiology: CHARM, BASEL, EUROPA and ESTEEM. *Eur J Heart Fail* 2003;5:697–704.
 72. Khand AU, Rankin AC, Kaye GC *et al*. Systematic review of the management of atrial fibrillation in patients with heart failure. *Eur Heart J* 2000;21:614–632.
 73. Khand AU, Rankin AC, Martin W *et al*. Digoxin or carvedilol for the treatment of atrial fibrillation in patients with heart failure? (Abstract). *Heart* 2000;83:30.
 74. Taylor AL, Ziesche S, Yancy C *et al*. Combination of isosorbide dinitrate and hydralazine in blacks with heart failure. *N Engl J Med* 2004;351:2049–2057.
 75. Cohn JN, Archibald DG, Ziesche S *et al*. Effect of vasodilator therapy on mortality in chronic congestive heart failure. Results of a Veterans Administration Cooperative Study. *N Engl J Med* 1986; 314:1547–1552.
 76. Cohn JN, Ziesche S, Smith R *et al*. Effect of the calcium antagonist felodipine as supplementary vasodilator therapy in patients with chronic heart failure treated with enalapril: V-HeFT III. Vasodilator-Heart Failure Trial (V-HeFT) Study Group. *Circulation* 1997;96:856–863.
 77. Thackray S, Witte K, Clark AL *et al*. Clinical trials update: OPTIME-CHF, PRAISE-2, ALL-HAT. *Eur J Heart Fail* 2000;2:209–212.
 78. Follath F, Cleland JG, Just H *et al*. Efficacy and safety of intravenous levosimendan compared with dobutamine in severe low-output heart failure (the LIDO study): a randomised double-blind trial. *Lancet* 2002;360:196–202.
 79. Cleland JG, Cowburn PJ, Falk RH. Should all patients with atrial fibrillation receive warfarin? Evidence from randomized clinical trials. *Eur Heart J* 1996;17:674–681.
 80. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. *BMJ* 2002;324:71–86.
 81. Cleland JG, Findlay I, Jafri S *et al*. The Warfarin/Aspirin Study in Heart failure (WASH): a randomized trial comparing antithrombotic strategies for patients with heart failure. *Am Heart J* 2004; 148:157–164.
 82. Teo KK, Yusuf S, Pfeffer M *et al*. Effects of long-term treatment with angiotensin-converting-enzyme inhibitors in the presence or absence of aspirin: a systematic review. *Lancet* 2002;360: 1037–1043.
 83. Cleland JG, Ghosh J, Freemantle N *et al*. Clinical trials update and cumulative meta-analyses from the American College of Cardiology: WATCH, SCD-HeFT, DINAMIT, CASINO, INSPIRE, STRATUS-US, RIO-Lipids and cardiac resynchronisation therapy in heart failure. *Eur J Heart Fail* 2004;6:501–508.
 84. The Cardiac Arrhythmia Suppression Trial. Preliminary report: effect of encainide and flecainide on mortality in a randomized trial of arrhythmia suppression after myocardial infarction. *New Engl J Med* 1989;321:406–412.
 85. López-Sendón J, Swedberg K, McMurray J *et al*. Expert consensus document on beta-adrenergic receptor blockers. *Eur Heart J* 2004; 25:1341–1362.
 86. Steinbeck G, Andresen D, Bach P *et al*. A comparison of electrophysiologically guided antiarrhythmic drug therapy with beta-blocker therapy in patients with symptomatic, sustained ventricular tachyarrhythmias. *N Engl J Med* 1992;327:987–992.
 87. Amiodarone Trials Meta-Analysis Investigators. Effect of prophylactic amiodarone on mortality after acute myocardial infarction and in congestive heart failure: meta-analysis of individual data from 6500 patients in randomised trials. *Lancet* 1997;350:1417–1424.
 88. Levy S, Breithardt G, Campbell RW *et al*. Atrial fibrillation: current knowledge and recommendations for management. Working Group on Arrhythmias of the European Society of Cardiology. *Eur Heart J* 1998;19:1294–1320.
 89. Singh SN, Fletcher RD, Fisher SG *et al*. Amiodarone in patients with congestive heart failure and asymptomatic ventricular arrhythmia. *N Engl J Med* 1995;333:77–82.
 90. Bardy GH, Lee KL, Mark DB *et al*. Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure. *N Engl J Med* 2005;352:225–237.
 91. Linde C, Leclercq C, Rex S *et al*. Long-term benefits of biventricular pacing in congestive heart failure: results from the Multisite STimulation in cardiomyopathy (MUSTIC) study. *J Am Coll Cardiol* 2002;40:111–118.
 92. Abraham WT, Fisher WG, Smith AL *et al*. Cardiac resynchronization in chronic heart failure. *N Engl J Med* 2002;346:1845–1853.

93. Bristow MR, Saxon LA, Boehmer J *et al.* Cardiac-resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. *N Engl J Med* 2004;**350**:2140–2150.
94. Bradley DJ, Bradley EA, Baughman KL *et al.* Cardiac resynchronization and death from progressive heart failure: a meta-analysis of randomized controlled trials. *JAMA* 2003;**289**:730–740.
95. Moss AJ, Hall WJ, Cannom DS *et al.* Improved survival with an implanted defibrillator in patients with coronary disease at high risk for ventricular arrhythmia. Multicenter Automatic Defibrillator Implantation Trial Investigators. *N Engl J Med* 1996;**335**:1933–1940.
96. Moss AJ, Zareba W, Hall WJ *et al.* Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. *N Engl J Med* 2002;**346**:877–883.
97. Kadish A, Dyer A, Daubert JP *et al.* Prophylactic defibrillator implantation in patients with nonischemic dilated cardiomyopathy. *N Engl J Med* 2004;**350**:2151–2158.
98. Jauhar S, Slotwiner DJ. The economics of ICDs. *N Engl J Med* 2004;**351**:2542–2544.
99. Nanthakumar K, Epstein AE, Kay GN *et al.* Prophylactic implantable cardioverter-defibrillator therapy in patients with left ventricular systolic dysfunction. A pooled analysis of 10 primary prevention trials. *J Am Coll Cardiol* 2004;**44**:2166–2172.
100. Desai AS, Fang JC, Maisel WH *et al.* Implantable defibrillators for the prevention of mortality in patients with nonischemic cardiomyopathy: a meta-analysis of randomized controlled trials. *JAMA* 2004;**292**:2874–2879.
101. Salukhe TV, Dimopoulos K, Sutton R *et al.* Life-years gained from defibrillator implantation: markedly nonlinear increase during 3 years of follow-up and its implications. *Circulation* 2004;**109**:1848–1853.
102. Bennett LE, Keck BM, Hertz MI *et al.* Worldwide thoracic organ transplantation: a report from the UNOS/ISHLT international registry for thoracic organ transplantation. *Clin Transpl* 2001;**25**–40.
103. Rose EA, Gelijns AC, Moskowitz AJ *et al.* Long-term mechanical left ventricular assistance for end-stage heart failure. *N Engl J Med* 2001;**345**:1435–1443.
104. Rimondini A, Cipolla CM, Della Bella P *et al.* Hemofiltration as short-term treatment for refractory congestive heart failure. *Am J Med* 1987;**83**:43–48.
105. Dormans TP, Huige RM, Gerlag PG. Chronic intermittent haemofiltration and haemodialysis in end stage chronic heart failure with oedema refractory to high dose frusemide. *Heart* 1996;**75**:349–351.
106. Fuster V, Rydén LE, Asinger RW *et al.* ACC/AHA/ESC Guidelines for the Management of Patients With Atrial Fibrillation: Executive Summary. A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines and Policy Conferences (Committee to Develop Guidelines for the Management of Patients With Atrial Fibrillation) Developed in Collaboration With the North American Society of Pacing and Electrophysiology. *Circulation* 2001;**104**:2118–2150.
107. Setaro JF, Zaret BL, Schulman DS *et al.* Usefulness of verapamil for congestive heart failure associated with abnormal left ventricular diastolic filling and normal left ventricular systolic performance. *Am J Cardiol* 1990;**66**:981–986.
108. Bonow RO, Dilsizian V, Rosing DR *et al.* Verapamil-induced improvement in left ventricular diastolic filling and increased exercise tolerance in patients with hypertrophic cardiomyopathy: short- and long-term effects. *Circulation* 1985;**72**:853–864.
109. Yusuf S, Pfeffer MA, Swedberg K *et al.* Effects of candesartan in patients with chronic heart failure and preserved left-ventricular ejection fraction: the CHARM-Preserved Trial. *Lancet* 2003;**362**:777–781.
110. The antiarrhythmics versus implantable defibrillators. A comparison of antiarrhythmic-drug therapy with implantable defibrillators in patients resuscitated from near-fatal ventricular arrhythmias. *N Engl J Med* 1997;**337**:1576–1583.
111. Buxton AE, Lee KL, Fisher JD *et al.* A randomized study of the prevention of sudden death in patients with coronary artery disease. Multicenter Unsustained Tachycardia Trial Investigators. *N Engl J Med* 1999;**341**:1882–1890.
112. Priori SG, Aliot E, Blomstrom-Lundqvist C *et al.* Task Force on Sudden Cardiac Death of the European Society of Cardiology. *Eur Heart J* 2001;**22**:1374–1450.
113. Torp-Pedersen C, Moller M, Bloch-Thomsen PE *et al.* Dofetilide in patients with congestive heart failure and left ventricular dysfunction. Danish Investigations of Arrhythmia and Mortality on Dofetilide Study Group. *N Engl J Med* 1999;**341**:857–865.
114. Rich MW. Heart failure disease management: a critical review. *J Card Fail* 1999;**5**:64–75.
115. McAlister FA, Lawson FM, Teo KK *et al.* Randomised trials of secondary prevention programmes in coronary heart disease: systematic review. *BMJ* 2001;**323**:957–962.
116. Stewart S, Pearson S, Horowitz JD. Effects of a home-based intervention among patients with congestive heart failure discharged from acute hospital care. *Arch Intern Med* 1998;**158**:1067–1072.
117. Stewart S, Marley JE, Horowitz JD. Effects of a multidisciplinary, home-based intervention on unplanned readmissions and survival among patients with chronic congestive heart failure: a randomised controlled study. *Lancet* 1999;**354**:1077–1083.
118. Stromberg A. Nurse-led heart failure clinics improve survival and self-care behaviour in patients with heart failure: results from a prospective, randomised trial. *Eur Heart J* 2003;**24**:1014–1023.
119. Weinberger M, Oddone EZ, Henderson WG. Does increased access to primary care reduce hospital readmissions? Veterans Affairs Cooperative Study Group on Primary Care and Hospital Readmission. *N Engl J Med* 1996;**334**:1441–1447.
120. Jaarsma T, Halfens R, Huijter Abu-Saad H *et al.* Effects of education and support on self-care and resource utilization in patients with heart failure. *Eur Heart J* 1999;**20**:673–682.
121. Ekman I, Andersson B, Ehnfors M *et al.* Feasibility of a nurse-monitored, outpatient-care programme for elderly patients with moderate-to-severe, chronic heart failure. *Eur Heart J* 1998;**19**:1254–1260.
122. McAlister FA, Stewart S, Ferrua S *et al.* Multidisciplinary strategies for the management of heart failure patients at high risk for admission: a systematic review of randomized trials. *J Am Coll Cardiol* 2004;**44**:810–819.
123. Nohria A, Tsang SW, Fang JC *et al.* Clinical assessment identifies hemodynamic profiles that predict outcomes in patients admitted with heart failure. *J Am Coll Cardiol* 2003;**41**:1797–1804.
124. Kearney MT, Fox KA, Lee AJ *et al.* Predicting death due to progressive heart failure in patients with mild-to-moderate chronic heart failure. *J Am Coll Cardiol* 2002;**40**:1801–1808.
125. Pulignano G, Del Sindaco D, Tavazzi L *et al.* Clinical features and outcomes of elderly outpatients with heart failure followed up in hospital cardiology units: data from a large nationwide cardiology database (IN-CHF Registry). *Am Heart J* 2002;**143**:45–55.
126. Yancy CW. Does race matter in heart failure? *Am Heart J* 2003;**146**:203–206.
127. Baldasseroni S, Opasich C, Gorini M *et al.* Left bundle-branch block is associated with increased 1-year sudden and total mortality rate in 5517 outpatients with congestive heart failure: a report from the Italian network on congestive heart failure. *Am Heart J* 2002;**143**:398–405.
128. Mancini DM, Eisen H, Kussmaul W *et al.* Value of peak exercise oxygen consumption for optimal timing of cardiac transplantation in ambulatory patients with heart failure. *Circulation* 1991;**83**:778–786.
129. Recommendations for exercise testing in chronic heart failure patients. *Eur Heart J* 2001;**22**:37–45.
130. Opasich C, Pinna GD, Bobbio M *et al.* Peak exercise oxygen consumption in chronic heart failure: toward efficient use in the individual patient. *J Am Coll Cardiol* 1998;**31**:766–775.
131. Vrtovec B, Delgado R, Zewail A *et al.* Prolonged QTc interval and high B-type natriuretic peptide levels together predict mortality in patients with advanced heart failure. *Circulation* 2003;**107**:1764–1769.
132. Cintron G, Johnson G, Francis G *et al.* Prognostic significance of serial changes in left ventricular ejection fraction in patients with congestive heart failure. The V-HeFT VA Cooperative Studies Group. *Circulation* 1993;**87**:V117–V123.
133. Lewis EF, Moye LA, Rouleau JL *et al.* Predictors of late development of heart failure in stable survivors of myocardial infarction: the CARE study. *J Am Coll Cardiol* 2003;**42**:1446–1453.
134. Hohnloser SH, Klingenhoben T, Bloomfield D *et al.* Usefulness of microvolt T-wave alternans for prediction of ventricular tachyarrhythmic events in patients with dilated cardiomyopathy: results from a prospective observational study. *J Am Coll Cardiol* 2003;**41**:2220–2224.

135. Felker GM, Shaw LK, O'Connor CM. A standardized definition of ischemic cardiomyopathy for use in clinical research. *J Am Coll Cardiol* 2002;39:210–218.
136. Nolan J, Batin PD, Andrews R *et al.* Prospective study of heart rate variability and mortality in chronic heart failure: results of the United Kingdom heart failure evaluation and assessment of risk trial (UK-heart). *Circulation* 1998;98:1510–1516.
137. La Rovere MT, Pinna GD, Maestri R *et al.* Short-term heart rate variability strongly predicts sudden cardiac death in chronic heart failure patients. *Circulation* 2003;107:565–570.
138. Corra U, Mezzani A, Bosimini E *et al.* Ventilatory response to exercise improves risk stratification in patients with chronic heart failure and intermediate functional capacity. *Am Heart J* 2002; 143:418–426.
139. Cohn JN, Johnson GR, Shabetai R *et al.* Ejection fraction, peak exercise oxygen consumption, cardiothoracic ratio, ventricular arrhythmias, and plasma norepinephrine as determinants of prognosis in heart failure. The V-HeFT VA Cooperative Studies Group. *Circulation* 1993;87:VI5–VI16.
140. Swedberg K, Eneroth P, Kjeksus J *et al.* Hormones regulating cardiovascular function in patients with severe congestive heart failure and their relation to mortality. CONSENSUS Trial Study Group. *Circulation* 1990;82:1730–1736.
141. St John SM, Lee D, Rouleau JL *et al.* Left ventricular remodeling and ventricular arrhythmias after myocardial infarction. *Circulation* 2003;107:2577–2582.
142. Koelling TM, Aaronson KD, Cody RJ *et al.* Prognostic significance of mitral regurgitation and tricuspid regurgitation in patients with left ventricular systolic dysfunction. *Am Heart J* 2002; 144: 524–529.
143. Dries DL, Sweitzer NK, Drazner MH *et al.* Prognostic impact of diabetes mellitus in patients with heart failure according to the etiology of left ventricular systolic dysfunction. *J Am Coll Cardiol* 2001; 38:421–428.
144. Gustafsson F, Torp-Pedersen C, Brendorp B *et al.* Long-term survival in patients hospitalized with congestive heart failure: relation to preserved and reduced left ventricular systolic function. *Eur Heart J* 2003;24:863–870.
145. Bittner V, Weiner DH, Yusuf S *et al.* Prediction of mortality and morbidity with a 6-minute walk test in patients with left ventricular dysfunction. SOLVD Investigators. *JAMA* 1993;270:1702–1707.
146. Opasich C, Pinna GD, Mazza A *et al.* Reproducibility of the six-minute walking test in patients with chronic congestive heart failure: practical implications. *Am J Cardiol* 1998;81:1497–1500.
147. Gronda E, Mangiavacchi M, Frigerio M *et al.* Determination of candidacy for mechanical circulatory support: importance of clinical indices. *J Heart Lung Transplant* 2000;19:S83–S88.
148. Anker SD, Negassa A, Coats AJ *et al.* Prognostic importance of weight loss in chronic heart failure and the effect of treatment with angiotensin-converting-enzyme inhibitors: an observational study. *Lancet* 2003;361:1077–1083.
149. Aaronson KD, Schwartz JS, Chen TM *et al.* Development and prospective validation of a clinical index to predict survival in ambulatory patients referred for cardiac transplant evaluation. *Circulation* 1997;95:2660–2667.
150. Dries DL, Exner DV, Domanski MJ *et al.* The prognostic implications of renal insufficiency in asymptomatic and symptomatic patients with left ventricular systolic dysfunction. *J Am Coll Cardiol* 2000; 35:681–689.
151. Ponikowski P, Francis DP, Piepoli MF *et al.* Enhanced ventilatory response to exercise in patients with chronic heart failure and preserved exercise tolerance: marker of abnormal cardiorespiratory reflex control and predictor of poor prognosis. *Circulation* 2001; 103:967–972.
152. Leite JJ, Mansour AJ, de Freitas HF *et al.* Periodic breathing during incremental exercise predicts mortality in patients with chronic heart failure evaluated for cardiac transplantation. *J Am Coll Cardiol* 2003;41:2175–2181.
153. Pozzoli M, Traversi E, Cioffi G *et al.* Loading manipulations improve the prognostic value of Doppler evaluation of mitral flow in patients with chronic heart failure. *Circulation* 1997;95:1222–1230.
154. Pinamonti B, Zecchin M, Di Lenarda A *et al.* Persistence of restrictive left ventricular filling pattern in dilated cardiomyopathy: an ominous prognostic sign. *J Am Coll Cardiol* 1997;29:604–612.
155. Horwich TB, Fonarow GC, Hamilton MA *et al.* Anemia is associated with worse symptoms, greater impairment in functional capacity and a significant increase in mortality in patients with advanced heart failure. *J Am Coll Cardiol* 2002;39:1780–1786.
156. Ghio S, Gavazzi A, Campana C *et al.* Independent and additive prognostic value of right ventricular systolic function and pulmonary artery pressure in patients with chronic heart failure. *J Am Coll Cardiol* 2001;37:183–188.
157. Polak JF, Holman BL, Wynne J *et al.* Right ventricular ejection fraction: an indicator of increased mortality in patients with congestive heart failure associated with coronary artery disease. *J Am Coll Cardiol* 1983;2:217–224.
158. Ammann P, Maggiorini M, Bertel O *et al.* Troponin as a risk factor for mortality in critically ill patients without acute coronary syndromes. *J Am Coll Cardiol* 2003;41:2004–2009.
159. Petrie MC, McMurray JV. It cannot be cardiac failure because the heart is not enlarged on the chest X-ray. *Eur J Heart Fail* 2003; 5:117–119.
160. Anker SD, Doehner W, Rauchhaus M *et al.* Uric acid and survival in chronic heart failure: validation and application in metabolic, functional, and hemodynamic staging. *Circulation* 2003;107: 1991–1997.
161. Cohn JN, Johnson G, Ziesche S *et al.* A comparison of enalapril with hydralazine-isosorbide dinitrate in the treatment of chronic congestive heart failure. *N Engl J Med* 1991;325:303–310.
162. The SOLVD Investigators. Effect of enalapril on survival in patients with reduced left ventricular ejection fractions and congestive heart failure. *N Engl J Med* 1991;325:293–302.
163. Packer M, Poole-Wilson PA, Armstrong PW *et al.* Comparative effects of low and high doses of the angiotensin-converting enzyme inhibitor, lisinopril, on morbidity and mortality in chronic heart failure. ATLAS Study Group. *Circulation* 1999;100:2312–2318.
164. The Cardiac Insufficiency Bisoprolol Study II (CIBIS-II): a randomised trial. *Lancet* 1999;353:9–13.
165. Murdoch DR, McDonagh TA, Farmer R *et al.* ADEPT: Addition of the AT1 receptor antagonist eprosartan to ACE-inhibitor therapy in chronic heart failure trial: hemodynamic and neurohormonal effects. *Am Heart J* 2001;141:800–807.
166. Pitt B, Poole-Wilson PA, Segal R *et al.* Effect of losartan compared with captopril on mortality in patients with symptomatic heart failure: randomised trial—the Losartan Heart Failure Survival Study ELITE II. *Lancet* 2000;355:1582–1587.
167. Dahlof B, Devereux RB, Kjeldsen SE *et al.* Cardiovascular morbidity and mortality in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol. *Lancet* 2002;359:995–1003.
168. Tonkon M. A study of the efficacy and safety of irbesartan in combination with conventional therapy, including ACE-inhibitors, in heart failure. Irbesartan Heart Failure Group. *Int J Clin Pract* 2000; 54:11–14.
169. Dunselman PH. Effects of the replacement of the angiotensin converting enzyme inhibitor enalapril by the angiotensin II receptor blocker telmisartan in patients with congestive heart failure. The replacement of angiotensin converting enzyme inhibition (REPLACE) investigators. *Int J Cardiol* 2001; 77:131–138.
170. McMurray JJ, Ostergren J, Swedberg K. *et al.* Effects of candesartan in patients with chronic heart failure and reduced left-ventricular systolic function taking angiotensin-converting-enzyme inhibitors: the CHARM-Added trial. *Lancet* 2003;362:767–771.
171. Cleland JG, Daubert JC, Erdmann E. *et al.* The effect of cardiac resynchronization on morbidity and mortality in heart failure. *N Engl J Med* 2005;352:1539–1549.