

Heart failure post-myocardial infarction: a review of the issues

H Dargie

Heart 2005;91(Suppl II):ii3-ii6. doi: 10.1136/hrt.2005.062018

In most patients with heart failure due to left ventricular systolic dysfunction, the underlying cause is coronary heart disease. To reduce progression to heart failure in a patient with acute myocardial infarction, it is important to achieve the earliest possible reperfusion, whether by thrombolysis or primary percutaneous coronary intervention. Every patient with acute myocardial infarction should have an assessment of their left ventricular function, the potential for reversibility should be considered, and reversible ischaemia should be identified. Left ventricular dysfunction does not only occur with ST segment elevation myocardial infarction but is also commonly associated with non-ST segment elevation myocardial infarction. Secondary prevention is crucial and this requires long term commitment by the patient and the health care system. Heart failure and left ventricular dysfunction are treatable but require a multidisciplinary, integrated network approach.

Of immediate importance in acute myocardial infarction are pain relief, sustaining life, and myocardial damage limitation—to contain the size of the infarct and also to prevent re-infarction. In addition, all patients with acute myocardial infarction, asymptomatic left ventricular dysfunction, or heart failure should undergo risk assessment in order to determine the options for further treatment. It is important to accept that when a patient is admitted with acute myocardial infarction, they are basically entering a system of acute and chronic disease management which has both “medical” and “interventional” components.

There has been substantial improvement in survival after acute myocardial infarction. In Scotland, during the decade 1986–1996, 30 day mortality after hospital admission with acute myocardial infarction improved from 25% to about 15%. This figure, which is likely to be even better now, is what would be expected for patients who survive to reach hospital and are admitted to a modern coronary care unit. The increased likelihood of surviving the initial episode is one reason why heart failure is becoming more common.

There is intense debate over the best method of limiting the damage after acute myocardial infarction. Thrombolysis is the standard treatment but interventional cardiologists have shown the benefit that can be achieved from primary percutaneous coronary intervention (PCI). A review of 23 randomised trials comparing the two treatments for acute ST segment elevation myocardial infarction showed primary PCI to be more effective than thrombolysis in restoring myocardial perfusion.² Mortality may be reduced by the invasive strategy and, of



Far from implying that progression to heart failure is an inevitable consequence of acute myocardial infarction, the title of this conference highlights the opportunity that the overt occurrence of a myocardial infarction presents for the secondary prevention of major cardiac events. This contrasts with the unfortunate fact that, for many patients, the first clinical expression of underlying coronary heart disease is chronic heart failure (CHF) caused by previous covert myocardial infarction.

In the great majority of patients with heart failure due to left ventricular systolic dysfunction, the underlying cause is coronary heart disease. Effective primary and secondary prevention of coronary heart disease is therefore a major priority. Data from the INTERHEART study show that most, if not all, cases of myocardial infarction are predictable from what is already known about the preventable risk factors.¹ It is also important to seek to improve out-of-hospital and in-hospital management of patients with acute myocardial infarction, and to appreciate that management is changing in relation to conventional versus invasive strategies. There is a need for effective implementation of evidence based treatments to try to prevent progression from acute myocardial infarction to left ventricular dysfunction and heart failure.

Abbreviations: BNP, B-type natriuretic peptide; CAPRICORN, carvedilol post-infarct survival control in LV dysfunction; CARE-HF, cardiac resynchronisation in heart failure; CHF, chronic heart failure; COMPANION, comparison of medical therapy, pacing and defibrillation in heart failure; CRT, cardiac resynchronisation therapy; GREAT, Grampian region early anistreplase trial; ICD, implantable cardioverter-defibrillator; LVAD, left ventricular assist device; MADIT II, multicenter automatic defibrillator implantation trial II; MIRACLE, multicenter InSync randomised clinical evaluation; MRI, magnetic resonance imaging; MUSTIC, multisite stimulation in cardiomyopathy; PCI, percutaneous coronary intervention; REMATCH, randomized evaluation of mechanical assistance for the treatment of congestive heart failure; SCD-HeFT, sudden cardiac death in heart failure trial; TACTICS TIMI 18, treat angina with Aggrastat and determine cost of therapy with an invasive or conservative strategy (TACTICS) – Thrombolysis in myocardial infarction (TIMI) 18

Correspondence to:
Professor Henry Dargie,
Western Infirmary,
Dumbarton Road,
Glasgow G11 6NT, UK;
h.dargie@bio.gla.ac.uk

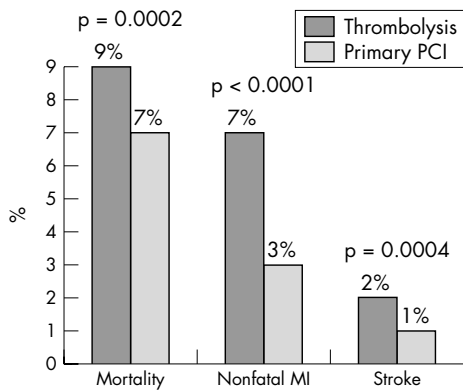


Figure 1 Comparison of short term end points after primary PCI and thrombolysis reperfusion treatment for acute myocardial infarction, from a review of 23 trials. Adapted with permission from Keeley *et al.*²

particular relevance in terms of preventing progression to heart failure, non-fatal re-infarction is substantially reduced (fig 1). This treatment has been taken on board in many parts of the world. In Switzerland, for example, all patients now receive primary PCI and thrombolysis has effectively been consigned to the history books. The UK and other European countries are following that trend, although not so rapidly.

However, there is renewed interest in the concept of pre-hospital thrombolysis. It has been shown that “the earlier the better” for thrombolytic treatment,³ with an estimated 10–50 lives lost/1000 patients for every hour delayed. The benefit of early treatment was shown in the GREAT trial, a small trial carried out in a semi-rural area of north east Scotland in the early 1990s to compare pre-hospital and in-hospital thrombolysis.⁴ This randomised study involved 311 patients with suspected myocardial infarction who were seen by their general practitioner within four hours of symptom onset and were given intravenous anistreplase either at home or on arrival at hospital. There was a saving of over two hours in “call to needle” time (101 minutes for pre-hospital thrombolysis versus 240 minutes for in-hospital treatment) and the 12 month death rate was 10.4% in patients treated at home compared with 21.6% in the hospital treated patients (relative reduction 52%, $p = 0.007$).

Ten year follow up of the GREAT trial was published in 2003 and showed sustained benefit for the early treatment.⁵ Improved survival with pre-hospital treatment was confined to patients with ST elevation or bundle branch block on the presenting ECG, in whom there was an average survival advantage of 1.6 years. Anistreplase, the thrombolytic agent

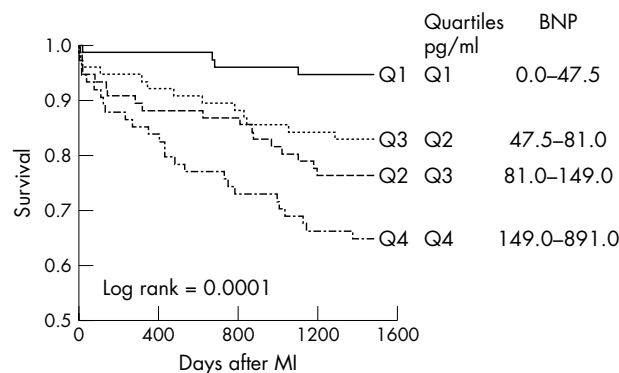


Figure 2 Data from a consecutive series of patients with myocardial infarction, showing how total mortality is associated with BNP concentration (pg/ml).

used in GREAT, could be given as a single injection, which enabled domiciliary use. Unfortunately, withdrawal of the drug following the development of alteplase probably put back pre-hospital thrombolysis by a number of years.

Early detection and management of acute heart failure is a prime function in the CCU and risk stratification can identify apparently stable patients who are at risk of further ischaemic events or chronic heart failure in the future. It is important to remember that it is not only patients with ST segment elevation myocardial infarction who have left ventricular dysfunction. This problem is also common in patients with non-ST segment elevation myocardial infarction. For example, in the CAPRICORN study⁶ evaluating use of a β blocker in myocardial infarction, in which one of the entry criteria was an ejection fraction of 40% or less, over 20% of the 1959 trial patients had non-ST segment elevation myocardial infarction. In other words, these patients with apparently mild myocardial infarction had left ventricular dysfunction.

Left ventricular function must therefore be assessed by echocardiography in all patients after an acute myocardial infarction and this should become a routine procedure in the coronary care unit.

NEW TECHNOLOGIES

One of the new technologies in acute myocardial infarction is the use of troponin measurement to identify those patients with non-ST segment elevation myocardial infarction who could benefit from early invasive treatment. Six month follow up of the TACTICS-TIMI 18 study⁷ showed advantages for troponin positive patients from an invasive strategy (early coronary angiography and revascularisation) rather than conservative management. In troponin positive patients there was a significant ($p < 0.001$) reduction in the composite end point of death, myocardial infarction, or rehospitalisation for acute coronary syndrome with the early invasive strategy. For troponin negative patients there was no significant difference between the two treatment strategies. Troponin measurement can therefore be used to identify high risk patients.

Risk assessment can be further refined by combining troponin measurement with measurement of natriuretic peptides. Figure 2 shows a consecutive series of patients with myocardial infarction in the Western Infirmary Glasgow. It shows that patients can be separated into low risk and high risk groups on the basis of their B-type natriuretic peptide (BNP) concentration.

In a recent review, Jernberg *et al.*⁸ reported that in patients with non-ST elevation myocardial infarction who were at low risk according to the BNP concentration there was no mortality advantage from an invasive treatment strategy rather than a conservative treatment approach. However, in patients with raised BNP concentrations there was a substantial advantage from the intensive strategy. It is therefore important to use all the available tools to identify an individual’s risk and then to decide the most appropriate treatment.

Magnetic resonance imaging (MRI), using injection of gadolinium contrast agent, remains experimental but studies indicate that in the future this technique might be used to identify tissue that has been stunned rather than killed by an infarction. Such tissue is potentially viable and may therefore respond to revascularisation.

While it may not be difficult to identify myocardial infarction if the patient presents with pain, many patients have truly “silent” myocardial infarction. With MRI, we can for the first time visualise the extent of infarction (fig 3). Thirty four per cent of patients attending our heart failure clinic with a diagnosis of idiopathic cardiomyopathy were found to have MRI evidence of a previous myocardial

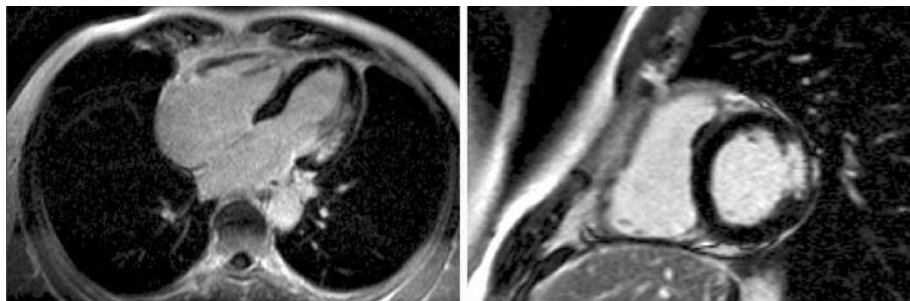


Figure 3 Magnetic resonance imaging scan showing a myocardial infarction—this was a “silent” infarction as the patient had experienced no chest pain.

infarction, without any history of chest pain. The new technique is therefore providing clinicians with much more information about causes of heart failure.

REMODELLING AND PHARMACOLOGICAL TREATMENT

The processes involved in progression from acute myocardial infarction to left ventricular dysfunction and heart failure include the development of myocardial stunning and hibernation, remodelling, and chronic neuroendocrine activation.

In a fully remodelled heart following infarction, the heart is dilated and hypertrophied, and there are areas of fibrosis within the myocardium. The neuroendocrine hypothesis proposes that these deleterious long term effects are caused by excess release of angiotensin II, aldosterone, and noradrenaline (norepinephrine) and can be prevented by blockade of these hormones with appropriate drug treatment.

Post-myocardial infarction pharmacological management involves four “standards”: antiplatelet treatment, statin, angiotensin converting enzyme inhibitor, and β blocker. The role of selective aldosterone receptor blockade is also now of interest because of the proven negative effects of this hormone on the heart.

USE OF DEVICES IN HEART FAILURE

In addition to the many pharmacologic agents available for heart failure management, there are many non-pharmacologic approaches. One developing area in the treatment of chronic heart failure, perhaps less so in acute myocardial infarction, is the use of devices.

By resynchronising the contraction of the ventricle following its injury by myocardial infarction, or other disease process, it is possible to improve cardiac function and to keep patients out of hospital. The MUSTIC⁹ and MIRACLE¹⁰ trials both showed clinical benefit from biventricular pacing. There is still debate about whether cardiac resynchronisation therapy (CRT) will improve mortality and that question is being investigated in the CARE-HF study.¹¹ Nevertheless, many patients are already receiving this form of treatment when all other options have failed.

A more difficult issue is the use of implantable cardioverter-defibrillators (ICDs) to prevent sudden cardiac death. There is now evidence of benefit from two trials: MADIT II¹² and SCD-HeFT (reported at the 2004 American College of Cardiology scientific sessions). The use of ICDs together with CRT has been investigated in the COMPANION study¹³ and the trial results suggest that mortality might be improved, but this is not proven.

It is essential that we use all the techniques at our disposal to identify patients who are most suitable for treatment with these electrical devices. However, often it is difficult to obtain funding for these technologies because of the “up front” costs, although they may be cost effective in the longer term.

Left ventricular assist devices (LVADs) are small implantable pumps that can assist the function of the heart. One published clinical trial, REMATCH,¹⁴ showed a definite benefit; however, this benefit was quite short lived, in part because of device failure. Technological developments are likely to lead to better, more effective devices for use in cases where all other treatment options have failed. One difficult group of patients is those admitted with an acute myocardial infarction who develop cardiogenic shock caused by pump failure. Pharmacological support is rarely successful in such cases and access to mechanical circulatory support is poor. Even intra-aortic balloon pumping, which is successful in some cases, is usually only available in centres equipped to perform PCI. The introduction on a regional basis of an efficient network for provision of effective mechanical circulatory support, including LVADs, could provide a “bridge” to revascularisation by PCI, transplantation or even recovery. In some patients, LVADs will provide “destination” therapy.

Based on published work from Scotland on the case fatality rate in patients admitted to hospital with a first myocardial infarction,¹⁵ an estimated 1000 people aged under 55 years who survive to reach hospital die each year in Britain within 30 days of their first myocardial infarction. There is currently little treatment for these patients. Urgent transplantation is

Learning points

- Coronary heart disease is the major cause of heart failure due to left ventricular systolic dysfunction. Since coronary heart disease is often asymptomatic, recognition of acute myocardial infarction offers a major opportunity in secondary prevention
- Progression to chronic heart failure after a myocardial infarction is multifactorial, involving the extent of myocardial damage at the time of the index event, recurrent ischaemia and the development of myocardial stunning and hibernation, remodelling and chronic neuroendocrine stimulation
- Adequate investigation to identify left ventricular dysfunction at the time of myocardial infarction is important as is the detection of potentially reversible myocardial dysfunction that might benefit from revascularisation
- Patients with significant left ventricular dysfunction after a myocardial infarction require particularly careful evaluation as they are at high risk of major cardiac events, including sudden death and heart failure
- Effective anti-remodelling treatment should be initiated as soon as possible and monitored in a chronic disease management strategy

not practicable because of the timescale, but the new mechanical assist devices may be suitable.

CONCLUSION

A patient who has had an acute myocardial infarction may or may not progress to develop left ventricular dysfunction and heart failure. The processes involved in this include myocardial stunning and hibernation, remodelling, and neuro-endocrine activation. Adequate investigation and prompt treatment are essential. The treatment of heart failure and left ventricular dysfunction post-myocardial infarction requires the same multidisciplinary, integrated network approach that we advocate for patients with chronic heart failure.

There are important issues on the journey from the coronary care unit to heart failure. It is apparent that the earliest possible reperfusion is important. Much has been achieved, using different strategies, and the time to thrombolysis has improved dramatically, but further improvement is required. One of the main problems is that patients often delay calling for medical help, which is now the major cause of delay in receiving reperfusion treatment. Public education programmes have not proven successful and we must find new ways of trying to alert patients to the need for prompt action so that they can get into the system earlier and so stand to benefit from treatment.

REFERENCES

- 1 Yusuf S, Hawken S, Öunpuu S, *et al.* on behalf of the INTERHEART Study Investigators. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet* 2004;**364**:937–52.
- 2 Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. *Lancet* 2003;**361**:13–20.
- 3 Boersma E, Maas AC, Deckers JW, *et al.* Early thrombolytic treatment in acute myocardial infarction: reappraisal of the golden hour. *Lancet* 1996;**348**:771–5.
- 4 Rawles J, on behalf of the GREAT group. Halving of mortality at 1 year by domiciliary thrombolysis in the Grampian Region early anistreplase trial (GREAT). *J Am Coll Cardiol* 1994;**23**:1–5.
- 5 Rawles J. GREAT: 10 year survival of patients with suspected acute myocardial infarction in a randomised comparison of prehospital and hospital thrombolysis. *Heart* 2003;**89**:563–4.
- 6 The CAPRICORN Investigators. Effect of carvedilol on outcome after myocardial infarction in patients with left-ventricular dysfunction: the CAPRICORN randomised trial. *Lancet* 2001;**357**:1385–90.
- 7 Morrow DA, Cannon CP, Rifai N, *et al.* for the TACTICS-TIMI 18 investigators. Ability of minor elevations of troponins I and T to predict benefit from an early invasive strategy in patients with unstable angina and non-ST elevation myocardial infarction: results from a randomized trial. *JAMA* 2001;**286**:2405–12.
- 8 Jernberg T, James S, Lindahl B, *et al.* Natriuretic peptides in unstable coronary artery disease. *Eur Heart J* 2004;**25**:1486–93.
- 9 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**:1111–8.
- 10 Abraham WT, Fisher WG, Smith AL, *et al.* for the MIRACLE study group. Cardiac resynchronization in chronic heart failure. *New Engl J Med* 2002;**346**:1845–53.
- 11 Cleland JG, Daubert JC, Erdmann E, *et al.*, CARE-HF study Steering Committee and Investigators. The CARE-HF study (cardiac resynchronisation in heart failure study): rationale, design and end-points. *Eur J Heart Fail* 2001;**3**:481–9.
- 12 Moss AJ, Zareba W, Hall WJ, *et al.*, for the Multicenter Automatic Defibrillator Implantation Trial II Investigators. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. *N Engl J Med* 2002;**346**:877–83.
- 13 Bristow MR, Saxon LA, Boehmer J, *et al.*, for the Comparison of Medical Therapy, Pacing and Defibrillation in Heart Failure (COMPANION) Investigators. Cardiac-resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. *N Engl J Med* 2004;**350**:2140–50.
- 14 Rose EA, Gelijns AC, Moskowitz AJ, *et al.*, for the Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) Study Group. Long-term use of a left ventricular assist device for end-stage heart failure. *N Engl J Med* 2001;**345**:1435–43.
- 15 McIntyre K, Stewart S, Capewell S, *et al.* Gender and survival: a population-based study of 201,114 men and women following a first acute myocardial infarction. *J Am Coll Cardiol* 2001;**38**:729–35.