

Why patients with heart failure die

See page 1601 for the article to which this Editorial refers

Understanding more about why patients who have heart failure die is paramount to improving their care. Quality of life is a key issue for those whose failure makes prognosis grave. Many are living an active life and their death is sudden and unexpected. It is difficult to envisage a cause of death other than from a further ischaemic or arrhythmic event for the majority of these patients who will have underlying ischaemic heart disease. Strokes or other catastrophic vascular events are alternatives but less likely. Increasing experience with interrogation of defibrillator devices will give more information about serious arrhythmias but not their immediate cause. A precipitating bout of ischaemia, the need for an appropriate substrate, electrolyte imbalance, sympathetic surge or various combinations will not be unravelled easily. For those smaller numbers with heart failure without large vessel coronary disease, one pathological component is removed. However the causes of non-ischaemic cardiomyopathy are not well understood, are likely to be heterogeneous and may themselves include an element of ischaemia in their aetiology.

For others the unrelenting progression of their heart failure is apparent with frequent hospitalization for breathlessness and oedema, dwindling exercise tolerance and near confinement to the home. Eventually the individual is cachectic, breathless at rest and bed-ridden. Sudden death in this state might be seen as a welcome relief of suffering. Although the course of the illness is protracted, the end may still come suddenly; more diverse precipitating factors like pneumonia and pulmonary embolus can be added to

the conditions discussed earlier. But what causes this decline? Here is opportunity to intervene. Rightly much has been made of the adverse effects of neuro-hormonal stimulation, given the substantial benefit seen with ACE inhibitors and beta-blockers. But in post myocardial infarction (MI) studies beta-blockers have been shown to prevent further myocardial infarction^[1] and the recent HOPE study has given credence to the previously retrospective claims for prevention of MI by ACE inhibitors^[2]. Could prevention of MI be a major mechanism in preventing the deterioration in heart failure?

In contrast to the ACE inhibitor studies^[3,4] the recent CIBIS-II^[5] and MERIT^[6] find few infarcts in their populations (Table 1). However, sudden death is common and is reduced by the beta-blockers. Apparently near identical patients entering different trials of heart failure find different routes to death. This highlights the difficulties of defining why patients die in large scale trials. Even when half die in hospital under observation the problem remains.

Cleland *et al.*^[7] deserve credit then for attempting to unravel the mechanism of death in the large heart failure population studied in ATLAS. It is difficult to disagree with their conclusion that ischaemic events and arrhythmias may contribute not just to sudden death but also to progression of failure. A similar exercise was undertaken in the AIRE study and is in broad agreement with the findings here^[8]. However, such evaluations cannot separate cause and effect from simple association. The more unwell patients more commonly have events including arrhythmias. Many patients have multiple events prior to their deaths and even witnessed deaths are not necessarily accompanied by objective evidence as to the exact

Table 1 Myocardial infarction rates in four major studies

Annual mortality (%)	Study	% non-fatal MI (n=)		
		EF %	Placebo % (n)	Enalapril % (n)
11.6	SOLVD-T ^[3] n=2569	25	6.5 (83)	Enalapril 5.1 (66)
5.1	SOLVD-P ^[4] n=4228	28	6.9 (147)	Enalapril 4.9 (103)
13.1	CIBIS II ^{[5]*} n=2647	28	0.6 (8)	Bisoprolol 0.5 (7)
11	MERIT ^[6] n=3093	28	2.2 (35)	Metoprolol 1.8 (27)

*Fatal MI is shown here for CIBIS II. In these trials, the number of fatal MIs reported ranges from 50–100% of non-fatal.

course of events, adding to difficulties of interpretation. Even postmortems are disappointing in resolving doubt. End-point committee members in my experience rarely disagree about the cause of death, once an arbitrary definition is in place, except when information is inadequate. Differences in definitions used in large-scale trials or their interpretation lead to apparent differences in cause of death.

Do any valuable lessons emerge from scrutinizing complex data in this way? One is glaringly obvious. Clinicians and researchers alike have no room for complacency. Control of ischaemic heart disease, made worse by the often concomitant problems of hypertension and diabetes, remains the major challenge. Since myocardial damage from ischaemic heart disease underlies heart failure in the majority in the first place, it is difficult to believe that the process does not continue. The current vogue for looking at heart failure as a disease in its own right is allowing investigators to lose sight of the need to prevent ischaemic damage from large vessel coronary heart disease. The development of overt heart failure or detection of ventricular dysfunction surely serve to emphasize the need for optimal management of coronary heart disease and the factors which predispose to it.

S. G. BALL

*Institute for Cardiovascular Research,
Leeds General Infirmary,
Leeds, U.K.*

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Early atrial defibrillation: ‘a stitch in time saves nine’ or ‘haste makes waste’?

See page 1613 for the article to which this Editorial refers

The paper by Vardas *et al.* in this issue reports a study in 19 patients with recurrent symptomatic atrial fibrillation in whom the atrial defibrillation threshold was determined both 30 s and 10 min after the electrical induction of atrial fibrillation for electrodes in the left pulmonary artery and lateral right atrium^[1]. The atrial defibrillation threshold energy was over 40% lower after 30 s of atrial fibrillation than after

10 min of atrial fibrillation, a highly significant difference.

While these results appear to be consistent with the few previous studies that deal, either directly or indirectly, with the effect of the duration of atrial fibrillation on the atrial defibrillation threshold^[2,3], they are not strongly supported by an animal study that specifically examined this issue^[4]. This animal study found no significant difference in atrial defibrillation threshold between shocks delivered 125 ms and 5 min following the induction of atrial fibrillation