Heart failure: we need more trials in typical patients

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A number of recent, landmark, clinical trials have further advanced our management of heart failure[1–4]. These include studies of the use of beta-blockade and spironolactone[1–4]. Earlier trials clarified the role of digoxin and identified the importance of ACE inhibitors[5–7].

While we can be justifiably proud of these studies we must also recognise their limitations and these have been clearly illustrated by the important survey carried out by the Myocardiology and Heart Failure Working Group of the French Society of Cardiology, the National College of General Hospital Cardiologists and the French Geriatrics Society, published in this issue[8].

Cohen-Solal and colleagues collected data, prospectively, on the first ten consecutive patients hospitalized with a main diagnosis of heart failure between 1 and 30 June 1997 in 120 hospital departments across France. Importantly, they surveyed medical (42) and geriatric (17) departments as well as cardiology ones (61), although it is not clear how representative these departments were of France as a whole. Analysable data were obtained on 1058 patients.

The median age of patients was 76 years and the proportion of females was 45%. These findings should be contrasted to those in recent clinical trials (Table 1). While several other reports have highlighted the age and sex discrepancy between clinical trials and hospital practice, this French survey also contains detailed information on other patient characteristics, particularly left ventricular function[9–11]. Echocardiography was carried out in 77% of patients and the left ventricular ejection fraction was above 40% in more than half. In other words, 53% of these patients would have been ineligible for most heart failure trials, to date, because they did not have left ventricular systolic dysfunction[1–4,6,7].

These data are tremendously important and rare. There have been few attempts to systematically collect information on ‘real’ patients with heart failure and, multidisciplinary, clinical epidemiological studies of this sort are to be encouraged in all countries. The present study highlights just how unrepresentative the patients in our current clinical trials are. Quite why and how they have excluded elderly patients is unclear; for example, the upper age limit in the US carvedilol trials was 85 years, yet the average age of patients in the studies was 58 years[1].

The exclusion of women at least in part reflects the exclusion of older patients, as females with heart failure are more elderly[12]. This age–sex interaction is shown in Table 1[13]. It is quite clear, therefore, that we still do not have an evidence base for treatment recommendations in a sizeable proportion of patients with heart failure.

In the future we must rectify this deficit in our trials. CHARM (Candesartan in Heart failure: Assessment of Reduction in Mortality and morbidity) is recruiting patients with preserved left ventricular systolic function and PEP-CHF (Perindopril in elderly people with chronic heart failure) is planning to recruit elderly patients with preserved systolic function[14,15]. More trials of this type will be needed.

Other important observations emerge from the work of Cohen-Solal and colleagues. Atrial fibrillation was common in ‘normal ejection fraction’ heart failure patients. Increasingly we are recognising the importance of atrial fibrillation as a cause of heart failure ‘progression’ and we need to think more about how its treatment might prevent clinical deterioration[16].

The rate of use of ACE-inhibitors in patients with reduced ejection fraction was commendably high, though was lower, overall, in women and the elderly (and amongst geriatricians). Hopefully, when this survey is repeated again similarly encouraging rates of use of beta-blockers and spironolactone will be found. Other, multinational, projects should also add to this French initiative[17].

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Intensive insulin treatment of diabetic patients with myocardial infarction is highly cost-effective

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As the variety of treatable diseases increases, so too does the health budget. As most communities have a limitation on the further expansion of health budgets, cost effectiveness of different treatment modalities has become increasingly important.

The calculations used for costs and savings differ, hampering comparison between different treatments. One example of such a discrepancy is the question whether future costs in a saved life period should be included in the comparison. This is discussed in the paper by Albrand et al.[11], in which the cost effectiveness of intensive insulin treatment after acute myocardial infarction in patients with diabetes mellitus is estimated.

Patients with type 2 diabetes have an increased morbidity and mortality from ischaemic heart disease. In a recent paper from Haffner et al.[10], it was shown that patients with type 2 diabetes without known ischaemic heart disease had the same risk of myocardial infarction and cardiovascular death as non-diabetic patients with known ischaemic heart disease. This and other findings suggest that patients with type 2 diabetes have a latent arteriosclerosis, and should be treated more aggressively according to guidelines for secondary prevention.

In patients with signs of ischaemic heart disease the mortality risk for the type 2 diabetic patient is considerably higher than for the non-diabetic patient. In several studies it has been shown in patients with acute myocardial infarction, that type 2 diabetics have a mortality twice that of non-diabetics[3,4]. In