whether a differentiation between circulatory failure and sudden death can be achieved with accuracy, especially if the patients dies out of hospital? Is it really justified to classify 93% out-of-hospital deaths as sudden?

Cleland et al.[2] correctly do not equate sudden death with arrhythmic death. In other studies of ACE inhibitors in heart failure and in Garg’s meta-analysis, however, sudden death was presumed to be arrhythmic[3]. The distinction between circulatory failure or progressive heart failure and sudden or arrhythmic death aims to give insight into the mechanisms by which ACE inhibitors reduce mortality in patients with heart failure. It is established[3] that ACE inhibitors reduce total mortality and hospitalization for congestive heart failure mainly by retarding the progression of heart failure. A direct antiarrhythmic effect of ACE inhibitors has neither been documented in clinical observations nor in animal experiments. This view is shared by Cleland et al.[2], who conclude that 'retarding the progression of heart failure appears to be a major factor contributing to the reduction in mortality both by reducing circulatory failure and by reducing sudden death'. Reduction in sudden death, as observed in the AIRE study, can be attributed to several mechanisms such as (1) reduction in acute circulatory failure, (2) reduction in secondary arrhythmic death causally related to less impaired left ventricular function and (3) reduction in the use of positive inotropic, potentially proarrhythmic drugs due to less severe heart failure. Alternatively, one would have to assume a reduction in primary arrhythmic death, which, however, has not convincingly been observed in any placebo-controlled trial.

Thus, it might well be that the reduction in sudden death suggested by Cleland et al.[2] still reflects the same beneficial effect of ACE inhibitors on left ventricular function as seen in other studies; the difference in the mode of death might be due to the definitions used and the assessment performed. In fact, retarding the progression of heart failure seems to be much more desirable and rewarding than fighting sudden death, which among all causes of death seems to be one of the more acceptable. At his 80th anniversary a former olympic silver medallist of the 400 m sprint and later Professor at the University of Heidelberg expressed one last wish, to die suddenly in the mountains which he loved so much. I can imagine that at his age I shall have the same wish and I hope that medical progress will not be able to prevent it.

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Epidemiology of dilated cardiomyopathy: a still undetermined entity

See page 117 for the article to which this Editorial refers

Epidemiological information on heart failure is obtained from various sources and the results can be difficult to compare because of differences in ascertainment and classification of the syndrome. According to the available data, the prevalence seems to range from 3 to 20 individuals/1000, rising to 30-100 individuals/1000 for those aged over 65 years. The incidence in the general population ranges from 1 to 5
cases/1000 population/annum increasing to 40/1000/annum for those aged over 75 years.

Coronary heart disease, arterial hypertension and valvular heart disease account for the great majority of patients with heart failure. In a minority of cases the aetiology is undetermined and the term cardiomyopathy is applied to describe these patients, qualifying their disease as dilated, hypertrophic or restrictive according to the anatomical and functional characteristics of the heart. So, the area of idiopathic dilated cardiomyopathy is a small fraction of the universe of patients with heart failure, but one brought into prominence by the fact that there is no specific treatment for the disease and also that it affects young and middle-aged patients, thus forming an important source of candidates for heart transplantation. This could have, in part, biased the quantitative dimension of the problem. In fact reliable data on the prevalence and incidence of dilated cardiomyopathy are scarce and for this reason studies dedicated to the subject are particularly important.

In this issue Rakar et al. report a very interesting clinical and post-mortem study carried out in the city of Trieste (Italy). The Trieste area is privileged for various reasons. (1) The population of about 250,000 inhabitants is settled, with few migratory shifts, and has a city hospital as the natural referral centre which ensures that when an inhabitant becomes ill he or she is referred there and not elsewhere. (2) The groups of cardiologists and pathologists are of high quality and have worked together for a long time. (3) There is a registry of cardiomyopathies which has been kept by the cardiologists for many years. Its evaluation protocol includes right and left cardiac catheterization and myocardial biopsy, such that all patients who died of suspected or known cardiomyopathy underwent exhaustive clinical assessment. (4) Finally the necropsy rate in the city population as a whole is exceptionally high, around 80%; thus it is unlikely that subjects not diagnosed in life were lost.

The clinically validated post-mortem prevalence of dilated cardiomyopathy in the Trieste population was 0.46%. The post-mortem incidence of the disease was estimated as 4.5/100,000/year. In the same period, the incidence of new cases diagnosed among the resident patients was 2.45/100,000/year. The authors sum the two incidence values as the overall estimated incidence of dilated cardiomyopathy. The estimation of the total incidence of a disease as the sum of autopsy plus clinical incidences does not seem to be fully appropriate. The post-mortem cases belong to a group of patients in whom diseases started several years before, while the new cases with clinical evidence of the disease are presumably going to die in some epoch in the future. So, the incidence of the disease (occurrence of cases in a given period) is not represented by the sum of the two. For example, if the prevalence of a disease in a given population is 50/100,000 cases with 10 deaths a year and 10 new cases a year, the annual incidence of the disease (clinical: new cases; autopsy post-mortem cases) is 10/100,000, not 20. If one further imagines that the disease does not allow survival beyond 5 years and that the observation lasts 5 years, in this period all the new cases diagnosed at the beginning of the observation will be reconsidered as deaths in the course of the observation. Summing the two would give an incidence higher than it really is.

Some other limitations, inevitable in research of this type, may be considered: (1) The stability of the population, which has advantages, gives an obvious characteristic of local specificity to the epidemiological data. Generalizing from such data could be problematic, particularly in a disease such as dilated cardiomyopathy in that a genetic influence is probably significant. (2) The uncertainty of the diagnostic limits, evident in the different choices made by the various authors who have dealt with the subject, exposes the study groups to heterogeneity. For example, the inclusion or otherwise of subjects with a given degree of arterial hypertension, the criteria adopted for the exclusion of a diagnosis of ischaemic heart disease, the inclusion or not of alcoholics could substantially affect the epidemiological profile of the disease. In the Trieste population as many as 41% of the subjects who died of cardiomyopathy drank alcohol excessively, and it is probably not coincidental that 29% had chronic liver disease. (3) Considering the limited size of the study group, the rates of the causes of death and co-morbidity should be viewed with caution: 12% with a family history, 33% with malignancy, 20% of deaths due to massive pulmonary embolism. On the basis of this last finding, the authors forward a cautious comment on the opportunity of using anticoagulants in heart failure. In fact, on the basis of larger studies the problem remains open, and probably further studies with a different design are needed to resolve it.

Apart from these remarks, the data reported by Rakar et al. confirm that the incidence of dilated cardiomyopathy is relatively low. Nevertheless, the relatively high number of subjects diagnosed only at post-mortem is striking. Taking into account the care given to the problem in the area, the rate of undiagnosed primary cardiomyopathy in common clinical practice is probably higher.

It is evident that an organized approach to the public health problem of heart failure requires much more knowledge about epidemiology and,
consequently, the real entity of medical needs. The limitations of the epidemiological data currently available on dilated cardiomyopathy have been pointed out by Rakar et al. who, in their paper, carry out a critical analysis of the literature. Their comments are also valid for heart failure in general. The problem must be tackled at national and international levels with the help of the medico-scientific Societies. I am thinking, in particular, of the European Society of Cardiology. The contribution given by the Trieste group is useful from this point of view, both for the results reported and for focusing attention on the problem.

By the way, in the Trieste population, out of 4629 autopsied residents <90 years old, 2804 (61%) had coronary artery disease. This is the real father of the problems!

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Reference