the heart rate of mice prolonged their life span and, more recently, that reducing the heart rate of monkeys with beta-blockers or sino-atrial node ablation retards coronary atherosclerosis. In humans, mortality reduction has been shown to occur, in persons with existing coronary disease, if the heart rate is reduced with beta-blockers by more than 14 beats.min⁻¹. Proof of the efficacy of reducing the heart rate to avoid atherosclerotic cardiovascular disease awaits long overdue clinical trials in hypertensive and non-hypertensive candidates for cardiovascular disease.

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References

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Prognosis in heart failure: the value of parameter-changes over time

See page 146 for the article to which this Editorial refers

Reliable prediction of prognosis and adequate risk stratification are of primary importance in chronic heart failure. In recent years the prognostic value of a great number of clinical, haemodynamic, ECG, laboratory and exercise parameters have been investigated. However, these efforts resulted only in a few parameters with consistently high power in predicting the progression of chronic heart failure. These conflicting results are not surprising, considering that the prognostic value of a given parameter may depend on and can be modified by several factors, such as the stage and aetiology of heart failure, the biological characteristics of patients and the treatment applied. Generally applicable prognostic factors in chronic heart failure are not yet available.

That is why the changes in parameters over time can be at least as important in prognostication as the values of parameters detected in a single point of time. However, the studies evaluating the significance of these changes are few. The study by Florea et al. dealt with a patient population with mild to moderate heart failure, treated with ACE inhibitors, diuretics, digitalis and direct vasodilators. The exercise duration, the mean peak oxygen consumption (VO₂), the ventilatory response to exercise (VE/VO₂) slope, the diameter of the left atrium and the left ventricular ejection fraction measured in a single point of time were all found to be predictive for the disease outcome in this study. However, among the parameter changes over time only the modification in peak VO₂ proved to be of prognostic benefit. The question arises why other parameters failed to prove predictive. The difficulties in evaluating the changes, as well as some limitations in applying them for prognostication, are surely contributing factors impeding the usability of those parameters. An inherent, unavoidable limitation of such an investigation is that the follow-up, i.e. the survival study must be performed on patients alive after the period of observation. By applying this set-up, patients considered to be most severely ill are...
obviously excluded from the study since their survival period is inherently limited. The higher the number of patients who died previously, the more select the patient population followed. Evidently, this patient group is not entirely comparable to a consecutively selected and double-blinded cohort of patients. To achieve optimal predictive power, the length of the observation period of changes should also be adjusted to the severity of heart failure, i.e. to the expected mortality rate.

The time course of changes in the investigated parameters is also a factor to be taken into account. The rate and the direction of changes — that are dependent mostly on the applied treatment — can also be greatly different depending on the time elapsed. The observation period during which changes are monitored should be long enough for the detection of those changes in order to yield valuable prognostic information. Proper selection of the observation time can reduce these shortcomings.

Taking into consideration the greatly differing time course of various changes, important limitations in evaluation may result from alterations in the length of the optimal observation time. Consequently, parameter changes observed patient to patient, in different periods of time, are not entirely consistent. Therefore, it is not reasonable to extrapolate changes during a given time period to other periods of similar length, but in a different period of disease progression. Another problem may emerge if there are significant treatment changes during the study. A steady treatment schedule is an important pre-requisite for attaining reliable prognostic information over time.

A special value of the study of Florea et al. — investigating mostly older patients with mild to moderate heart failure — is that the obtained information can be extrapolated to the large outpatient population. In this population, the detection and prevention of disease progression may have much greater significance than in the advanced stage of the disease. Nevertheless, the prognostic significance of the changes, particularly in exercise parameters, might be quite different in the groups of patients treated with or without beta-blocking drugs.

Peak VO₂, and its change over time, the prognostic parameter selected by Florea et al., had been proved to be predictive in other studies, mostly in patient populations with severe heart failure awaiting heart transplantation. Stelken et al., after adjusting this parameter for age, gender and weight in moderate heart failure, found that the value of the achieved actual peak VO₂ and its relationship to predicted peak oxygen uptake were prognostically important.

By reviewing the literature, left ventricular ejection fraction measured by echocardiography — with rare exception — failed to predict prognosis, most probably reflecting the investigator-dependency of this technique. On the other hand, when determining left ventricular ejection fraction with other, possibly more exact methods (i.e. by radionuclid-ventriculography) several factors may reduce the prognostic value of this parameter, i.e. the presence and extent of mitral regurgitation, and decreased left ventricular diastolic function.

Echocardiographic parameters reflecting left ventricular diastolic function, such as deceleration time, also proved to be important prognosticators. Few data are available regarding the significance of the left atrial diameter, however, its predictive value can be explained by the fact that it can reliably mirror left ventricular diastolic function and the grade of mitral regurgitation.

Mild and moderate heart failure patients are mostly in the hands of primary care physicians. Therefore, in traditional care the need for simple and readily available prognostic indicators is imperative. In spite of the reliable prognostic value of the cardio-respiratory exercise test, this method is not entirely suitable for risk stratification of the great majority of heart failure patients. The parameters obtainable by this method have their specific role in higher, referral centres; their evaluation may result in a much broader understanding of heart disease progression and thereby a more efficient therapy in the large group of patients suffering chronic heart failure.

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References