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Editorial

Exercise training in chronic heart failure: is it really safe?

See page 872 for the article to which this Editorial refers

There is little doubt that tailored moderate exercise training programmes using aerobic exercises and calistenics can result in improved exercise capacity, ventilatory efficiency, symptomology and quality of life, and reduced neuroendocrine activation in patients with chronic heart failure[1]. The CHANGE (Chronic Heart Failure and Graded Exercise) study, as reported in this issue[2] has once again supported this concept, which has been demonstrated from other research and from experience. Because there were no adverse cardiac events in this study, exercise training has been deemed safe in chronic heart failure patients categorized as New York Heart Association class II and III. The relatively large sample size of 80 patients was considered unique, and it was hoped that this would provide stronger evidence for the safety of exercise training in chronic heart failure than was previously available. Should we agree that the evidence from the CHANGE study is sufficient to conclude that exercise training in most chronic heart failure patients is safe?

In terms of the question, 'Is exercise training in chronic heart failure patients really safe?' we should consider only randomized controlled trials that involve patients with *defined* congestive heart failure, meaning chronically low cardiac output with compensatory sodium and water retention, neurohumoral activation, and thoracic congestion. Additionally, according to standard aerobic training methods, only studies in which large muscle groups were trained should be considered. In some studies, patients with left ventricular dysfunction, with and without signs of heart failure, were lumped together in one pot, and thus not properly categorized[1].

Based on these arguments, which studies have been conducted which fit the above criteria? Including the CHANGE study and the not-yet-published EXERT study (McKelvie), there are 10 randomized controlled trials involving 431 chronic heart failure patients[3–10]; this is still a relatively small number, statistically considered. The mean age of patients was 56 years, the majority under 60. This relatively young age does not take into consideration the fact that the incidence of chronic heart failure increases with advancing age. Patients from these studies demonstrated a narrow range difference in left ventricular dysfunction, with mean values of left ventricular ejection fraction between 19 and 27%, and functional capacity ranging between mean maximum values of 12 and 21 ml . kg^{-1} . min^{-1} $\dot{V}O_2$. In most studies, including the CHANGE study, the aetiology of coronary heart disease and dilated cardiomyopathy was similarly distributed. Usually, myocardial ischaemia and angina were considered exclusion criteria, and the baseline cardiac rhythm status was not precisely defined; this was also true for the CHANGE study. Prior to training, patients were clinically stable for 1 to 3 months.

Were there adverse cardiac events during these studies? If we believe what was reported, no adverse cardiac events occurred during exercise training sessions. During the entire study period lasting between 3 and 52 weeks, the following was reported in four of 10 randomized controlled trials: one death due to worsening heart failure, two sudden cardiac deaths (training groups), one case of right heart failure (control group), one case of AV re-entry tachycardia (training group), two cases of atrial fibrillation (training group and control group), and one case of myocardial infarction. No event was reported to be related to physical exercise. Additionally, there was no difference in distribution of adverse cardiac events for training groups versus control groups, or in terms of location of training (in-hospital supervised vs home-based unsupervised vs combined supervised/home-based programme). These data indicate that exercise training really seems to be safe.

Nevertheless, exercise training studies may not reflect the *real* world. As mentioned above, study patients were highly selected, using exclusion criteria associated with high risk, such as documented myocardial ischaemia and malignant rhythm disorders. Also to be considered is that in two-third of the patients chronic heart failure is due to coronary artery disease, and myocardial ischaemia is the most frequent reason for sudden cardiac death in these patients. Additionally, patients who were not clinically stable for less than 4 weeks, as well as patients with severe symptomology falling between

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New York Heart Association classification III and IV, were excluded. As suggested from Wilson *et al.*[11] clinically stable chronic heart failure patients with severely impaired exercise tolerance (such as <10 ml . kg^{-1} . min^{-1} peak $\dot{V}O_2$) should be involved in an exercise training programme to improve cardiopulmonary exercise reserve, but these patients usually were also excluded. The maximum training period studied so far lasted 52 weeks.

In summary, the available studies on exercise training are characterized by a statistically small number of patients, heterogeneous study design and inclusion criteria, stringent exclusion criteria, an application of various training methods, and a short training period in relation to mean survival time of chronic heart failure patients. Do these studies alone allow one to conclude that exercise training in chronic heart failure is safe? How safe is exercise training in patients with a documented serious rhythm disorder, documented myocardial ischaemia, angina at low work rates, or a history of frequent need for change in diuretics? What can we expect from training periods of 3 years and longer, while primary disease continues? Is it safe in the long-term and is it prognostically effective? There are some indications that exercise training might cause slow myocardial deterioration (significant increase in brain natriuretic peptide blood levels, and pathological levels of troponin I) although no change in left ventricular end-diastolic volume could be appreciated[12]. When involving patients >75 years of age in exercise training programmes, is there a similar benefit-to-safety relationship to that found in younger patients?

The real world of exercise training in chronic heart failure looks like this: we have to consider many patients in a broad range of age and severity of disease. Patients have concurrent disorders such as insulin-dependent diabetes, renal insufficiency with an enhanced risk for electrolyte disturbances and acute heart failure, among others, and a propensity to orthostatic dysregulation. There are patients with a New York Heart Association classification greater than III and/or with a severely impaired exercise tolerance awaiting heart transplantation. It is precisely these patients who often have an urgent need for physical mobilization. During daily routine examination prior to exercise training, discrete rales and/or peripheral oedema are sometimes found, as well as undetected rhythm changes or general discomfort which prompts withdrawal of a patient from exercise training for the day. During exercise training, for example, a third heart sound may develop, and mitral insufficiency may worsen, which may compromise the safety of a patient. Additionally, compliance to the training routine may affect the safety of some patients. For some, exercise training may be considered the 'last hope', and thus the more, the better. In this context it might be understandable when patients deny symptoms and/or repress discomfort, or are not compliant with the prescribed exercise instruction.

All these items have to be taken into account when deciding whether exercise training per se is safe. The CHANGE study provided additional support for efficacy and the general safety of exercise training in a very selected sample of chronic heart failure patients. But this is no justification for encouraging exercise training across the broad chronic heart failure population, which is seen daily. Current experience with exercise training in chronic heart failure probably corresponds to a point between the clinical phases II and III of a pharmaceutical study. In other words, the current state of the art is not advanced enough to state categorically that exercise training for chronic heart failure patients is risk free. Thus, there is still a need for statistically sufficient prospective, randomized controlled long-term trials using patients whose characteristics are different from those studied so far, and using a broader range of training methods (mode, intensity, duration) which have not yet been assessed. Results would then allow us to develop a comprehensive view on the safety of exercise training in patients with chronic heart failure.

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The revival of heart rate

See *European Heart Journal Supplements* Suppl. H which accompanies this issue

Nowadays, 'modern cardiologists' and, in general, MDs, deal with complex theories and sophisticated approaches in their clinical practice: they rely on elaborate diagnostic tools which have, through the years, succeeded in identifying and evaluating those more hidden parts of the hearts and vessels of their patients.

As a result, so-called bedside medicine is no longer a daily clinical practice when compared to 'high tech' medicine. Equally, evidence-based medicine has ruled out intuitive medicine.

The aim of the *European Heart Journal Supplement* which accompanies this issue is to amaze modern cardiologists with an ancient and apparently banal concept, i.e. the heart rate. In our daily activities, we are all concerned with using the best available technique to ensure the proper diagnosis, prognosis and therapeutic intervention. Palpation and ausculation are no longer used. Imaging is the preferred manner of diagnosis, and therefore we often forget to measure heart rate in our patients. Who does this any more?

It is a pity that this method is no longer used, as 'taking the pulse' has always been the first point of contact between doctor and patient and succeeds in reassuring and gaining the confidence of the patient. Besides its value as an easy patient approach, measuring the heart rate also has scientific worth, as we all know that a fast or an extremely slow heart rate is an unequivocal sign of a 'suffering' heart, as is frequently shown in romantic literature, paintings and music. This unsophisticated sign can be considered the means of communication chosen by the body to 'speak' to the doctor. Heart rate is not only the language of romantic times, it also seems to be the language of our modern high tech times, since change in heart rate is the language chosen by the body to communicate with its own cells. It has recently been suggested that the heart rate corresponds to the rate of energy needed by the body. There are theories hypothesizing that the body controls its own metabolic rate and energy needs by altering its heart rate. In fact, heart rate controls nitric oxide release from the endothelium through shear stress. Nitric oxide, in turn, regulates the degree of vasodilatation and thus the amount of blood supplied to the muscles. In this way, heart rate contributes to the metabolic needs of the muscles and, therefore, to their metabolic rate.

Not only this! Heart rate negatively affects the metabolic rate of the heart itself, thus negatively influencing its own 'supplier'! It is surprising to realise that a reduction in heart rate of $10\ \text{beats} \cdot \text{min}^{-1} \cdot \text{day}^{-1}$, saves 5 kg of ATP! In addition, an increase in heart rate of $5\ \text{beats} \cdot \text{min}^{-1}$ corresponds to an increase in the atherosclerosis progression score of 0·21 and to an increase in the stenosis progression score of 0·27!

By analysing heart rate variability one can properly assess autonomic tone, better appraise the control of sinus node functionality and, in general, evaluate the function of the entire body. You may be surprised to learn that animal studies show that life expectancy is related to heart rate! Take a look at these examples: a rat from the pyramids has a heart rate of about $240\ \text{beats} \cdot \text{min}^{-1}$ and lives no longer than 5 years, while the life expectancy of a tortoise from the Galapagos islands, which has a heart rate of $6\ \text{beats} \cdot \text{min}^{-1}$, is 177 years!

Please, don't take your pulse now! We know that human beings are exceptions. We have relatively fast heart rates which correspond to relatively long life expectancy. Why? Changes in the social environment, as well as an improvement in scientific and, more specifically, therapeutic tools have played a role in increasing life expectancy. We know, for instance, that drugs which reduce cardiovascular mortality,