EDITORIAL

Oxygen uptake in heart failure: how much, how fast?

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Patients with chronic heart failure (CHF) have limited exercise capacity. Exercise intolerance in CHF is associated with increased mortality;[1] moreover, several studies suggest that interventions that increase exercise capacity in CHF improve prognosis.[2-4] Therefore, as Kemps and colleagues state in this issue of the *Netherlands Heart Journal*,[5] exercise testing is an important tool for evaluating and monitoring heart failure.

Multiple exercise testing variables are in use or have been proposed to represent exercise capacity. These variables are often assessed by a symptom-limited incremental exercise test. During such a test in CHF patients, the exercise intensity level at which the objective criteria for maximal oxygen uptake ($\dot{V}O_{2max}$) are met is often not achieved. Hence, in CHF patients, symptom-limited exercise tests yield only a peak $\dot{V}O_2$ value. However, the interpretation of the peak $\dot{V}O_2$ value is difficult because it depends on the motivation of the patient and test leader, and on the choice of exercise testing protocol.[6,7] Therefore, in CHF, exercise testing variables are to be preferred that can be obtained from submaximal exercise data. For example, the oxygen uptake efficiency slope (OUES) and the ventilatory response ($\dot{V}E/\dot{V}CO_2$ slope) can easily be computed from respiratory gas exchange results obtained during the test, and both have important prognostic value.[1,8] Meaningful results can already be derived from the data generated during the lower 75% of the covered exercise intensity range.[9-11]

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Also relevant are variables referring to the oxygen uptake kinetics, exercise testing derived variables that depend on the oxygen delivery and utilisation systems, i.e., cardiac, pulmonary, vascular and skeletal muscle systems.[12] In their review article, Arena and co-authors[12] give an overview of variables that characterise VO_2-onset kinetics. These are time constants in steady state exercise protocols and, in progressive exercise protocols, the change in oxygen uptake per unit change in workload, and the time interval from onset of exercise to the linear increase in oxygen uptake. VO_2-recovery kinetics, expressed in a time constant, can be measured by observation of the recovery period of a constant[13] or incremental exercise protocol.[14] As it is not necessary to attain the ventilatory threshold for any of these variables,[13,14] the variables characterising oxygen uptake kinetics can be computed from data obtained during routine exercise testing with respiratory gas exchange analysis in hospitals and in institutions for cardiopulmonary rehabilitation.

Several studies have demonstrated the prognostic relevance of oxygen uptake kinetics in heart failure,[15-19] hence it is relevant that in this issue of the *Netherlands Heart Journal* a review about oxygen uptake kinetics is published.[5] The paper by Kemps and colleagues stresses the potential importance of oxygen onset and recovery kinetics for the clinical management of CHF patients, for risk assessment, and, equally or even more important, to measure the effect of therapeutic interventions. Also, Kemps and colleagues explore the physiological determinants of oxygen onset and offset kinetics, herewith underscoring the multitude of mechanisms involved in oxygen delivery and utilisation. Moreover, the authors would like to have more insight in the pathophysiological mechanisms of oxygen uptake/recovery kinetics in patients with CHF.

When the time constants of the oxygen uptake kinetics during onset and recovery of exercise are compared with the time constants of the cardiac output kinetics, a conclusion can be drawn about whether oxygen delivery or oxygen consumption is the limiting factor. In healthy persons, cardiac output kinetics is faster than oxygen uptake kinetics during onset of exercise, and slower during recovery of exercise. This suggests that oxygen delivery is always in excess of oxygen utilisation. Hence, in healthy subjects, oxygen utilisation mechanisms are likely the limiting factor in onset and recovery of exercise. In a recently published paper by Kemps and colleagues,[20] data are presented that suggest that in almost uniquely NYHA-II CHF patients cardiac output and oxygen uptake kinetics are slower than in healthy subjects, but also, that there was no longer a clear difference between the time constants describing oxygen uptake and cardiac output kinetics. This would imply that, in these patients, not only the oxygen delivery and consumption had deteriorated, but also that it seems that oxygen delivery is the limiting factor for oxygen uptake kinetics.

It is conceivable that in a specific CHF patient, depending on, for example, aetiology, stage of heart failure, treatment, amount of physical activity, the limiting factor in exercise is predominantly either in the oxygen delivery (e.g., cardiac dysfunction, vasoconstriction, endothelial dysfunction) or in the oxygen consumption mechanisms (skeletal muscle dysfunction). A diagnostic procedure that can discriminate between these two possibilities could obviously help in establishing an optimal therapeutic regimen in the individual patient, and could also be helpful in assessing the effect of the instituted therapy.

When limited exercise capacity restricts the daily life activities of a CHF patient, it impairs quality of life, and deprives the patient from being physically active. As physical activity is essential for normalisation of the neurohumoral activation in heart failure and for the improvement in oxygen delivery and oxygen consumption systems,[21] the development of diagnostic and therapeutic approaches that can help to improve exercise capacity in CHF patients is warranted. ■

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