Cardiopulmonary exercise testing for heart failure patients: a hodgepodge of techniques, parameters and interpretations. In other words, the need for a time-break

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This editorial refers to 'Enhanced prognostic value from cardiopulmonary exercise testing in chronic heart failure by non-linear analysis: oxygen uptake efficiency slope'[‡] by L. Ceri Davies *et al.*, on page 684

It is reported in several papers, and is widely accepted by most scientists, that cardiopulmonary exercise test (CPET) is the best way to evaluate exercise capacity and, more importantly, to identify the prognosis of chronic heart failure patients.[1] However, several technical issues can effectively influence the results obtained by CPET. Some of these issues are known, but frequently forgotten or ignored, and some are simply unknown. I will report a few examples. First, we have known since the work of Elborn *et al.*[2] that for properly determined peak oxygen consumption (VO_2) in heart failure patients, a familiarization procedure is needed. Unfortunately, it is unclear how often this is done in either clinical practice or research studies. It seems to me that familiarization procedures are almost never done or, in any case, are almost never reported with the underlying concept that nobody is paying for the second test. Secondly, we have known for many years that ergometers are different. Indeed, we know that, in normal subjects, peak VO_2 is ~10% greater with treadmill than with cyclo-ergometer,[3] but it is unknown whether this is true in heart failure as well. Furthermore, it is also unknown whether walking and biking generate comparable cardiovascular responses in heart failure subjects, although we do know that it is not the case in respiratory patients.[4] Thirdly, which protocol should be chosen? It is now clear that an exercise should last around 10 min and that a

protocol which generates a shorter or longer exercise by itself affects measurements.[5] However, a personalized ramp protocol is rarely used. Indeed, in the great majority of studies, a standard incremental protocol, such as 10 W/min for the cyclo-ergometer or a modified Bruce protocol for the treadmill, is used in heart failure, but exercise capacity is different among heart failure patients. For example, a 10 W/min test which lasts, as it should, 10 min, implies that workload at peak exercise is 100 W, a workload which is rarely obtained in heart failure. Furthermore, the exercise duration is only occasionally reported, so that, I believe, we are frequently dealing with data obtained by test which is often too short and sometimes, though more rarely, too long.

Another issue which is unclear is which CPET parameter we should look at first. Parameters can be grouped into two major categories: the VO_2-related parameters and the ventilation (VE)-related parameters. These two groups analyse two different but interrelated aspects of exercise performance in heart failure. The VO_2-related parameters depend on the efficacy of VE, which includes lung diffusion, cardiac output, oxygen extraction by the muscles, and muscle function, whereas the VE-related parameters depend on the ventilatory efficiency which is related to reflex activity, dead space VE, and, possibly, the amount of gas to be exchanged. So, none of these parameters looks at a singular body function. Another issue is that several parameters are related to a specific moment of exercise, such as peak or the anaerobic threshold, and it is crucial to precisely define these specific moments: is peak the real peak, is anaerobic threshold determination correct, and so on. In the recent years, more attention has been dedicated to gas kinetics analysis. This has the advantage of not being related to a specific time frame, although it might suffer from its difficult mathematical approach and from the pretence that a single phenomenon guides a process throughout the entire exercise. The fact that none of the possible parameters obtained by CPET is 'the perfect prognostic parameter for heart failure', regardless of heart failure severity or treatment, can be

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confirmed by the plethora of tentatives to improve prognostic capability done by adding to CPET parameters one or more non-CPET variables such as cardiac output,[6] blood pressure,[7] or several parameters grouped in more complex scores.[8]

Ceri Davies *et al.*[9] bring our attention to the oxygen uptake efficiency slope (OUES), an index obtained by analysing VO_2 and VE kinetics. Indeed, OUES is obtained by the mathematical analysis of the VE/VO_2 relationship. It is an attempt to combine VO_2 with VE-related parameters. OUES is a good prognostic indicator which remains so also if only a portion, as low as 50%, of the exercise is evaluated. This is an extremely important finding. Apparently, in this regard, OUES is better than VE/VCO_2, but in Ceri Davies study,[9] as in many other studies,[10] the VE/VCO_2 relationship is calculated throughout the entire exercise, even though it is well known that, due to acidosis-induced hyperventilation, the slope of the VE/VCO_2 relationship is steeper in the last part of the exercise. However, before extensive application of OUES can be carried out in clinical practice, a few issues should be resolved: (i) Is OUES related to exercise duration? (ii) Is OUES obtained with a treadmill exercise similar to that obtained with a cyclo-ergometer exercise? (iii) Is OUES the same at altitude? So, as is usually the case in an intriguing paper, more questions are brought out than answers.

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