Working Group Report

Recommendations for exercise testing in chronic heart failure patients

Working Group on Cardiac Rehabilitation & Exercise Physiology and Working Group on Heart Failure of the European Society of Cardiology

Introduction

In the chronic heart failure patient, exercise intolerance is one of the hallmarks of disease severity. However, symptoms are modestly related to measures of functional capacity, and symptom scores during exercise tend to under-estimate the level of functional disability[1], suggesting that clinical symptoms are not reliable indices of exercise intolerance.

Therefore, exercise testing has been widely used in the assessment of chronic heart failure patients. Directly measured VO_2 has been shown to be a reproducible marker of exercise tolerance in chronic heart failure, and to provide objective and additional information regarding the patient's clinical status and factors which limit exercise performance[2–8]. 'Maximal VO_2' is traditionally defined as a plateau of the maximum oxygen consumption reached during exercise (it does not increase any more while external work increases). VO_2 max is generally not achieved in chronic heart failure patients, because they are usually limited by symptoms of fatigue or dyspnoea. 'Peak VO_2' (VO_2 at peak exercise) is the better term to describe the highest oxygen uptake achieved in chronic heart failure. Like maximal workload and exercise duration, peak VO_2 is dependent upon motivation and perceived symptoms (of both patient and physician). It is more reliable than other indicators of exercise tolerance. Moreover, exceeding the anaerobic threshold (which generally occurs at 60–70% of the peak VO_2) or a respiratory exchange ratio (the ratio of VCO_2 to VO_2) exceeding 1·0 at peak exercise suggests adequate patient effort.

Determinants of exercise intolerance

The main determinants of peak exercise capacity are summarized in Table 1.

Peak VO_2 is generally poorly correlated with haemodynamic parameters measured at rest. Resting haemodynamic variables do not accurately reflect pump function reserve, which can accurately be evaluated during exercise. During exercise, maximal cardiac output correlates with peak VO_2 and inadequate cardiac output reserve is the primary determinant of the impairment in aerobic capacity in asymptomatic or mildly symptomatic heart failure patients[9]. Maximal pulmonary capillary wedge pressure does not correlate with peak VO_2, suggesting a more complex mechanism between pulmonary circulation and limitations of exercise capacity[9–11]. While heart failure worsens, several neurohormonal systems are gradually hyperstimulated, among others the adrenergic system. The heart responds to the increased level of catecholamines with a downregulation/desensitization of beta-adrenergic receptors which drops the heart rate response to exercise (and contributes to limit the exertional increase on cardiac output). The blunted chronotropic reserve causes the pump function reserve to deteriorate further.

In moderate to severe chronic heart failure patients, the decreased skeletal muscle vasodilation in response to exercise appears to be an important determinant of decreased peak VO_2. While normal subjects distribute close to 90% of total cardiac output to exercising skeletal muscle during maximal exercise in the lower extremities, patients with chronic heart failure distribute only 50–60% of total cardiac output to the exercising skeletal muscle. Failure to redistribute available cardiac output reserve to the lower extremities during exercise is probably caused by multiple factors, including increased vascular resistance of the skeletal muscle vasculature and endothelial dysfunction. The main mechanisms responsible for functional abnormalities of peripheral perfusion are systemic neurohormonal hyperactivity, with predominance of vasoconstrictor and antinatriuretic systems (sympathetic nervous system, renin-angiotensin-aldosterone system, endothelin, vasopressin,

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Table 1 *Main determinants of exercise capacity in chronic heart failure*

Central haemodynamics
    Heart rate response to exercise
    Stroke volume response to exercise
    Left and right ventricular ejection fraction
Neurohormones
    Sympathetic drive during exercise
    Beta-adrenergic sensitization
    Balance between vasoconstrictor and antinatriuretic systems
    versus vasodilatory and natiuretic systems
Peripheral response
    Skeletal muscle perfusion and vasodilatory capacity
        muscle vasculature resistance
        vascular endothelial function
        cytokines, local growth factors and sodium content in the
        vessel wall (vascular remodelling)
    Skeletal muscle mass
    Skeletal muscle function
Pulmonary function
    Breathing pattern
    Bronchial reactivity
    Gas diffusion
    Ventilation/perfusion ratio
    Ventilatory response

constrictive prostaglandins) and abnormalities in vascular endothelial function (decreased production of nitric oxide and overexpression of the endothelin-1 pathway). Chronically reduced peripheral blood flow, neurohormonal activation, increased release of cytokines and local tissue growth factors may reduce the calibre of the resistance arterioles (hypertrophy of smooth muscle cells, increase in the sodium content of the vessel wall) and therefore decrease maximal vasodilatory capacity in the peripheral circulation in severe chronic heart failure patients[10]. Exaggerated ergoreceptor activity has also been demonstrated in chronic heart failure patients[12], which is responsible for hyperstimulation of circulatory and respiratory sympathetic-mediated responses, leading to both inappropriate hyperventilation/dyspnoea and early muscular fatigability/asthenia.

In severe chronic heart failure patients the skeletal muscle typology and enzyme profile change. Modification of muscle fibre distribution (increase of glycolytic at the expense of oxidative fibres), reduction of mitochondria which are smaller and with a reduced surface area of the cristae, and a selective reduction in the enzymes involved in the oxidative pathway have been found in the muscle biopsies of such patients and are related to peak VO_2 limitation. The overall result of such changes is reduced metabolic efficiency (early increase in anaerobic metabolism, higher release of lactate)[2,13]. Recent studies suggest that skeletal muscle myopathy, among other factors, might be related more to deconditioning than to a chronic reduction in peripheral flow. However, the concomitant alterations and weakness of both skeletal and respiratory muscles (which are likely to be used more rather than less) raises questions about inactivity being the predominant cause of muscle dys-

function. In fact muscle atrophy is frequent in chronic heart failure patients, and has been linked to underperfusion, malnutrition, direct action of cytokines, and genetics (reduction in myosin-I heavy chain)[14], but does not appear to be a major determinant of peak VO_2 per se. Clinical consequences of skeletal myopathy are decreases in strength and muscle endurance capacity, both of which contribute to the reduction in peak VO_2[15].

In the process of distribution, diffusion and utilization of oxygen, respiratory abnormalities may play a role[9,11]. A restrictive pulmonary pattern is common in chronic heart failure patients (increased cardiac size, interstitial, alveolar and pleural fluid). Bronchial hyperreactivity and alterations in oxygen diffusing capacity[16,17] have also been described. However, it is not clear if and to what extent these pulmonary abnormalities contribute to exercise limitation, given that arterial oxygen desaturation is not generally observed in chronic heart failure patients. A reduction in respiratory muscle and diaphragm strength and endurance is observed in more severe chronic heart failure patients and can lead to a reduction in maximal voluntary and maximal sustainable ventilation. Recently, when measuring respiratory muscle force with non-volitional and more reliable tests[18], only a slight weakness of the diaphragm was demonstrated in chronic heart failure patients, but the overall respiratory muscle force was preserved, suggesting that respiratory force is not a major determinant of peak VO_2. Chronic heart failure patients show a steeper increase in respiratory rate during exercise and greater ventilation at a given workload. The severity of these ventilatory abnormalities is reflected in the elevated slope of the relation between ventilation and carbon dioxide production (VE/VCO_2), which is related to peak VO_2. Ventilation is increased due to haemodynamic mechanisms such as a ventilation–perfusion mismatching in the lung (increased ventilation of dead space due to pulmonary hypoperfusion), possibly heightened hypoxic carotid chemosensitivity and skeletal muscle alterations (early accumulation of lactate in the blood, exaggerated ergoreflex activity[12,19]).

In summary, the major determinant of exercise intolerance is most likely cardiac output reserve in asymptomatic and mildly symptomatic chronic heart failure patients, while abnormal peripheral mechanisms have a greater role in moderate and severe chronic heart failure patients.

Exercise testing protocols in chronic heart failure

The question concerning the most appropriate exercise test protocol with which to assess prognosis and functional capacity in patients with chronic heart failure has been intensely debated in recent years [20–28]. The protocol chosen often depends on the experience of the testing physician.

Protocols can differ considerably in terms of the rate with which work is incremented, the duration of time between stages, and total exercise time. Large and rapid work increments have been shown to result in less accurate estimates of exercise capacity, particularly for patients with heart failure. The test duration can have a considerable influence on the evaluation of therapy, how accurately oxygen uptake is estimated, and the symptom limiting exercise[26,29–31].

Thus the selection of protocols for testing heart failure patients appears to be of considerable importance. It should yield the maximum amount of information and assess a patient's maximal or near maximal function with a high degree of confidence and reproducibility[32,33]. Patients with heart failure stop exercising usually due to one of two reasons: breathlessness or fatigue. Breathlessness may be the salient symptom during rapidly incremented protocols, whereas fatigue predominates during gradually incremented tests[26]. Many patients with chronic heart failure have been tested using the modified Naughton protocol, which increases in approximately 1 MET increments at each 2 min stage[24]. This protocol has the advantage in that a great deal of functional and prognostic data have been generated with its use among chronic heart failure patients. The Ellestad and modified Astrand protocols employ work rates that may be too difficult for most patients with heart failure to achieve. Similarly, the Bruce protocol is too demanding because of its large increments in workload per stage, resulting in a duration of exercise for the heart failure patient which is too short[30,32]. For most patients with chronic heart failure, stage increments of approximately 1 MET (2·5% increase in grade on the treadmill, 10 to 15 Watt increments on the cycle ergometer) are recommended.

Recent exercise testing guidelines published by the American College of Cardiology, the American Heart Association and the American College of Sports Medicine have consistently recommended that the exercise protocol be individualized for each patient, that the increments in work be reduced and that the total duration of the exercise test be maintained between 8–12 min[33,34]. These conditions would appear to be facilitated by the ramp approach, in which work increases continuously[30,33–35]. Because this test allows increments in work to be individualized, a given test duration can be targeted. The linear increase in heart rate and oxygen uptake with the ramp protocol permits improved interpretation of gas exchange responses not possible with protocols employing large, abrupt, or unequal changes in work between stages. Oxygen uptake has been shown to be over-estimated from tests that contain large increments in work compared with individualized tests such as with the ramp protocol. The importance of gas exchange measurements in patients with heart failure has been mentioned above. Ramp software is now available both for cycle ergometer and treadmill testing from many of the system manufacturers.

Table 2   *Exercise testing in chronic heart failure: key points*

1. Exercise testing in stable chronic heart failure only
2. Directly measured oxygen uptake is preferable to estimate of METs
3. Individualized protocol (ramp, Naughton)
4. Stage increments of 1 MET are recommended
5. Optimal test duration 8–12 min
6. Walking test for submaximal testing

Testing of heart failure patients can be performed either on a treadmill or on a bicycle ergometer. The bicycle ergometer offers the convenience of a stable sitting position and is more familiar in Europe, whereas the treadmill is the more common testing mode in the U.S.A. Peak VO_2, the ventilatory threshold, and minute ventilation are generally 10 to 20% higher with treadmill testing[25,30–35]. It should be noted, however, that major multicentre trials in heart failure have found similar peak VO_2 values to be important in predicting mortality, using either the treadmill or cycle ergometer[36].

The 6-min walk test has become more popular in recent years due to its ease of administration and its approximation to daily tasks. The test uses a 20 m long, level, enclosed corridor. Instructions are given to the patient to cover as much ground as possible in 6 min by walking continuously if possible, and performance is quantified by distance walked. This test is less likely to discriminate between NYHA Class II and III than the measurement of peak VO_2, but may be well suited for patients with moderate to severe heart failure in whom repeated testing is used for serial monitoring[37–41] (see section on functional and treatment assessment). A substudy of the SOLVD registry reported that the 6-min walk test was an independent predictor of mortality and morbidity[42].

An exercise test should be performed with the patient in a stable clinical condition for a duration of at least 2 weeks. Clinical stability is defined by stable symptoms, absence of resting symptoms and postural hypotension, stable fluid balance (need of an increase in diuretic dosage no more than once a week), freedom from evidence of congestion, stable renal function (i.e. creatine level) and normal or near-normal electrolyte values[43]. Caution is advocated when the systolic blood pressure drops below 80 mmHg, resting heart rate is below 50 beats . min^{-1} or increases above 100 beats . min^{-1}, symptomatic arrhythmias occur (AID firing ≤ 1 . $month^{-1}$) or when dressing and body caring are associated with clinical symptoms.

In summary, the choice of the exercise test protocol in patients with chronic heart failure for prognostic, functional, and treatment applications is important to ensure an optimal information yield. Ideally the protocol should be tailored to the physical capabilities of each patient (individualized) and should be challenging enough yet of sufficient duration to achieve target endpoints within 8–12 min. Increments in work should be

Table 3   Cardiopulmonary exercise testing for differential diagnosis of dyspnoea

	Cardiac disease	Pulmonary disease
Peak VO_2	Reduced	Reduced
Anaerobic threshold	Precox	Normal
Oxygen pulse	Early plateau	Normal
VO_2 workload ratio	Reduced	Normal
Chronotropic response	Normal, increased, decreased	Normal or increased
Ventilatory reserve	Normal	Reduced
PaO_2	Normal	Decreased
Oxygen saturation	Normal, unchanged	Decreased
A-V oxygen difference	Normal	Decreased
Respiratory rate	Increased	Excessive
Vd/Vt	Normal reduction	Constant

Table 4   Correlation between self-administered activity questionnaire and objective measures of exercise tolerance

Correlation with	NYHA	CCS	SAS	DASI	VSAQ
Treadmill time	− 0·54	− 0·64	− 0·66		0·82
Peak VO_2	− 0·28	0·49	0·30	0·58	0·57
Reference	[49]	[49, 50]	[49, 50]	[50]	[51, 52]

NYHA=New York Heart Association classification; CCS=cardiovascular class; SAS=specific activity scale; DASI=Duke Activity Status Index; VSAQ=Veterans Specific Activity Questionnaire.

used that are no larger than 1 MET between stages. The ramp approach (treadmill or bicycle ergometer) appears to facilitate these recommendations for maximal testing. For submaximal testing the 6 min walk test may provide important prognostic information (Table 2).

Application of exercise testing in chronic heart failure

Diagnosis

Exercise testing in patients with suspected chronic heart failure is generally of little value for diagnostic purposes. The European Society's Guidelines[44] for the diagnosis of heart failure suggest that a normal exercise test in a patient with suspected heart failure (not receiving treatment for heart failure) excludes heart failure as a diagnosis. Exercise intolerance due to fatigue or dyspnoea is a finding supporting the diagnosis of heart failure, but it lacks specificity. The results of a cardiopulmonary exercise test may be taken for differential diagnosis of dyspnoea (Table 3): a marked fall in oxygen saturation, PaO_2 and arterovenous oxygen difference, a reduced ventilatory reserve, normal oxygen pulse and a normal ratio between VO_2 and workload suggest pulmonary disease[45–47].

The use of exercise testing for determining the aetiology of the disease is generally not helpful, particularly in patients with moderate-to-severe chronic heart failure, due to the high prevalence of resting ECG abnormalities, which prevent meaningful ECG analysis. The combination with imaging techniques may be of some value in confirming an ischaemic aetiology. The main applications of exercise testing in chronic heart failure are focused therefore on functional and treatment assessment and on prognostic stratification.

Functional and treatment assessment

Modest correlations have been found between peak VO_2 and measures of daily function obtained by a self-administered activity questionnaire [like the Specific Activity Scale (SAS), Cardiovascular Class[48], the Duke Activity Status Index (DASI)[49], and the Veterans Specific Activity Questionnaire[50,51] (Table 4)], as well as those obtained by monitoring body motion, heart rate, or pedometer scores[52,53]. These findings suggest the inability of these methods to measure functional capacity accurately in an individual and underscore the need for objective measures.

Functional capacity should be expressed as the MET value estimated from the workload achieved or, better, as the peak VO_2 achieved during an exercise test. Functional assessment is commonly classified by peak VO_2 on a symptom-limited exercise test using the Weber criteria (Table 5[2]). If the patient is seriously deconditioned, submaximal exercise testing (such as the 6 min walk) is suggested.

While exercise testing for functional assessment in chronic heart failure patients is broadly accepted among

Table 5 Weber functional classification for heart failure

Weber class	Peak VO$_2$ ml . kg^{-1} . min^{-1}	Anaerobic threshold ml O$_2$. kg^{-1} . min^{-1}	Deterioration of functional capacity
A	>20	>14	Mild or absent
B	16–20	11–14	Mild–Moderate
C	10–15	8–11	Moderate–Severe
D	<10	<8	Severe

most cardiologists, debate exists about is value in assessing changes that may occur with interventions[54–58]. It has been argued that there is a poor relationship between exercise test results and mortality rates in clinical trials with angiotensin converting enzyme inhibitors and with beta-blockers; for example there was only a modest effect on exercise capacity despite a significant improvement in survival in the SOLVD and V-HEFT Trials[36,42].

Many authors have therefore called for optimizing the exercise test for treatment assessment[29–33,54–61]. It is often argued that the quality of studies that use exercise to objectively evaluate the efficacy of interventions depends heavily on how the test is carried out. For instance, exercise time may increase in a standard protocol with serial testing on the same day and on different days even without interventions. Changes in treadmill time with serial testing have even been observed without changes in maximal heart rate or double product. In contrast, a number of investigators have observed that measured oxygen uptake remains relatively stable with serial testing whereas exercise time continues to increase[59–63]. This suggests that measured oxygen uptake is a more stable and reliable measure of exercise tolerance than exercise time. Another important consideration is the time of testing with respect to the time medication effect.

These observations emphasize the importance of measuring, rather than predicting, oxygen uptake when studying treatment effects. Several investigations have confirmed that substantial errors can result when using certain protocols, studying certain disease states, or both. Again, it appears that more modestly-incremented or ramp-type protocols are superior choices for optimizing cardiopulmonary assessment when evaluating interventions in patients with heart failure. Regardless of the specific protocol chosen, the exercise test should be adapted to the subject and purpose of the test.

It is suggested that, in addition to data at rest, a number of points during exercise, both maximal and submaximal, should be obtained in order to improve the yield of information concerning treatment effects[59,63,64]. A matched (placebo vs drug) submaximal workload is particularly important when studying oxygen uptake in patients with chronic heart failure (i.e. with a beta-blocker). Patients with chronic heart failure are known to have a reduced cardiac output for a given level of submaximal work. Because most medications have the primary goal of increasing cardiac performance, reducing afterload, or both, a comparison of the oxygen requirements at a matched submaximal workload can add significantly to the assessment. In none of the large clinical trials were these additional points of analysis considered[56].

Finally, mortality and exercise capacity may not be influenced equally by a given intervention. In other words, a given drug may improve survival, but not exercise tolerance. Furthermore, some exercise trials in chronic heart failure have demonstrated marked improvements in peak VO$_2$, without changes in left ventricular function[58]. Moreover, the influence of exercise training on mortality in these patients has not yet been studied. Therefore, the lack of relationship between exercise test results and mortality may not necessarily be due to the inability of the exercise test to detect changes in work capacity, but may be a true finding.

Exercise testing is a useful tool for the functional assessment of patients with chronic heart failure. Gas exchange techniques should be included whenever possible. When these methods are unavailable, functional capacity should be expressed as a MET value, estimated from the workload achieved. Submaximal tests (such as the 6 min walk) can be used to complement maximal tests, and both have been shown to have prognostic value. A wide variety of protocols can be chosen; however, gradually incremented or ramp approaches appear to have advantages over other protocols.

When exercise testing is performed for treatment assessment in the context of a study protocol, several points of analysis should be used (maximal, submaximal and matched workloads). Submaximal testing with the 6 min walk test may provide reasonable complementary information.

Prognosis

Prognosis remains a major concern for patients with chronic heart failure. Despite significant advances in treatment options for this condition, the risk of death in patients with severe chronic heart failure can exceed 50% annually[65–68].

In recent years, exercise testing has been used for prognostic purposes and exercise capacity has been demonstrated to be an important component to the risk profile in chronic heart failure. Peak VO$_2$ was shown

to be a strong predictor of hospitalization and death in the broad population of patients from the Veterans Administration Heart Failure Trial[69] and a predictor of survival in patients with more advanced heart failure considered for heart transplantation. Transplantation has been demonstrated to improve prognosis considerably; the 1 year survival rate is approximately 85–90% and the 5-year survival approximately 70–75%. Successful transplantation is usually associated with improvements in exercise capacity[70,71]. However, there remains a paucity of available donor hearts relative to the demands[72]. In order to direct the limited number of donor hearts to patients who need them the most, a great deal of effort has been directed toward stratifying risk in patients with severe chronic heart failure using clinical, haemodynamic and exercise data. In particular, directly measured oxygen uptake has, in some studies, outperformed clinical, haemodynamic and other exercise test data in predicting 1–2 years mortality[3,73–77]. This variable has been categorized differently by many investigators. In a widely-cited study Mancini *et al.*[3] found that patients with a peak $VO_2 \leq 10$ ml . kg^{-1} . min^{-1} had the worst prognosis. Other cut-offs proposed for risk stratification have been >10 to 14, >18 and >18 ml . kg^{-1} . min^{-1}. Recently, a 4-year follow-up study[78] showed that, when expressed using the common cutpoint of 14 ml . kg^{-1} . min^{-1}, measured peak VO_2 was a significant predictor of death, whereas exercise capacity predicted from the work rate was not. Several investigators have reported that patients who achieve a peak VO_2 >14 ml . kg^{-1} . min^{-1} appear to have a prognosis similar to that observed in patients who receive transplantation (i.e. mortality rate roughly 10% at 1 year[3,73–77]), implying that transplantation can be safely deferred in these patients.

However, the available data concerning an optimal cut-off point to discriminate survivors from non-survivors remains sparse. First, a large follow-up study[78] confirmed some of the cut-off points proposed by Mancini *et al.*[3], where a peak VO_2 ≤ 10 ml . kg^{-1} . min^{-1} identifies high risk patients, a peak VO_2 >18 ml . kg^{-1} . min^{-1} identifies low risk patients, but all other values in between these cut-off values define a gray area of medium risk patients, without any further possible stratification by the VO_2 value per se. This result has been confirmed by other reports in the literature[75,79]. Moreover, in that study the cut-off of 14 ml . kg^{-1} . min^{-1} previously proposed did not discriminate patients at different risk.

Second, the simplistic use of the same cut-off values in all patients with moderate to severe heart failure might be inappropriate. In the same study mentioned above[78], the prognostic power of peak VO_2 was confirmed only in patients in functional class I or II. Although the cardiac event rate was higher in functional class III or IV, survival curves corresponding to the peak VO_2 strata were not significantly different. In these patients the presence of a clinical contraindication to performing the exercise test, despite optimized medical treatment, is a simple and strong negative prognostic indicator.

Thirdly, some technical limits exist. The prognostic stratification according to peak VO_2 is less if the value of anaerobic threshold is not detectable[3,78]. When fourthly the prognostic value of the measured peak VO_2 and the percentage of normal peak VO_2 achieved are compared, the reported data are conflicting[73–77]. In theory, expressing peak VO_2 relative to a normal standard should improve its predictive accuracy because VO_2 is influenced by sex, body weight, and most importantly, by age. However, various factors may account for the negative results. The relation between peak VO_2 and age in the various published regression equations is relatively weak. Moreover, peak VO_2 is related to other variables that are not so easily measured, such as psychological factors, muscle mass and strength.

Because of safety concerns, muscle weakness, and deconditioning, some patients with chronic heart failure are not appropriate candidates for, or may not be able to perform, a symptom-limited maximal exercise text. In such patients submaximal testing may be more appropriate. As mentioned above, the 6 min walk test has been shown to be helpful in stratifying high from low risk patients[42], but its addictive prognostic power is still controversial[40,80–82].

Another useful submaximal parameter is the VO_2 at the ventilatory or lactate threshold. VO_2 at the ventilatory threshold was recently demonstrated to be a significant univariate predictor of death, although it did not outperform peak VO_2[75]. This measurement, however, carries inherent problems related to definition, determination and application[83]. Nevertheless, this observation suggests that it may have a complementary role in the prognostic assessment of patients with chronic heart failure.

Other exercise variables, like the kinetics of oxygen consumption during and after exercise (entity of the oxygen debt), an abnormally high ventilatory response (VE/VCO_2), an abnormally low chronotropic response, a peak systolic blood pressure lower than 120 mmHg showed predictive properties, in some cases better than peak VO_2[84–89]. These parameters are easy to be measured and worth considering: the combination of all prognostic variables could lead to an increase of the predictive power of the exercise test. Coupling of haemodynamic measurements with oxygen consumption during exercise showed controversial results in the risk stratification of patients with heart failure[90,91].

Two recent studies have assessed whether serial peak VO_2 can help in identifying patients at high or low risk. Stevenson *et al.*[92] reported that 38 of 68 patients increased peak VO_2 by a degree greater than or equal to 2 ml . kg^{-1} . min^{-1} to a level greater than or equal to 12 ml . kg^{-1} . min^{-1} after a mean of 6 ± 5 months, and the 2-year survival rate in these patients was 100%. These results strongly suggest that subtle increases in peak VO_2 in severe chronic heart failure patients portend an excellent prognosis, and such patients could safely be removed from a transplant list. In contrast, Gullestad *et al.* observed 263 severe chronic heart failure patients with heart failure who underwent two exercise

ests a mean of 8 months apart after baseline evaluation and stabilization, and found that subtle changes in peak VO_2 did not contribute to prognosis[8]. The conflicting results of these studies suggest the need for additional data.

Safety concerns

The only data available which has focused on safety was reported by Tristani and colleagues[93] on 607 mild-to-moderate chronic heart failure patients assessed for the Veterans Cooperative-(VHeFT) trial. The initial baseline test was stopped in only 1·6% of patients for arrhythmias and in one patient for hypotension. The incidence of ventricular arrhythmias was assessed before, during and after a second baseline test for a period of about 5 h. They reported no significant differences in the incidence of arrhythmias during exercise testing compared with the pre and post exercise period and concluded that exercise testing was safe.

To date there have been no reports of serious problems related to exercise testing or training in chronic heart failure. The partial exclusion from the studies of patients with evidence of significant arrhythmias or abnormal blood pressure responses should be taken into account when these data are applied in the clinical setting.

Relative and absolute contraindications outlined in the available exercise testing guidelines[94] (unstable symptoms, arrhythmia, aortic stenosis, etc.) would be more commonly observed in patients with chronic heart failure, in addition to the specific precautions already addressed in this document. All these factors should be carefully considered before testing any patient in this condition.

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