Prediction of peak oxygen uptake in chronic fatigue syndrome

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Abstract

Objectives—To establish a simple, valid, and acceptable method of predicting peak oxygen uptake (VO₂peak) in patients with chronic fatigue syndrome (CFS), which could provide a basis for subsequent exercise prescription at an appropriate intensity as part of a clinical rehabilitation programme.

Methods—A total of 130 patients who met UK research criteria for CFS were taken from consecutive referrals for chronic fatigue to the University Department of Medicine at Withington Hospital, Manchester. VO₂peak was determined using an incremental graded exercise test to exhaustion. Respiratory gas exchange, work rate, and heart rate were monitored throughout.

Results—In all patients, VO₂peak was found to correlate strongly and significantly with peak work rate (WRpeak) during testing (r² = 0.88, p<0.001). In patients who exercised for longer than two minutes (n = 119), regression analysis established the relation as VO₂peak = 13.1 × WRpeak + 284, where VO₂ is given in ml/min and WR in W. The mean error between the measured VO₂peak and the predicted value was 10.7%. The relation between increase in work rate and oxygen uptake across the group was highly significant (r² = 0.87, p<0.001), and given as VO₂increase = 12.0 × WRincrease, this value being similar to that expected for healthy individuals. Almost all (97%) subjects reported no exacerbation of symptoms after maximal exercise testing.

Conclusions—Using a simple to administer maximal exercise test on a cycle ergometer, it is possible to predict accurately the VO₂peak of a patient with CFS from peak work rate alone. This value can then be used as an aid to setting appropriate exercise intensity for a rehabilitation programme. The increase in VO₂ per unit increase in workload was consistent with that expected in healthy individuals, suggesting that the physiological response of the patients measured here was not abnormal. Contrary to the belief of many patients, maximal exercise testing to the point of subjective exhaustion proved to be harmless, with no subjects suffering any lasting deterioration in their condition after assessment.

Keywords: chronic fatigue syndrome; work rate; exercise prescription

The research criteria produced by Sharpe et al describe chronic fatigue syndrome (CFS) as a symptomatically defined illness of definite onset, characterised by fatigue as the principal symptom. The fatigue is severe, disabling, and affects physical and mental functioning, and must have been present for a minimum of six months during which it was evident for more than 50% of the time. Other symptoms may be present, particularly myalgia, arthralgia, and mood and sleep disturbance. Certain patients are excluded from the definition including those with established medical conditions known to produce chronic fatigue.

Investigations into the exercise capacity of CFS suffersers have shown a reduced aerobic work capacity, reduced peak heart rate, reduced time to exhaustion on a standardised exercise protocol, and higher heart rates at submaximal levels of exertion compared with control subjects. Graded exercise has been recommended as a possible treatment for CFS in a Joint Working Party Report from the Royal Colleges of Physicians, Psychiatrists and General Practitioners. This approach has since been shown to be effective in two independent clinical trials.

Any exercise prescription should include specific recommendations for mode of activity, frequency, duration, and most importantly, intensity. The maximal oxygen uptake (VO₂MAX) of a subject performing gross whole body activity is readily measured in the laboratory by respiratory gas analysis during subjection to gradually increasing workloads to the point of exhaustion. The appropriate training intensity or work rate is then commonly expressed as a percentage of the measured VO₂MAX, and specific work rates can be prescribed across a variety of common exercise ergometers or modes of activity.

The equipment required to perform respiratory gas analysis and thereby directly measure VO₂ is rarely available during clinical rehabilitation, although an estimation during either steady state or incremental leg ergometry (cycling) and some other modes of activity (commonly walking or running on a powered treadmill) is possible in normal healthy subjects. Alternatively, the Astrand Rhyming Nomogram provides a simple means of predicting VO₂MAX from steady state submaximal measures of heart rate and workload, and is widely used within the health and fitness industry. However, the validity of employing an extrapolative technique to obtain a predicted VO₂MAX is dependent on the assumption that age related predicted maximal heart rate would be achievable during activity. If this is not the...
Subjects breathed through a one way valve system which was attached to a 6 V Fleisch pneumotachograph. This was calibrated using a 3 litre calibration syringe. A gas sample line was connected to a PK Morgan gas analyser (PK Morgan Ltd, Chatham, Kent, UK). This system uses a paramagnetic oxygen analyser which was calibrated to span between 15 and 21% using certified reference gases from CryoService Ltd, Worcester, UK. The infrared carbon dioxide analyser was calibrated to span between 0 and 4%. Calibration was performed each day before testing and between patients. Interface to a Dabs Press microprocessor allowed minute by minute monitoring of respiratory variables including oxygen consumption (VO2), carbon dioxide production (VCO2), and minute volume. The VO2peak was taken as the highest recorded 60 second average during the course of the exercise test.

Immediately after cessation of the test, patients were asked to rate on the Borg RPE scale their own perception of their overall exertion at the end of the test. Patients had to position themselves on a scale with values ranging from 6 (marked “No exertion at all”) at one end to 20 (marked “Maximal exertion”) at the other. At a subsequent appointment one week later, they were asked specifically if they had experienced any adverse after effects following testing, including excess fatigue or additional pain.

STATISTICAL ANALYSIS
This was carried out using SPSS for Windows (release 8.0). A Pearson correlation coefficient was calculated to establish the strength of the association between VO2peak and WRpeak. Linear regression was used to determine the relation between variables. Statistical significance was set at p<0.05 (two tailed).

RESULTS
Of the 136 patients who were initially screened and found to be eligible to undergo testing, four dropped out during the initial assessment before all physiological measures were taken and two patients chose to do a step test for their exercise assessment. This left 130 patients who

| Table 1 Summary of demographic details and selected physiological variables after exhaustive cycle ergometer exercise in 130 patients with chronic fatigue syndrome |
|---------------------------|---------------------------|
| Demographic detail/variable | Value                     |
| Sex                       | 94F/36M                   |
| Age (years)               | 38.9 (10.7)               |
| Weight (kg)               | 69.6 (14.8)               |
| Illness duration (months) | 37.9 (28.7)               |
| Resting VO2 (ml/min)      | 343 (327 to 360)          |
| VO2peak (litres/min)      | 1.612 (1.494 to 1.730)    |
| Work rate (W)             | 101 (92 to 109)           |
| Test duration (min)       | 5.1 (4.6 to 5.5)          |
| Peak heart rate (bpm)     | 140 (136 to 144)          |
| % Predicted max heart rate| 77 (74 to 79)             |
| Peak RER                  | 0.95 (0.93 to 0.97)       |
| RPE                       | 17 (15 to 18)             |

Values are mean (SD) or mean (95% confidence interval) as applicable. Subjects were seated erect on cycle ergometer to measure resting VO2. Predicted max heart rate was calculated as (210−0.65 × age). RER, respiratory exchange ratio (VCO2/VO2); RPE, rating of perceived exertion (median (interquartile range)).
completed the cycling protocol. Table 1 gives a summary of demographic details and data obtained from physiological testing.

Figure 1 shows that VO₂peak and WRpeak correlated strongly and significantly ($r^2 = 0.88$, $F = 930$, Df = 129, $p<0.001$). Linear regression analysis determined the line of best fit to be defined as:

$$VO₂_{peak} = 12.73 \times WR_{peak} + 332$$

where VO₂peak is in ml/min and WRpeak is given in W.

The percentage error encountered when comparing the actual measured VO₂peak with the predicted value (using the regression derived equation) was calculated. These residuals were then plotted against the measured values (fig 2).

In 104 cases out of 130 (80%), the error in the prediction was less than 20% when compared with the measured VO₂peak. The error was less than 35% in 126 cases (97%). It can be seen that in four cases, the error of the predicted value when compared with the measured value was greater than 35%. There were 11 patients who failed to exercise for more than two minutes, and this subgroup included all four cases with high error values. In those patients who exercised for more than two minutes (n = 119), the mean (SD) error between the predicted and measured values was only 10.7 (8.9)%.

A linear regression analysis on this subgroup of 119 patients (details given in table 2) determined the corrected line of best fit to be defined as:

$$VO₂_{peak} = 13.1 \times WR_{peak} + 284$$

VO₂ during exercise may be divided into two separate components: the basal metabolic requirement (resting VO₂) and the additional oxygen cost of the actual work involved. The concept of VO₂ reserve (the additional oxygen utilisation capacity above and beyond basal metabolic requirements) has recently been recommended as a means of describing potential for exercise performance. The slope of the VO₂ to work rate relation in healthy subjects has been previously reported.

When questioned in the clinic one week after the exercise test, 126/130 patients (97%) stated that they had not been aware of any relapse in their condition. Two patients said that they had experienced leg pain (one for four days, one for seven days), which they felt was due to the exercise protocol. A further two patients experienced an increase in general tiredness, which they attributed as much to the stress of their lengthy journey to the hospital clinic as to the exercise test.

### Discussion

The main findings of this study suggest that CFS suffers can safely undergo maximal exercise testing on a cycle ergometer, and that the work rate/oxygen uptake relation is sufficiently strong to allow prediction of VO₂peak from WRpeak alone. However, a cautious approach should be taken where patients are unable to exercise for more than two minutes. In four out of the 11 cases where this occurred in this trial, the predicted VO₂peak was subject to an error of greater than 35%. Where the exercise test lasted for more than two minutes, the error in the prediction was always less than 35% and the mean difference was reduced to 10.7%.

The physiological measurements taken in this trial showed a similar pattern of intolerance to exercise by patients with CFS to that observed by other workers. Peak heart rate
attained during exhaustive exercise reached a mean of only 77% of age related predicted maximum.

This confirms the findings of Montague et al. and Gibson et al., both of whom used a similar cycle ergometer protocol to that used in this study. The onset of disabling exhaustion coincided with a mean peak respiratory exchange ratio (V̇CO₂/V̇O₂) of only 0.95, suggesting that patients were suffering the feeling of gross fatigue before the onset of a significant level of anaerobiosis had occurred. Combined, these findings suggest that oxygen transport was not the limiting factor to exercise performance in this trial group, further supporting the argument that extrapolative methods of predicting VO₂peak are inappropriate for patients with CFS.

Many patients initially expressed a concern that excessive activity would be detrimental to their condition. However, the patients’ own perception of the level of effort that they had exerted during testing equated to “Very Hard” on the Borg scale (a median score of 17). This would suggest that many were at least partially prepared to put aside any predetermined convictions they may have had about the negative effect of higher levels of activity. It is also known that leg fatigue is commonly cited as the cause of test cessation in cycle ergometry. It is still possible that these factors may have influenced the amount of exercise induced discomfort that patients were prepared to tolerate, before fear of a subsequent exacerbation of their symptoms caused them to discontinue cycling.

The protocol described here requires maximal effort from the patient (exhaustive or symptom limited), and therefore does not rely upon extrapolation to obtain a theoretical age related predicted value. The strong relation shown (r² = 0.88) provides a means of predicting VO₂peak from WR alone. In clinical rehabilitation, where direct measurement of expired gas content is rarely an option, the therapist can obtain a close estimate of VO₂peak of a patient with CFS by following the simple method described above, armed solely with an accurately calibrated cycle ergometer. The value calculated, as well as providing an additional outcome measure, can serve as a basis for the prescription of rehabilitation exercise. Patients can be instructed to work at a specified percentage of their estimated VO₂peak from work rate guidelines based upon the known oxygen cost of standard modes of activity. The estimate of absolute VO₂peak (ml/min) can readily be converted into a body-weight specific value (ml/kg/min) if appropriate—that is, for prescribing intensity in weightbearing activities. Although it is known that VO₂peak can vary depending on the exercise modality used, this method has been successfully employed in the prescription of both walking and overland cycling exercise for CFS sufferers.

The VO₂ reserve (the additional oxygen utilisation capacity above and beyond basal metabolic requirements) has recently been recommended as a means of describing potential for exercise performance. Subtraction of the rest-
Take home message
Prediction of peak oxygen uptake for the prescription of exercise at an appropriate intensity for chronic fatigue syndrome sufferers can be achieved within the clinical environment by following the protocol outlined above, and requires no more than an accurately calibrated cycle ergometer.