Peak exercise cardiac power output

A direct indicator of cardiac function strongly predictive of prognosis in chronic heart failure


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Objectives This study assessed the prognostic value of peak cardiac power output, measured non-invasively during maximal cardiopulmonary exercise testing, against other exercise-derived haemodynamic variables in patients with chronic congestive heart failure.

Method and Results Two hundred and nineteen unselected, consecutive patients with congestive heart failure (166 men, mean (±SD) age of 56±13 years) who underwent maximal symptom limited cardiopulmonary treadmill exercise testing with non-invasive estimation of cardiac output using carbon dioxide re-breathing techniques, were followed-up for a mean period of 4·64 (4·47–4·82, 95% CI) years. Cardiac power output was calculated from the product of cardiac output and mean arterial blood pressure. All cause mortality was 12·3% (27 deaths). Peak and resting cardiac power output, peak mean arterial blood pressure, peak and resting cardiac output and peak VO2 were all predictive of outcome on univariate analyses. Peak cardiac power output, either entered continuously or categorically with a cut-off value of 1·96 watts, was the only independent predictor of mortality (P=0·0004 for values <1·96 watts and P=0·001 for continuous values) using multivariate analysis. A relative risk ratio of 5·08 (1·94–13·3, 95% CI) was obtained for a cardiac power output <1·96 watts.

Conclusion Peak cardiac power output is an independent predictor of mortality that can be measured non-invasively using cardiopulmonary exercise testing. It can give further prognostic power to a peak VO2 in the assessment of patients with congestive heart failure.

Key Words: Chronic heart failure, cardiac power output, prognosis, non-invasive cardiopulmonary exercise testing.

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Introduction

Chronic congestive heart failure is becoming increasingly prevalent as new effective therapies reduce cardiovascular mortality and the proportion of elderly patients increases[1]. With the resultant burden on health care resources it is imperative that patients with the highest risks are identified, ideally with objective indicators of cardiac dysfunction, in order that appropriate and effective treatment can be instituted. Many studies published in the last decade have shown peak oxygen consumption (VO2) to be a significant independent predictor of mortality[2–5]. However, peak VO2 may be influenced by non-cardiac factors such as muscle conditioning, motivation, age and gender[6,7]. This has led several groups to look at exercise-derived variables other than peak VO2 as predictors of outcome. Parameters such as blood pressure response to exercise[8–12], the ratio of minute ventilation to carbon dioxide production (VE/VCO2)[13,14] and oxygen recovery post exercise[15] have emerged in recent years as independent predictors of outcome. However, these variables are only indirectly related to cardiac function, and therefore can only be considered as markers of severity of organ failure, with direct means to improve these values not necessarily indicating an improvement in cardiac function. More direct measurements of cardiac work (represented by peak stroke work index[16,17], or peak cardiac power output[18,19], have emerged as powerful independent predictors of prognosis over peak VO2. The major...
drawback in measuring these exercise derived haemodynamic parameters is the invasive methodology that needs to be applied, raising safety issues and questioning the validity and reliability of true measurements at peak exercise.

Cooke and colleagues\[20\] described a non-invasive method for measuring peak exercise cardiac power output using carbon dioxide (CO\(_2\)) re-breathing techniques in conjunction with conventional cardiopulmonary exercise testing. In this study, we applied these techniques to measure haemodynamic variables, at rest and peak exercise in a group of patients with congestive heart failure undergoing cardiopulmonary exercise testing as part of their clinical evaluation. Univariate and multivariate analyses were then performed to assess whether peak cardiac power output (or any other haemodynamic variables) added further prognostic information to peak VO\(_2\).

Methods

Patients

The study group included 219 unselected consecutive patients (166 men, 53 women) with stable congestive heart failure, secondary to left ventricular impairment assessed by echocardiography, angiography or radionuclide scintigraphy, referred to a secondary and tertiary referral cardiac centre for clinical assessment of their condition by cardiopulmonary exercise testing between November 1993 and March 1998. Exclusion criteria included inability to perform a familiarization test, reduced exercise tolerance due to myocardial ischaemia or non-cardiac factors, congestive heart failure secondary to congenital or valvular heart disease or a myocardial infarction or revascularization procedure in the preceding 3 months.

All patients were followed up for a minimum of 24 months or until death. Outcomes were assessed directly (by questioning the patients) or by assessing the hospital records. No patient was lost to follow-up. The date and cause of death was documented in all cases. Death was defined as sudden when it occurred unexpectedly without known symptomatic worsening of heart failure in the previous 24 h.

Cardiopulmonary exercise testing and estimation of cardiac power output

Exercise testing was conducted on a Marquette 2000 treadmill (Marquette Electronics, Milwaukee, U.S.A.) using the standard or modified Bruce protocol. A preliminary familiarization procedure identified patients not able to exercise for reasons other than cardiac limitation — these patients were excluded. The same supervisors (G.A.C., R.L.R.) conducted the tests throughout the study. All patients performed symptom limited exercise tests unless termination was indicated for safety reasons. Patients were exercised after a 2 h postprandial period and were asked not to consume alcohol or caffeine in the preceding 12 h. The room in which the tests were carried out was maintained at a constant temperature between 21–23 °C using an air conditioning system controlled by a thermostat. Beta-blockers and other rate slowing drugs (e.g. diltiazem) were stopped for 48 h before the exercise test.

The first stage consisted of an incremental exercise test. ECG and blood pressure were monitored throughout. Rates of oxygen consumption (VO\(_2\)), carbon dioxide production (VCO\(_2\)), end-tidal partial pressure of carbon dioxide (PETCO\(_2\)), tidal volume (V\(_T\)), and respiratory rate were recorded breath by breath using the Medgraphics CardiO2 analytic system (Medgraphics, Minnesota, U.S.A.). Respiratory exchange ratio (RER = VCO\(_2\)/VO\(_2\)), minute ventilation (V\(_E\) = V\(_T\) × respiratory rate), and VO\(_2\)/kg were calculated from the above variables. The V-slope method\[21\] was used to calculate anaerobic threshold.

The second stage began following 40 min of recovery. Resting cardiac output was measured using the equilibrium CO\(_2\) re-breathing technique of Collier\[22\] and calculated using the indirect Fick method. Validation and reproducibility have previously been described for our laboratory\[20\]. At least three measurements of cardiac output were taken in order to calculate an average. The patient then performed a constant maximum workload exercise test for at least 4 min to a VO\(_2\) of at least 95% of the maximum level obtained during the incremental test. Peak cardiac output was measured in duplicate using the exponential CO\(_2\) re-breathing technique of Defares\[23\].

Cardiac power output, in watts, was calculated from the equation: cardiac power output = (CO × MAP) × K, where MAP is the mean arterial pressure in mmHg, CO is the cardiac output in l/min and K the conversion factor 2.22 × 10\(^{-3}\). Mean arterial pressure was calculated from the equation: MAP = (systolic pressure + 2 × diastolic pressure)/3.

Statistical analysis

All continuous variables included in the analysis are presented as means ± standard deviations (SD). Statistical significance was set at the 5% level and analysis of all variables by univariate and multivariate analysis was carried out using SPSS statistical software version 8 (SPSS\textsuperscript{R} for Windows/SPSS Inc. Michigan).

Univariate analysis was performed on continuous variables using two sample t-tests and chi-squared tests for categorical data. Odds ratios with 95% confidence intervals were calculated using multivariate logistic regression. The variables predictive of survival by univariate analysis were entered into the logistic regression to determine their significance as independent predictors of outcome in a multivariate model. The variables included in the stepwise model were as follows: peak exercise heart rate, exercise time, resting and peak exercise
Table 1  Clinical, cardiopulmonary and haemodynamic characteristics of the study population

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n (%)</td>
<td>166 (76%)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>53 (24%)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>56±14±13±13</td>
</tr>
<tr>
<td>NYHA class, n (%)</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>119 (54%)</td>
</tr>
<tr>
<td>III</td>
<td>76 (35%)</td>
</tr>
<tr>
<td>IV</td>
<td>24 (11%)</td>
</tr>
<tr>
<td>Cause, n (%)</td>
<td></td>
</tr>
<tr>
<td>Ischaemic</td>
<td>115 (53%)</td>
</tr>
<tr>
<td>Other</td>
<td>104 (47%)</td>
</tr>
<tr>
<td>Exercise time (min)</td>
<td>9±4±4±21</td>
</tr>
<tr>
<td>Resting VO2 (ml. min⁻¹)</td>
<td>334±6±70±1</td>
</tr>
<tr>
<td>Resting HR (min⁻¹)</td>
<td>76±4±21±2</td>
</tr>
<tr>
<td>Resting CO (l. min⁻¹)</td>
<td>4±8±1±1</td>
</tr>
<tr>
<td>Resting MAP (mmHg)</td>
<td>93±7±13±9</td>
</tr>
<tr>
<td>Resting CPO (watts)</td>
<td>0±99±0±29</td>
</tr>
<tr>
<td>VO2 at anaerobic threshold (ml. min⁻¹)</td>
<td>1157±1±498</td>
</tr>
<tr>
<td>Peak VO2 (ml. kg⁻¹ min⁻¹)</td>
<td>23±06±9±23</td>
</tr>
<tr>
<td>Peak HR (min⁻¹)</td>
<td>14±6±25±2</td>
</tr>
<tr>
<td>Peak CO (l. min⁻¹)</td>
<td>12±0±3±4</td>
</tr>
<tr>
<td>Peak MAP (mmHg)</td>
<td>10±2±2±29</td>
</tr>
<tr>
<td>Peak CPO (watts)</td>
<td>2±96±1±2</td>
</tr>
<tr>
<td>Peak CPO &lt;1±96 (watts), n (%)</td>
<td>38 (17%)</td>
</tr>
</tbody>
</table>

All values expressed as mean ± standard deviation.

NYHA=New York Heart Association; HR=heart rate; CO=cardiac output; MAP=mean arterial pressure; CPO=cardiac power output.

Results

Cardiac output, resting and peak exercise cardiac power output, anaerobic threshold, peak VO2 and peak mean arterial blood pressure. Peak cardiac power output (< and >1±96 watts) and peak VO2 (< and >14 ml. kg⁻¹ min⁻¹) were also entered as categorical variables.

A Kaplan–Meier cumulative survival curve was plotted to the end of the follow-up period for cardiac power output (using the 1±96 watts cut-off) risk factor. The survival curve was compared using the log-rank test.

Survival

All-cause mortality was 12±3% (27 deaths) over a mean follow-up period of 4±64 years (4±47–4±82, 95% CI). Cumulative survival for the entire study group was 98±6% at 6 months, 96±7% at 1 year, 91±2% at 2 years, 87±6% at 3 years and 85±8% at 4 years (Fig. 1). The cause of death was progressive heart failure in 19 patients (70%) and sudden death in the remaining eight patients (30%). The haemodynamic characteristics of survivors vs non-survivors is shown in Table 2. There were no significant differences in age, sex, NYHA class and aetiology between survivors and non-survivors.

Univariate and multivariate predictors of survival

Results of analyses for univariate and multivariate predictors of survival are shown in Table 3. By univariate analysis, rest and peak cardiac power output (either continuous or dichotomized at 1±96 watts), rest and peak cardiac output and peak VO2 (continuous values) were predictive of survival. When peak VO2 was dichotomized at 14 ml. kg⁻¹ min⁻¹, the common cut-off used for transplantation[1], this was not predictive of survival using a univariate model.

Multivariate analysis identified peak cardiac power output (entering either continuous or dichotomized values into the model) as the only independent predictor of death (P=0.0004 for dichotomized values and P=0.001 for continuous values). When dichotomized at 1±96 watts, a relative risk ratio of 5±08 (1±94–13±3, 95% CI) was obtained for a peak cardiac power output <1±96 watts. None of the other variables predictive of survival on univariate analysis were found to be predictive on multivariate analysis.

Kaplan–Meier survival analysis

A total of 38 patients had a peak cardiac power output <1±96 watts. During a mean follow-up of 4±71 years (4±15–5±25, 95% CI), 12 patients died (32% of this group). Mean survival time was 3±51 years (2±97–4±04, 95% CI) with a cumulative survival of 89±2% at 1 year, 75±7% at 2 years, 67±4% at 3 years and 43±4% at 4 years. Of the remaining 181 patients having a peak cardiac power output >1±96 watts, cumulative survival (15 deaths) was 98±3%, 94±2%, 91±4% and 90±5% at 1, 2, 3 and 4 years, respectively, with a mean survival time of 4±82 years (4±67–4±98, 95% CI) during a mean follow-up.

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of 5·14 years. Kaplan–Meier survival curves for peak cardiac power output <1·96 watts are shown in Fig. 2.

### Discussion

In the present study, we examined the relative prognostic value of standard cardiopulmonary and non-invasively measured resting and exercise haemodynamic derived variables in the assessment of a group of patients with congestive heart failure. We found by means of univariate analysis that in addition to peak VO₂, various haemodynamic variables were predictive of prognosis. Multivariate analysis showed peak cardiac power output, entered into the model either as a continuous variable or dichotomized at a level of 1·96 watts, to be the best predictor of outcome over a 5-year follow-up period in our group of consecutive, unselected ambulatory patients with congestive heart failure.

Of the patients with a peak cardiac power output <1·96 watts, the mortality rate was considerably higher than those with a peak cardiac power output of >1·96 watts (log rank Chi-square=21·77, P<0·00001). This result is in close agreement with a finding highlighted in a previous report by Roul and colleagues[19] who were the first group to evaluate the prognostic value of peak cardiac power output during maximal exercise testing. Roul et al.[19] assessed 50 patients with NYHA class...
II–III congestive heart failure using invasive measurements of haemodynamic parameters during maximal supine exercise on a flywheel. Mean follow-up was 21.2 ± 1.17 months. Multivariate analysis revealed peak cardiac power output to be the best independent predictor of death or a major cardiac event ($P<0.0001$). Peak cardiac power output <2 watts was found to accurately identify patients with a poor short-term prognosis ($P<0.003$). It is remarkable that despite marked differences in methods and patient population, the two results are highly consistent.

Peak oxygen consumption is an important prognostic measurement in the evaluation of patients with congestive heart failure and is used to monitor the progress of the condition, especially in selecting patients for transplantation, where a cut-off level of 14 ml·kg$^{-1}$·min$^{-1}$ has been routinely used\cite{1}. A cut-off value of <14 ml·kg$^{-1}$·min$^{-1}$ for peak VO$_2$ did not predict prognosis in our study group and peak VO$_2$ dichotomized at 14 ml·kg$^{-1}$·min$^{-1}$ was not statistically different using Kaplan–Meier survival analysis. Of the 34 patients with a peak VO$_2$ <14 ml·kg$^{-1}$·min$^{-1}$, only 7 (21%) died. Conventionally, these patients would have been categorized into a poor prognostic group. In the group of patients with a peak VO$_2$ of >14 ml·kg$^{-1}$·min$^{-1}$, there were 20 deaths (11%). Of the 34 patients with a peak VO$_2$ of <14 ml·kg$^{-1}$·min$^{-1}$, only 15 (44%) had a peak cardiac power output <1.96 watts. Over half of the patients that would conventionally be categorized into a poor prognostic group on the grounds of peak

Table 3 Univariate and multivariate predictors of survival

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate (P)</th>
<th>Multivariate (P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak CPO</td>
<td>0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>Peak CPO, dichotomized at 1.96 watts</td>
<td>&lt;0.001</td>
<td>0.0004</td>
</tr>
<tr>
<td>Peak CO</td>
<td>&lt;0.001</td>
<td>0.078</td>
</tr>
<tr>
<td>Resting CPO</td>
<td>0.016</td>
<td>0.061</td>
</tr>
<tr>
<td>Resting CO</td>
<td>0.002</td>
<td>0.057</td>
</tr>
<tr>
<td>Peak VO$_2$</td>
<td>0.020</td>
<td>0.134</td>
</tr>
<tr>
<td>Peak VO$_2$, dichotomized at 14 ml·kg$^{-1}$·min$^{-1}$</td>
<td>0.163</td>
<td>0.160</td>
</tr>
<tr>
<td>Peak HR</td>
<td>0.063</td>
<td>0.104</td>
</tr>
<tr>
<td>Peak MAP</td>
<td>0.319</td>
<td>0.057</td>
</tr>
<tr>
<td>Exercise time</td>
<td>0.074</td>
<td>0.693</td>
</tr>
<tr>
<td>Anaerobic threshold</td>
<td>0.120</td>
<td>0.106</td>
</tr>
</tbody>
</table>

All values expressed as mean ± standard deviation.

CPO=cardiac power output; CO=cardiac output; HR=heart rate; MAP=mean arterial pressure.

![Figure 2](image-url) **Figure 2** Kaplan–Meier survival curves for peak cardiac output (CPO), greater or less than 1.96 watts (log rank Chi-square=21.77, df=1, $P<0.0001$).
Peak exercise cardiac power output 1501

VO₂ (<14 ml . kg⁻¹ min⁻¹), had an adequate peak cardiac power output (≥1.96 watts). Of these 19 patients with a peak VO₂ <14 ml . kg⁻¹ min⁻¹ and a peak cardiac power output >1.96 watts, only two (11%) died. That peak VO₂, dichotomized at 14 ml . kg⁻¹ min⁻¹, was not predictive of survival is not a new finding as peak VO₂ has several key limitations in the assessment of congestive heart failure. It can be influenced by non-cardiac factors such as muscle deconditioning, motivation for performing exercise and obesity[6,7]. The expected peak VO₂ varies according to the age and sex of the patient[24,25] and evaluation using a percentage of the predicted peak VO₂ has been suggested to be more predictive than peak VO₂ alone[26]. Also, no statistical difference in survival between patients with peak VO₂ levels of 10–14 ml . kg⁻¹ min⁻¹ and those with levels of 14–18 ml . kg⁻¹ min⁻¹ has previously been shown in some studies[27,28]. The non-predictive value of peak VO₂ may be linked to the fact that it is only an indirect indicator of peak exercise cardiac performance[27,29,30] and cardiac functional reserve. This has led several groups to look beyond peak VO₂ to assess whether a more direct assessment of cardiac function, using exercise derived haemodynamic variables, yields more precise prognostic information than standard cardiopulmonary derived data.

Several investigators have shown cardiac work related performance to be prognostically superior to peak VO₂ in the evaluation of patients with congestive heart failure, using indexes such as peak stroke work index[16,17], cardiac output response to exercise[19] and peak cardiac power output[19]. Although cardiac output response to exercise has been shown to be prognostically important, it must be remembered that the heart generates pressure as well as flow. A number of groups[8–12] have shown the prognostic importance of the pressure generating ability of the heart and have concluded peak exercise blood pressure to be independently predictive of prognosis. The incorporation of pressure into exercise haemodynamic assessment is therefore crucial. Cardiac power output, a prognostic index first introduced by Tan in the late 1980’s[31,32] takes into account both the flow and pressure generating ability of the heart, and can therefore be viewed as a comprehensive indicator of cardiac function. One may anticipate, therefore, that cardiac power output would provide a more accurate prognostic indicator than peak VO₂ alone, or either of its two components, cardiac output and arterial blood pressure. Our study supports this hypothesis.

Previous studies have measured haemodynamic variables invasively, using right heart catheterization. We are the first group to evaluate the prognostic power of cardiac power output measured non-invasively, using relatively little equipment in addition to the standard cardiopulmonary exercise testing. Non-invasive measurement has the advantage that it does not have the complications associated with Swan–Ganz catheterization, e.g. pneumothorax. From the patients’ point of view, it obviates the discomfort associated with in-situ intravenous (± intra-arterial) catheters which can result in indeterminate extents of vasovagal reaction. With less constraints, patients are more likely to attain their true maximum exercise capability. Non-invasive measurements are therefore more likely to provide a true reflection of peak exercise haemodynamic data.

Over the years, there have been many indicators found to be predictive of prognosis in congestive heart failure. They can be broadly classified into (i) those predictive markers that are surrogates of outcomes of cardiac failure e.g. plasma brain natriuretic peptide[33–36], plasma urate[37,38] or nor-adrenaline levels[39,40] and (ii) those which are direct indicators of cardiac failure or dysfunction. Improvement of any of the former variables, for instance, by inhibiting the synthesis or release of the marker substances, is not expected to lead directly to improvement of cardiac failure. A test of whether any variable belongs to the latter category may take the form of asking the question whether improvement of the variable can lead directly to an improvement of the condition. Since peak exercise cardiac power output has not only been found to be predictive of prognosis, but also an indicator of cardiac function that correlates well with exercise capacity[20,41,42] it is more likely to belong to the latter category of prognostic indicators.

**Study limitations**

There are several limitations to this study. Our mortality rate (12.5% over 4.64 years) was considerably lower than any of the other patient populations in studies assessing haemodynamic response to exercise (Roul et al.[19]—26% mortality over 21.2 ± 1.7 months, Metra et al.[17]—15% mortality over 19 ± 25 months, Griffin et al.[17]—33% mortality at 1 year, Chomsky et al.[18]—17% mortality over 307 ± 192 days). The results obtained may thus not reflect other populations (e.g. cohorts of patients undergoing cardiopulmonary exercise testing for transplant assessment or geriatric populations) with more severe disease. Our low mortality rate may reflect the fact that our group consisted of an unselected consecutive cohort reflecting clinical practice in general cardiology in a secondary and tertiary referral centre which is not a cardiac transplant unit. It was also standard clinical practice that the patients were tested when their treatment had been optimized and their functional status was as good as could be achieved medically, such that by the time the patients attended for cardiopulmonary exercise testing, 54% of our patients were in NYHA functional class II heart failure, whereas only 11% had class IV. Only 16% of our patients had a peak VO₂ <14 ml . kg⁻¹ min⁻¹ (the recommended cut-off point for consideration of transplantation[43]).

A second limitation is the lack of quantitative echocardiographic, radionuclide or magnetic resonance data which may have been included in the statistical analyses. These variables are invariably measured in the assessment of patients for transplantation. However, the role of left ventricular dimensions and ejection fraction
is well defined in the assessment of congestive heart failure. This study was not designed to rediscover these known facts, but to compare variables obtained from non-invasive haemodynamic measurements and those from respiratory gaseous exchange.

Unlike VO₂, which with modern technology can be measured breath-by-breath continuously during strenuous exercise, it is as yet not technically possible to measure cardiac output or blood pressure non-invasively in a similar continuous manner. Since the extreme peak of exercise can only be sustained only transiently, estimation of cardiac output and blood pressure at this point would not approach the same technical reliability and accuracy as the measurement of peak VO₂. Also, measurement of diastolic blood pressure is notoriously difficult during exercise. The time required to perform repeated CO₂ re-breathing measurements of cardiac output during exercise (a requisite 2–3 min between measurements for the washout of CO₂) meant that it was necessary to perform two separate exercise tests for the measurement of peak VO₂ and peak cardiac output. Because at least 4 min were required to perform two peak cardiac output readings, the workload was necessarily slightly below the maximal (peak VO₂ during the second test was on average 5% less than that achieved during the incremental first test). Therefore, in our study, there may be a systematic underestimation of the values obtained for peak cardiac power output.

### Conclusion

Our results show that in a relatively low risk population, reflecting a broad spectrum of hospital patients with congestive heart failure, assessment of peak cardiac power output (a direct indicator of cardiac work), measured non-invasively by cardiopulmonary exercise testing has a superior prognostic impact than peak VO₂. A peak cardiac power output of <1.96 watts distinguishes a group of patients with a significantly worse prognosis. By application of these methods, risks associated with invasive measurement of haemodynamic variables can be avoided, thus giving a safe, easy and accurate method in the future prognostic assessment of patients with congestive heart failure.

### References

[1] Steering Committee and membership of the advisory council to improve outcomes nationwide in heart failure. Consensus recommendations for the management of chronic heart failure. Am J Cardiol 1999; 83: 2–38A


