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# Exercise testing in survivors of intensive care—is there a role for cardiopulmonary exercise testing?

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**Abstract**

**Purpose:** The aims of this study were to assess the feasibility of cardiopulmonary exercise testing (CPET) for the early assessment of cardiorespiratory fitness in general adult intensive care unit (ICU) survivors and to characterize the pathophysiology of exercise limitation in this population.

**Methods:** Fifty general ICU survivors (ventilated for ≥5 days) performed a maximal cycle ergometer CPET within 6 weeks of hospital discharge. Health-related quality of life was measured by the Medical Outcome Study Short Form 36 version 2.0 questionnaire.

**Results:** Fifty patients (median age, 57 years; median Acute Physiology And Chronic Health Evaluation II score, 16) completed a CPET 24 ± 14 days after hospital discharge with no adverse events. Significant exercise limitation was present with peak $V_{O_2}$ 56% ± 16% predicted and anaerobic threshold (AT) 41% ± 13% of peak predicted $V_{O_2}$. Prospectively stratified subgroup comparison showed that patients ventilated for 14 days or more had a significantly lower AT and peak $V_{O_2}$ than those ventilated for 5 to 14 days (AT: 9.6 vs 11.7 mL/kg per minute $O_2$, $P = .009$; peak $V_{O_2}$: 12.9 vs 15.3 mL/kg per minute $O_2$, $P = .022$). At peak exercise, heart rate reserve was 25% ± 14%, breathing reserve was 47% ± 19%, and the respiratory exchange ratio was 0.96 ± 0.11. Ventilatory equivalents for $CO_2$ ($Eq_{CO_2}$) were 39 ± 9.

**Conclusions:** Significant exercise limitation is evident in patients who have had critical illness. Etiology of exercise limitation appears multifactorial, with general deconditioning and muscle weakness as major contributory factors. Early CPET appears a practical method of assessing exercise capacity in ICU survivors. Cardiopulmonary exercise testing could be used to select patients who may benefit most from a targeted physical rehabilitation program, aid in exercise prescription, and help assess the response to intervention.



## 1. Purpose

The deleterious effect of critical illness on physical function is well described, with exercise limitation and neuromuscular abnormalities persisting for long periods after hospital discharge [1,2]. The rehabilitation of patients after critical illness has gained increased prominence in the United Kingdom recently after the publication of a national guideline. This provides a broad framework for patient assessment but falls short of providing details of how best to improve physical function [3].

In contrast to conditions such as chronic obstructive airways disease and congestive cardiac failure, there is little published evidence regarding the optimal physical rehabilitation strategy

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for survivors of critical illness after hospital discharge. In these patients, the relative contribution of cardiac, respiratory, and musculoskeletal impairment to exercise limitation is also not well characterized. Commonly used assessment tools such as the 6-minute walk test (6MWT) are well validated and simple measures of exercise capacity but are subject to a learning effect and do not differentiate between the many potential causes of exercise limitation in intensive care unit (ICU) survivors [4,5].

Cardiopulmonary exercise testing (CPET) provides an objective, noninvasive global assessment of the integrated physiologic response to exercise. A major advantage over other objective measures of exercise capacity (eg, 6MWT) is that it provides information that may identify cardiac, respiratory, or musculoskeletal contributions to any exercise limitation present. The anaerobic threshold (AT) is an objective measure of functional or aerobic capacity that normally occurs at 50% to 60% of peak exercise capacity. Importantly and unlike peak oxygen consumption (peak $V_{O_2}$), it is less influenced by either learning effect or patient effort. Cardiopulmonary exercise testing is advocated as a tool to guide exercise prescription in chronic obstructive pulmonary disease and heart failure [6,7]. To date, its use after critical illness has been restricted to the study of specific patient populations including survivors of the severe acute respiratory syndrome and the acute respiratory distress syndrome (ARDS) [8,9]. To our knowledge, CPET has never been used in the assessment of general adult ICU survivors in the immediate post–hospital discharge period. The purpose of our study was therefore 2-fold:

1. To determine the feasibility and safety of CPET as a tool for the objective assessment of exercise capacity in unselected adult general ICU survivors.
2. To help to further characterize the pathophysiology of any exercise limitation present in this patient population.

## 2. Materials and methods

### 2.1. Patient selection

Fifty survivors of critical illness were recruited into the study and underwent a CPET within 6 weeks of hospital discharge. No changes were made to patients' medications in preparation for the test (eg, withholding of $\beta$-blockade). All patients ventilated for at least 5 days during their general ICU admission were eligible for inclusion; patients were prospectively stratified into 2 groups based on the duration of ventilation (5-14 days and >14 days). Exclusion criteria were age younger than 18 years, duration of mechanical ventilation less than 5 days, inability to perform CPET because of physical or mental impairment, pregnancy, terminal illness, and acute coronary syndrome within the preceding 30 days. Approval for the study was obtained from the local research ethics committee. Written informed consent was obtained from all participants.

### 2.2. Cardiopulmonary exercise testing

A maximal, symptom-limited incremental CPET using a cycle ergometer was conducted according to a standard ramped protocol [10]. Patients were seated on a bicycle ergometer with 12-lead electrocardiogram and gas exchange monitoring using a Jaeger Oxycon Pro ergospirometry system (Jaeger, Wurzburg, Germany). Peripheral oxygen saturations ($Sp_{O_2}$) and noninvasive blood pressure were monitored throughout the test. After a period of observation at rest to allow the respiratory exchange ratio (RER) to plateau (typically 1-3 minutes), subjects completed 3 minutes of unloaded cycling at 60 revolutions per minute. Load was then applied to the pedals in a ramp-like fashion increasing by 10 to 15 W/min until maximum exercise capacity was reached. For safety reasons, the study protocol required immediate termination of the test if the subject experienced any of the following adverse events: chest pain, altered sensorium, ST depression greater than 2 mm on the exercise electrocardiogram, and emotional distress. Two intensive care physicians with advanced life support skills were present throughout all tests. After termination of the test, subjects were monitored until cardiorespiratory parameters returned to baseline levels.

Anaerobic threshold was determined using a combination of the V-slope and ventilatory equivalents methods as described by Wasserman et al [10].

Data for the following parameters were collected: AT, peak $V_{O_2}$, ventilatory equivalents for $CO_2$ ($Eq_{CO_2}$), oxygen pulse ($V_{O_2}$/HR), heart rate reserve (HRR), breathing reserve (BR) at peak exercise and static spirometry. Values of $Eq_{CO_2}$ were taken at AT or recorded as the lowest value achieved during incremental exercise when AT was not able to be determined. Maximum voluntary ventilation (MVV) was determined indirectly: MVV (L/min) = Forced expiratory volume in 1 second ($FEV_1$) × 40. Heart rate reserve at peak exercise was expressed as an absolute value or as a percentage: HRR (beats per minute) = peak predicted HR − HR at peak exercise or %HRR = (1 − [HR at peak exercise/peak predicted HR]) × 100. Breathing reserve at peak exercise was expressed as both an absolute value and as a percentage: BR (L/min) = MVV − $V_E$ at peak exercise or %BR = (1 − [$V_E$ at peak exercise/MVV]) × 100.

### 2.3. Health-related quality of life assessment

Exercise capacity has been shown to correlate with various measures of quality of life [11]. Patients' health-related quality of life (HRQL) was assessed using the Medical Outcome Study Short Form 36 version 2.0 (SF-36v2) questionnaire (Quality Metric, Lincoln, RI) [12]. This was performed immediately before their CPET. Physical