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Peak circulatory power is a strong prognostic factor in patients with idiopathic pulmonary arterial hypertension

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ABSTRACT

Background: Studies have shown that peak circulatory power (peak CircP; peak oxygen uptake × peak systolic blood pressure) is a variable predictor of prognosis in patients with left heart failure. It remains unknown whether peak CircP also predicts outcome in patients with idiopathic pulmonary arterial hypertension (IPAH).
Methods: Patients with newly diagnosed IPAH who underwent symptom-limited cardiopulmonary exercise testing (CPET) from 1 January 2011 to 1 January 2014 in Fuwai Hospital were prospectively enrolled and followed for up to 66 months for cardiac events (mortality and lung transplantation).
Results: One hundred forty patients with IPAH (104 female, mean age: 33 ± 11 years) were studied. During follow-up (mean: 42 ± 14 months), 24 patients died and 1 patient underwent lung transplantation. In the univariate analysis, peak oxygen uptake(VO_2), oxygen uptake at anaerobic threshold, ventilation (VE)/carbon dioxide output (VCO_2) slope, end-tidal partial pressure of carbon dioxide at anaerobic threshold, peak systolic blood pressure (SBP), the change of SBP, the change of heart rate, peak work rate, peak CircP, pulmonary vascular resistance, cardiac index and World Health Organization functional class were predictive of cardiac events (all $P < .05$).In the multivariate analysis, Peak CircP in the fourth model had the highest significance compared with peak VO_2 and VE/VCO_2 slope in the second and third model (chi-square = 5.26, $P < .02$, HR: 0.99, 95% CI: 0.99 to 1.00).
Conclusions: Peak CircP, better than peak VO_2 and VE/VCO_2slope, was a strong predictor of cardiac events among exercise parameters in patients with IPAH.

1. Introduction

Pulmonary arterial hypertension (PAH) is a progressive and devastating disease characterised by increased pulmonary vascular resistance that eventually leads to right heart failure and death. The 5-year survival rate for patients with newly diagnosed group 1 PAH is 61.2%, even when they were treated in a professional hospital with specific and expensive drugs, such as endothelin receptor antagonists, phosphodiesterase type 5 inhibitors, prostacyclin analogues and prostacyclin receptor agonists [1]. Therefore, to improve the 5-year survival rate of patients with PAH, early identification of those patients with higher risk of poor outcome is important. Cardiopulmonary exercise testing (CPET) is now considered as a very useful and powerful tool in comprehensively assessing disease severity, therapeutic responses and prognosis estimation in patients with PAH, as there is no single variable that can provide sufficient diagnostic and prognostic information [2].

Several studies have already shown that important indications of poor prognosis in patients with PAH were low peak oxygen uptake (peak VO_2), low end-tidal partial pressure of carbon dioxide at anaerobic threshold ($PETCO_2$@AT) and high ventilation/carbon dioxide output slope (VE/VCO_2slope) [3–5]. Peak circulatory power (peak CircP), a new index, which is calculated by the product of peak oxygen

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uptake (peak VO_2) and peak systolic blood pressure (SBP), was demonstrated to have greater prognostic power than peak VO_2 in patients with left heart failure [6–8], and the results also applied to patients with congenital heart disease [9]. The pathophysiological mechanisms account for the results is that peak CircP can best represent the performance of the cardiac pump [7]. However, it remains unknown whether peak CircP, better than peak VO_2 or VE/VCO_2 slope, can predict outcome in patients with idiopathic pulmonary arterial hypertension (IPAH). Therefore, we aimed to assess the prognostic value of peak CircP on long-term outcomes in patients with IPAH.

2. Methods

2.1. Study participants

Consecutive patients with newly diagnosed IPAH at Fuwai Hospital from 1 January 2011 to 1 January 2014 were prospectively enrolled. IPAH was defined according to 2009 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension [10]. The diagnosis of IPAH was based on clinical symptoms, routine blood test and immunological test, electrocardiogram (ECG), high-resolution chest and contrast enhanced pulmonary artery computed tomography, ventilation-perfusion lung scanning, echocardiography and abdominal ultrasonography, pulmonary function tests, CPET, and right heart catheterisation (RHC). All patients received the examinations mentioned above including RHC. Patients with absolute and relative contraindications to CPET were excluded (Fig. 1).Data regarding basic demographics, medications, hemodynamic measurements from right-heart catheterisation, and World Health Organization (WHO) functional classification were collected. The study complies with the Declaration of Helsinki and was approved by the Ethics Committee of Fuwai Hospital (No. 2011-331). Written informed consents were obtained from all the participants.

2.2. Cardiopulmonary exercise testing

Symptom-limited CPET was performed on all recruited patients with IPAH at baseline before they received specific drug therapy. All patients rested for 3 min followed by 3 min of unloaded pedaling, and exercised using a progressively increasing work rate of 5–20 W/min to maximum tolerance on a cycle ergometer with electromagnetic brake. Gas exchange variables were measured by a metabolic cart (Cosmed, Italy) on a breath-by-breath basis and averaged over 10-second intervals. Peak VO_2 was defined as the highest 30-second average of oxygen consumption in the last minute of exercise, and other peak parameters were also calculated at the same time. Anaerobic threshold (AT) was detected by a combination of the V-slope method and ventilatory equivalents. A standard 12-lead ECG and oxyhaemoglobin saturation (SpO_2) were continuously recorded, Blood pressure was measured every 3 min and at the peak of the exercise. The blood pressure at the previous stage was used when blood pressure measurement was not obtained at peak exercise. The test was performed by experienced medical staff, and the equipment was calibrated before each test. Oxygen therapy was ceased for at least half an hour before patients underwent CPET. PeakVO_2/HR was calculated as peak VO_2 divided by peak heart rate, and ventilatory efficiency was evaluated by VE/VCO_2 slope and $PETCO_2$@AT. VE/VCO_2 slope was determined by linear regression using the whole exercise period. Peak CircP was defined as the product of peak VO_2 and peak SBP.

2.3. Follow-up

Patients were followed up every 3 months for 1 year after they were discharged, and were followed up every 6 months thereafter. WHO function class, medications and side effects, the date and cause of lung transplantation, and death were documented at each follow-up. Cardiac events were defined as mortality and lung transplantation due to IPAH. The follow-up time was calculated as time from the date of CPET to the end point date or 1 May, 2016.

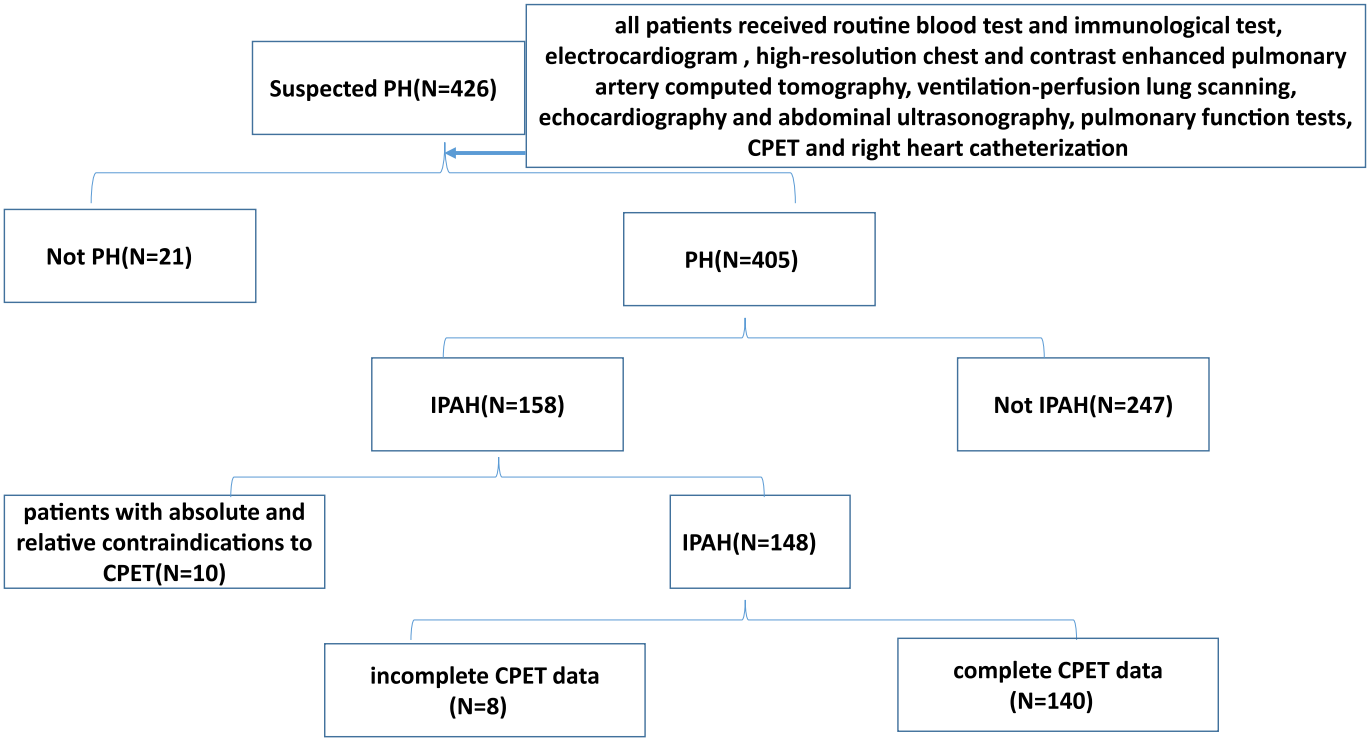

Fig. 1. Patients ' flow-chart with the included and excluded patients in our study.