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ORIGINAL ARTICLE

Cardiorespiratory optimal point during exercise testing as a predictor of all-cause mortality

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KEYWORDS
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Abstract
Introduction and Aim: The cardiorespiratory optimal point (COP) is a novel index, calculated as the minimum oxygen ventilatory equivalent (VE/VO_2) obtained during cardiopulmonary exercise testing (CPET). In this study we demonstrate the prognostic value of COP both independently and in combination with maximum oxygen consumption (VO_2max) in community-dwelling adults.
Methods: Maximal cycle ergometer CPET was performed in 3331 adults (66% men) aged 40-85 years, healthy (18%) or with chronic disease (81%). COP cut-off values of <22, 22-30, and >30 were selected based on the log-rank test. Risk discrimination was assessed using COP as an independent predictor and combined with VO_2max.
Results: Median follow-up was 6.4 years (7.1% mortality). Subjects with COP >30 demonstrated increased mortality compared to those with COP <22 (hazard ratio [HR] 6.86, 95% confidence interval [CI] 3.69-12.75, p<0.001). Multivariate analysis including gender, age, body mass index, and the forced expiratory volume in 1 s/vital capacity ratio showed adjusted HR for COP >30 of 3.72 (95% CI 1.98-6.98; p<0.001) and for COP 22-30 of 2.15 (95% CI 1.15-4.03, p<0.001). Combining COP and VO_2max data further enhanced risk discrimination.
Conclusions: COP >30, either independently or in combination with low VO_2max, is a good predictor of all-cause mortality in community-dwelling adults (healthy or with chronic disease). COP is a submaximal prognostic index that is simple to obtain and adds to CPET assessment, especially for adults unable or unwilling to achieve maximal exercise.

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PALAVRAS-CHAVE
Consumo de oxigênio;
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Teste cardiopulmonar de exercício

Ponto ótimo cardiorrespiratório como preditor de mortalidade por todas as causas

Resumo
Introdução e objetivos: O ponto ótimo cardiorrespiratório (POC) representa o menor valor do equivalente ventilatório de oxigênio (VE/VO2), obtido durante um teste cardiopulmonar de exercício (TCPE). Neste estudo, demonstramos a utilidade prognóstica do POC de forma independente e associado ao VO2max.
Métodos: Foram avaliados TCPE máximos em cicloergômetro de 3331 adultos (66% homens) com idades entre 40-85 anos, saudáveis (18%) e com doenças crônicas (81%). Ao POC foram atribuídos pontos de corte para a criação de grupos < 22, 22-30 e > 30, com base no teste *log-rank*. As associações de risco foram verificadas por meio de regressões de Cox, utilizando o POC como preditor independente e combinado com VO2max.
Resultados: O seguimento médio foi de 6,4 anos (7,1% das mortes). Indivíduos com POC > 30 demonstraram maior mortalidade, em comparação com POC < 22; HR = 6,86 (intervalo de confiança [IC] 95% = 3,69-12,75, p < 0,001). A análise multivariada ajustada, incluindo idade, sexo, índice de massa corporal, e a capacidade vital 1-s volume expiratório forçado mostraram HR POC > 30 de 3,72 (IC 95% = 1,98-6,98; p < 0,001) e para a POC 22-30 de 2,15 (IC 95% = 1,15-4,03, p < 0,001). Combinando POC e VO2max, aumentou-se a discriminação do risco.
Conclusões: O POC > 30, de forma independente ou combinado com baixo VO2max, é um bom preditor de mortalidade por todas as causas em adultos (saudáveis ou com doença crónica). Simples de se obter, o POC como índice prognóstico submáximo acrescenta ao TCPE uma nova possibilidade de avaliação de risco de mortalidade, especialmente para adultos incapazes ou não dispostos a alcançar o exercício máximo.

List of abbreviations

COP	cardiorespiratory optimal point
CPET	cardiopulmonary exercise testing
FEV1	forced expiratory volume in 1 s
FVC	forced vital capacity
HR	heart rate
OUES	oxygen uptake efficiency slope
VAT	ventilatory anaerobic threshold
VE	ventilation
VE/VO_2	oxygen ventilatory equivalent
VO_2	oxygen uptake
VO_2max	maximum oxygen uptake

Introduction

Quantification of gas exchange during exercise with cardiopulmonary exercise testing (CPET) is used in healthy and diseased populations.[1–6] Previous studies have indicated the prognostic importance of several CPET ventilatory variables,[7] including maximum oxygen uptake (VO_2max),[8] ventilatory anaerobic threshold (VAT),[9] oxygen uptake efficiency slope (OUES)[10,11] and ventilatory equivalent for CO_2 (VE/VCO_2),[12,13] as well as in the immediate recovery after CPET, such as the recently proposed O_2 kinetics.[14] While a submaximal measure of exercise performance may be useful in adults who are physiologically unable to reach a peak level of exercise, such theoretical utility is often offset by methodological limitations in the assessment of some of these variables.[15]

The cardiorespiratory optimal point (COP) constitutes a novel submaximal CPET index which provides an alternative approach to respiratory physiology.[16,17] The COP represents the lowest value of the oxygen ventilatory equivalent (the ratio between ventilation [VE] in l/min and oxygen consumption [VO_2] in l/min, VE/VO_2) in a given minute during incremental exercise. As an index that quantifies the lowest ventilation required to extract 1 l of oxygen, COP characterizes the interplay between the circulatory and respiratory systems.[17] COP is simple to identify and occurs at modest exercise levels (30-50% of VO_2max), much earlier than VAT.[17] While COP has been shown to be reliable[16] and reference values are available,[17] its utility as a clinical prognostic indicator has not been evaluated. Therefore, our objective was to assess the ability of COP, as an independent prognostic index and in combination with VO_2max, to predict all-cause mortality in middle-aged and older adults with and without chronic disease.

Methods

In a retrospective observational study, clinical data from 5643 subjects assessed in an exercise medicine clinic between January 1996 and July 2013 were reviewed. A subset that had completed maximal CPET and were aged between 40-85 years old narrowed the study population to 3331 adults. Among these subjects, 2220 (66.6%) were male,