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Patients With Heart Failure in the “Intermediate Range” of Peak Oxygen Uptake:

ADDITIVE VALUE OF HEART RATE RECOVERY AND THE MINUTE VENTILATION/CARBON DIOXIDE OUTPUT SLOPE IN PREDICTING MORTALITY

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Abstract

PURPOSE: While patients with heart failure who achieve a peak oxygen uptake (peak $\dot{V}O_2$) of 10 mL·kg⁻¹·min⁻¹ or less are often considered for intensive surveillance or intervention, those achieving 14 mL·kg⁻¹·min⁻¹ or more are generally considered to be at lower risk. Among patients in the “intermediate” range of 10.1 to 13.9 mL·kg⁻¹·min⁻¹, optimally stratifying risk remains a challenge.

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The authors declare no conflict of interest.

METHODS: Patients with heart failure (N 1167) referred for cardiopulmonary exercise testing were observed for 21 ± 13 months. Patients were classified into 3 groups of peak $\dot{V}O_2$ (10 , 10.1 – 13.9 , and 14 mL·kg⁻¹·min⁻¹). The ability of heart rate recovery at 1 minute (HRR₁) and the minute ventilation/carbon dioxide output ($\dot{V}_E/\dot{V}_{CO_2}$) slope to complement peak $\dot{V}O_2$ in predicting cardiovascular mortality were determined.

RESULTS: Peak $\dot{V}O_2$, HRR₁ (16 beats per minute), and the $\dot{V}_E/\dot{V}_{CO_2}$ slope (>34) were independent predictors of mortality (hazard ratio 1.6, 95% CI: 1.2–2.29, $P=.006$; hazard ratio 1.7, 95% CI: 1.1–2.5, $P=.008$; and hazard ratio 2.4, 95% CI: 1.6–3.4, $P=.001$, respectively). Compared with those achieving a peak $\dot{V}O_2 \geq 14$ mL·kg⁻¹·min⁻¹, patients within the intermediate range with either an abnormal $\dot{V}_E/\dot{V}_{CO_2}$ slope or HRR₁ had a nearly 2-fold higher risk of cardiac mortality. Those with both an abnormal HRR₁ and $\dot{V}_E/\dot{V}_{CO_2}$ slope had a higher mortality risk than those with a peak $\dot{V}O_2 10$ mL·kg⁻¹·min⁻¹. Survival was not different between those with a peak $\dot{V}O_2 10$ mL·kg⁻¹·min⁻¹ and those in the intermediate range with either an abnormal HRR₁ or $\dot{V}_E/\dot{V}_{CO_2}$ slope.

CONCLUSIONS: HRR₁ and the $\dot{V}_E/\dot{V}_{CO_2}$ slope effectively stratify patients with peak $\dot{V}O_2$ within the intermediate range into distinct groups at high and low risk.

Keywords

cardiopulmonary exercise test; heart failure; mortality

Despite recent improvements in medical therapy, the mortality rate in patients with heart failure (HF) remains high. The continued scarce availability of donor hearts makes the accurate selection of those with a poor prognosis and who may benefit most from intensive therapy or cardiac transplantation a major challenge.^{1,2} Since the landmark study by Mancini et al³ 2 decades ago, peak oxygen uptake (peak $\dot{V}O_2$) has been considered one of the most important variables used to guide the selection of transplant recipients. While patients who achieve peak $\dot{V}O_2$ values 10 mL·kg⁻¹·min⁻¹ or less are generally considered to benefit most from transplantation, those with peak $\dot{V}O_2$ values 14 mL·kg⁻¹·min⁻¹ or more are generally considered to have an acceptable short-term survival, and surgical intervention is usually deferred.^{1,2}

However, the limitations of peak $\dot{V}O_2$ in stratifying risk have been well-documented.^{4–7} Fundamental to these limitations is the fact that peak $\dot{V}O_2$ does not accurately reflect ventricular performance,⁷ or the level of circulatory, metabolic, or ventilatory dysfunction during exercise,⁶ and that it is dependent on subject effort. In part for this reason, evaluating risk in medically optimized patients who achieve a peak $\dot{V}O_2$ in the range of 10 to 14 mL·kg⁻¹·min⁻¹ has been debated. In recent years, cardiopulmonary exercise test (CPX) variables other than peak $\dot{V}O_2$, in particular the slope of the relationship between minute ventilation and carbon dioxide production ($\dot{V}_E/\dot{V}_{CO_2}$ slope) and heart rate recovery (HRR₁), have been shown to powerfully predict mortality in HF.^{8–10} In many instances, these responses have been stronger predictors of adverse events than peak $\dot{V}O_2$.^{8,9} Multivariate approaches, which

combine CPX variables, may be an optimal method for estimating risk.^{11,12} However, few studies have investigated the prognostic value of such variables within the “intermediate range” of peak $\dot{V}O_2$ (10–14 mL·kg⁻¹·min⁻¹).^{13,14} Therefore, our objective was to test the hypothesis that the $\dot{V}_E/\dot{V}_{CO_2}$ slope and HRR₁ would improve risk stratification in patients with HF who have peak $\dot{V}O_2$ values within this range.

METHODS

This was a multicenter analysis including patients with HF from the CPX laboratories at San Paolo Hospital, Milan, Italy; Virginia Commonwealth University, Richmond, Virginia; LeBauer Cardiovascular Research Foundation, Greensboro, North Carolina; and the VA Palo Alto Health Care System, Palo Alto, California. A total of 1167 consecutive patients with chronic HF were included in the study. Inclusion criteria consisted of a diagnosis of HF, defined by symptoms compatible with HF, and evidence of left ventricular systolic dysfunction (left ventricular ejection fraction [LVEF] < 45%) or abnormal filling pattern and ejection fraction greater than 45% by 2-dimensional echocardiography obtained within 1 month of exercise testing (those with HF symptoms and an ejection fraction < 45% were defined as diastolic HF patients). Patients with pacemakers were excluded. All subjects completed a written informed consent, and institutional review board approval was obtained at each institution. All authors have read and approved the manuscript.

CPX Procedure and Data Collection

Symptom-limited CPX was performed on all patients using ramp protocols.¹⁵ A treadmill was used for testing in the American centers, while a cycle ergometer was used in the European center. Previous studies have demonstrated optimal peak $\dot{V}O_2$, $\dot{V}_E/\dot{V}_{CO_2}$ slope and HRR₁ prognostic threshold values are similar regardless of the mode of exercise in patients with HF.¹⁶ Ventilatory-expired gas analysis was performed with a metabolic system (MedGraphics CPX-D, Minneapolis, MN, or SensorMedics Vmax29, Yorba Linda, CA). Before each test, the equipment was calibrated in a standard fashion with reference gases. In addition, each center routinely performed validation procedures.¹⁷ A standard 12-lead electrocardiogram was obtained at rest, each minute during exercise, and for at least 5 minutes during the recovery phase; blood pressure was measured with a standard cuff sphygmomanometer. Minute ventilation ($\dot{V}_E$), oxygen uptake ($\dot{V}O_2$), carbon dioxide output ($\dot{V}_{CO_2}$), and other cardiopulmonary variables were acquired on a breath-by-breath basis and averaged over 10- or 15-second intervals. Peak $\dot{V}O_2$ and peak respiratory exchange ratio were expressed as the highest averaged samples obtained during the exercise test. $\dot{V}_E$ and $\dot{V}_{CO_2}$ values, acquired from the initiation of exercise to peak, were used to calculate the $\dot{V}_E/\dot{V}_{CO_2}$ slope via least squares linear regression ($y = mx + b$, where m = slope). Previous work has shown that this method of calculating the $\dot{V}_E/\dot{V}_{CO_2}$ slope is prognostically optimal.^{18,19} Heart rate recovery was measured 1 minute post-CPX and termed HRR₁.

End points—Subjects were followed for cardiac-related death for 3 years after CPX via hospital and outpatient medical chart review. Subjects were followed by the HF programs at their respective institutions, which provided a high likelihood that all major events were

captured. Cardiac-related mortality was defined as death resulting from failure of the cardiac system. Individuals conducting the CPX were not involved in decisions regarding cause of death.

Statistical analysis—Continuous data are reported as mean SD. Oneway ANOVA was used to compare differences in continuous variables, whereas chi-square analysis was used to compare differences in categorical variables between peak $\dot{V}O_2$ subgroups. Bonferroni *post hoc* tests were used when appropriate. The optimal abnormal cut points for the $\dot{V}_E/\dot{V}CO_2$ slope (>34), peak $\dot{V}O_2$ ($<14 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$), and HRR_1 (<16 beats per minute) were established by receiver operating characteristic curves. Univariate Cox regression analysis was used to assess the prognostic value of key baseline and CPX variables. Multivariate Cox regression analysis was used to determine the prognostic value of the $\dot{V}_E/\dot{V}CO_2$ slope, peak $\dot{V}O_2$, LVEF, HRR_1 , and etiology of HF. In addition, all variables retained in the multivariable model were included in the Cox regression model, which assessed the predictive power of $\dot{V}_E/\dot{V}CO_2$ slope and HRR_1 in the intermediate range group of peak $\dot{V}O_2$. All analyses were adjusted for age, etiology, LVEF, and β -blocker use.

Patients were divided into 3 peak $\dot{V}O_2$ subgroups: $14 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$, 10.1 to $13.9 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ (intermediate range), and $10 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ or less. Kaplan-Meier analysis with log-rank testing was used to assess survival within each subgroup. Kaplan-Meier analyses were also used to assess the ability of the $\dot{V}_E/\dot{V}CO_2$ slope, HRR_1 , or their combination to stratify those within the intermediate range into high- and low-risk mortality groups.

RESULTS

Demographic characteristics for all subjects and peak $\dot{V}O_2$ subgroups are presented in Table 1. Age was higher and male gender was less prevalent in patients in the 2 lower peak $\dot{V}O_2$ groups. Left ventricular ejection fraction was lower in those with peak $\dot{V}O_2$ values $10 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ or less. There were no differences in HF etiology, respiratory exchange ratio, and β -blocker or angiotensin-converting enzyme inhibitor use between groups.

Table 2 shows the results of univariate and multivariate Cox regression analyses. Univariately, the $\dot{V}_E/\dot{V}CO_2$ slope, HRR_1 , peak $\dot{V}O_2$, and LVEF were all independent predictors of mortality. In the multivariate analysis, those with an abnormal $\dot{V}_E/\dot{V}CO_2$ slope response had 2.4 times higher risk of cardiac mortality when compared with patients with a normal response. HRR_1 (1.7-fold higher risk) and peak $\dot{V}O_2$ (1.6-fold higher risk) were also multivariate predictors of cardiac mortality, while LVEF was removed from the regression. When added to the multivariate model as a continuous variable, peak $\dot{V}O_2$ was also an independent predictor of mortality with an 11% reduction in risk of mortality per unit increment in $\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$.

Kaplan-Meier curves, illustrating survival rates between the peak $\dot{V}O_2$ tertiles, are shown in Figure 1; survival was progressively lower as peak $\dot{V}O_2$ was reduced. Compared with those

with a peak $\dot{V}O_2 > 14 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$, patients within the intermediate range with either an abnormal $\dot{V}_E/\dot{V}_{CO_2}$ slope or HRR_1 had a nearly 2-fold higher risk of cardiac mortality (Figure 2). Importantly, patients within the intermediate range with both an abnormal $\dot{V}_E/\dot{V}_{CO_2}$ slope and an abnormal HRR_1 response had an even higher mortality risk than those with a peak $\dot{V}O_2 > 10 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ (hazard ratio [HR] 3.51, 95% CI: 2.33–5.29, $P < .001$, and HR 3.11, 95% CI: 2.07–4.68, $P < .001$, respectively) (Table 3). Survival was not different between those with a peak $\dot{V}O_2 > 10 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ or less and those within the intermediate range with either an abnormal HRR_1 or $\dot{V}_E/\dot{V}_{CO_2}$ slope.

DISCUSSION

Traditionally, HF patients who achieve a peak $\dot{V}O_2 > 14 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ have been considered to have an acceptable prognosis and generally do not benefit from surgical or other intensive intervention.¹ Conversely, patients with a peak $\dot{V}O_2 < 10 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ have a poor short-term prognosis and interventions such as transplantation have been shown to significantly improve outcomes.^{1–3} However, classifying risk in patients who achieve a peak $\dot{V}O_2$ in what has been termed the *intermediate range* ($10\text{--}14 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$) has been less clear. A potential application of CPX variables other than peak $\dot{V}O_2$ would likely be in the specific group of patients with peak $\dot{V}O_2$ values in this intermediate range, among whom peak $\dot{V}O_2$ alone is often limited in differentiating high and low mortality risk.

To our knowledge, this study is the first to focus on the prognostic value of the $\dot{V}_E/\dot{V}_{CO_2}$ slope and HRR_1 in patients with HF who fall within the intermediate range of peak $\dot{V}O_2$. The present results suggest that the $\dot{V}_E/\dot{V}_{CO_2}$ slope and HRR_1 , markers of ventilatory efficiency, and autonomic function, respectively, are strong predictors of cardiovascular mortality among HF patients in this subgroup. Importantly, these responses stratify patients with peak $\dot{V}O_2$ in the range of 10.1 to $13.9 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ into distinct groups with high and low risk for cardiovascular mortality. Patients within this range who exhibit abnormal responses for both the $\dot{V}_E/\dot{V}_{CO_2}$ slope and HRR_1 had an even higher mortality risk than those with peak $\dot{V}O_2$ values $10 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ or less, underscoring their utility in identifying high-risk patients in this important category.

Over the last decade, there have been numerous studies demonstrating the prognostic significance of an abnormal $\dot{V}_E/\dot{V}_{CO_2}$ slope in HF patients.^{5,8–11,13,16,18,19} An elevated $\dot{V}_E/\dot{V}_{CO_2}$ slope has been linked to poor pulmonary perfusion,^{20,21} an impaired cardiac output both at rest²² and during exercise,²³ early lactate accumulation, heightened skeletal muscle, and chemoreceptor sensitivity,^{24,25} and deconditioning. The optimal cut point for the $\dot{V}_E/\dot{V}_{CO_2}$ slope in our population was 34, which is in accordance with previous studies.^{8,10,11} We observed that the addition of the $\dot{V}_E/\dot{V}_{CO_2}$ slope in patients within the intermediate range of peak $\dot{V}O_2$ stratified patients into distinct groups of high and low cardiovascular mortality (Table 3, Figure 2). Corrá et al¹³ reported that the $\dot{V}_E/\dot{V}_{CO_2}$ slope discriminated high-and

low-risk patients within a wider peak $\dot{V}O_2$ range (10–18 mL·kg⁻¹·min⁻¹); HF patients with a $\dot{V}_E/\dot{V}_{CO_2}$ slope greater than 35 had a mortality rate that was similar to that in patients with a peak $\dot{V}O_2 < 10$ mL·kg⁻¹·min⁻¹. Conversely, we observed that patients in the intermediate range for peak $\dot{V}O_2$ who had both an abnormal $\dot{V}_E/\dot{V}_{CO_2}$ slope and HRR₁ had a higher mortality risk than those with a peak $\dot{V}O_2 > 10$ mL·kg⁻¹·min⁻¹ (Figure 2, Table 3).

While HRR₁ has been shown to have prognostic value in patients with coronary disease for some time,^{26,27} such studies in patients with HF are more recent.^{9,11,28} We previously observed that HF patients with an HRR₁ < 6 beats per minute had a high mortality risk; the combination of an abnormal $\dot{V}_E/\dot{V}_{CO_2}$ slope and impaired HRR₁ resulted in an approximate 90% event rate 1 year after CPX.²⁹ In subsequent analyses, we observed that HRR₁ was a powerful prognostic marker when adjusted for β -blocker use, EF, HF etiology, and mode of exercise, and that HRR₁ consistently added prognostic value to the $\dot{V}_E/\dot{V}_{CO_2}$ slope and other CPX responses.^{9,11} The present findings confirm these earlier results in a larger population of patients with HF. HRR₁, together with $\dot{V}_E/\dot{V}_{CO_2}$ slope, provided powerful risk prediction for cardiac mortality in both univariate and multivariate analyses. Among patients specifically within the intermediate range of peak $\dot{V}O_2$, we observed that an abnormal HRR₁ was particularly helpful in estimating risk, providing a doubling of the HR in patients with a heightened $\dot{V}_E/\dot{V}_{CO_2}$ slope. Thus, these results suggest that the $\dot{V}_E/\dot{V}_{CO_2}$ slope and HRR₁ should be routinely measured when using CPX to estimate risk in patients with HF.

Previous studies have observed that patients with both an abnormal HRR₁ and a high $\dot{V}_E/\dot{V}_{CO_2}$ slope have particularly high mortality rates.^{9,11,28,29} The current results confirm the value of these responses among patients who fall within the intermediate range for peak $\dot{V}O_2$. Because the pathophysiology of HF is multifactorial, variables that incorporate different mechanisms that may be underlying exercise intolerance in these patients may provide better risk stratification. The improved estimates of risk using these variables in the current study might be explained by the fact that they represent distinct manifestations of HF, including autonomic imbalance (HRR₁) and ventilation-perfusion mismatching in the lungs ($\dot{V}_E/\dot{V}_{CO_2}$ slope).^{30,31}

This study has several limitations. Our sample represents a generalized group of HF patients, among whom few were being evaluated specifically for transplantation. Had the analysis been performed in patients with more severe disease, the prognostic characteristics of the CPX responses would likely have differed. The fact that we only assessed heart rate in the first minute of recovery is another limitation since the second minute in recovery and other time points have been shown to provide improved risk stratification in some studies.^{32,33} Our exercise tests included an active cool-down phase, which differs from some studies in measuring HRR₁ in which patients were placed in the supine position immediately. Further research is needed to determine the optimal recovery protocol for estimating risk in patients with HF.

SUMMARY

The application of 2 easily derived variables from CPX, the $\dot{V}_E/\dot{V}_{CO_2}$ slope and HRR_1 , effectively stratifies risk among HF patients who fall into the intermediate range for peak $\dot{V}_{O_2}$. The inclusion of these responses in the risk paradigm, when evaluating patients with HF, may help to better select candidates for transplantation or identify those who require closer clinical followup and/or device therapy.

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Figure 1.
Kaplan-Meier survival curves for peak oxygen uptake ($\dot{V}O_2$) subgroups.

Figure 2.

Kaplan-Meier survival curves for peak oxygen uptake ($\dot{V}O_2$) subgroups adding the minute ventilation/carbon dioxide production ($\dot{V}_E/\dot{V}_{CO_2}$) slope and heart rate recovery at first minute (HRR_1) for subjects in the intermediate range.

(A) Peak $\dot{V}O_2$ $14 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$.

(B) Peak $\dot{V}O_2$ $10.1\text{--}13.9 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ and abnormal $\dot{V}_E/\dot{V}_{CO_2}$ slope or HRR_1 .

(C) Peak $\dot{V}O_2$ $10 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$.

(D) Peak $\dot{V}O_2$ $10.1\text{--}13.9 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ and abnormal $\dot{V}_E/\dot{V}_{CO_2}$ slope and HRR_1 .

Table 1 •

Demographics and Clinical Characteristics ($M \pm SD$ Unless Otherwise Indicated)

Variable	All Subjects	Peak $\dot{V}O_2$ ($\text{mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$)		
		(A) 14	(B) 10.1–13.9	(C) 10
Subjects, n	1167	671	330	166
Age, y	58 $\pm$ 13	57 $\pm$ 13	59 $\pm$ 13 ^a	60 $\pm$ 14 ^a
Male gender, n (%)	854 (73)	550 (82)	203 (61) ^a	101 (61) ^a
Etiology, % nonischemic/ischemic	54.1/45.9	53.4/46.6	56.1/43.9	54.1/45.9
Systolic/diastolic HF, %	79/21	78/22	78/22	87/13 ^{a,b}
NYHA functional class	2.4 $\pm$ 0.8	2.1 $\pm$ 0.8	2.6 $\pm$ 0.7 ^{a,b}	2.9 $\pm$ 0.6 ^a
Ejection fraction, %	32.6 $\pm$ 14.2	33.8 $\pm$ 13.7	32.4 $\pm$ 14.8 ^b	28.4 $\pm$ 13.9 ^a
Peak $\dot{V}O_2$, $\text{mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$	15.7 $\pm$ 5.9	19.4 $\pm$ 5.1	12.1 $\pm$ 1.1 ^{a,b}	8.1 $\pm$ 1.4 ^a
$\dot{V}_E/\dot{V}CO_2$ slope	35.1 $\pm$ 9	31.8 $\pm$ 6.7	37.6 $\pm$ 8.4 ^{a,b}	43.7 $\pm$ 13.0 ^a
Heart rate recovery at 1 min, bpm	19 $\pm$ 12	21 $\pm$ 12	16 $\pm$ 10 ^a	14 $\pm$ 12 ^a
Peak respiratory exchange ratio	1.08 $\pm$ 0.15	1.09 $\pm$ 0.14	1.08 $\pm$ 0.13	1.07 $\pm$ 0.18
Prescribed β -blocker, %	64	62	64	68
Prescribed angiotensin-converting enzyme inhibitor, %	72	74	68	72
Prescribed diuretic, %	71	63	81 ^a	84 ^a
Cardiac mortality, n (%)	204 (17)	86 (13)	74 (22) ^a	44 (26) ^a

Abbreviations: HF, heart failure; NYHA, New York Heart Association class; $\dot{V}O_2$, oxygen uptake; $\dot{V}_E/\dot{V}CO_2$ slope, minute ventilation/carbon dioxide production slope.^a $P < .05$ (A) vs others.^b $P < .05$ (B) vs C.

Table 2 •Univariate and Multivariate Cox Regression Analysis^a

Variable	Hazard Ratio	95% CI	P Value
Univariate			
Ejection fraction	1.75	1.26–2.43	<.001
Peak $\dot{V}_{O_2}$ < 14 mL·kg ⁻¹ ·min ⁻¹	2.52	1.83–3.47	<.001
$\dot{V}_E/\dot{V}_{CO_2}$ slope	3.19	2.28–4.46	<.001
HRR ₁	2.29	1.57–3.34	<.001
Multivariate			
Ejection fraction	1.28	0.91–1.81	.15
Peak $\dot{V}_{O_2}$	1.62	1.15–2.29	.006
$\dot{V}_E/\dot{V}_{CO_2}$ slope	2.36	1.64–3.40	<.001
HRR ₁	1.70	1.14–2.51	.008

Abbreviations: $\dot{V}_{O_2}$, oxygen uptake; $\dot{V}_E/\dot{V}_{CO_2}$ slope, minute ventilation/carbon dioxide production slope; HRR₁, heart rate recovery at the first minute.

^aAdjusted for ejection fraction, age, and etiology.

Table 3 •Relative Risks Associated With Peak $\dot{V}O_2$, $\dot{V}_E/\dot{V}CO_2$ Slope, HRR_1 , and Their Combination

Groups	Hazard Ratio	95% CI	P Value
Peak $\dot{V}CO_2$ 14 mL·kg ⁻¹ ·min ⁻¹	1 (Ref)	...	...
Peak $\dot{V}CO_2$ 10.1–13.9 with $\dot{V}_E/\dot{V}CO_2$ 34 or $HRR_1 < 16$	1.81	1.07–3.05	.02
Peak $\dot{V}O_2$ 10.1–13.9 mL·kg ⁻¹ ·min ⁻¹ with $\dot{V}_E/\dot{V}CO_2$ 34 and $HRR_1 < 16$	3.51	2.33–5.29	<.001
Peak $\dot{V}O_2$ 10 mL·kg ⁻¹ ·min ⁻¹	3.11	2.07–4.68	<.001

Abbreviations: $\dot{V}O_2$, oxygen uptake; $\dot{V}_E/\dot{V}CO_2$ slope, minute ventilation/carbon dioxide production ($\dot{V}CO_2$) slope; HRR_1 , heart rate recovery at the first minute.