

Associations Between Exercise Blood Pressure Responses and Oxygen Pulse During Cardiopulmonary Exercise Testing: A Cross-Sectional Study

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Objective: To observe the impact of exaggerated blood pressure response during exercise on oxygen pulse (O_2 pulse), facilitating earlier and more precise identification of the subclinical threat of hypertension.

Methods: This cross-sectional study consecutively enrolled 262 patients with exaggerated blood pressure response (EBPR) (March 2023–March 2025). Based on peak O_2 pulse $\geq 80\%$ of predicted value, patients were divided into Normal ($n=149$) and Reduced O_2 pulse ($n=113$) groups. Baseline characteristics, laboratory findings, and CPET parameters were collected. Binary logistic regression analysis was used to identify independent factors associated with reduced peak O_2 pulse ratio. Multiple linear regression models were employed with the relative increase of O_2 pulse before and after the anaerobic threshold (AT) as dependent variables to explore the associations of blood pressure increase and metabolic equivalent (MET)-adjusted blood pressure increase with changes in O_2 pulse relative increase.

Results: Compared with the Normal O_2 pulse group, the Reduced O_2 pulse group had a higher proportion of males, younger age, higher BMI, and worse metabolic profiles. Logistic regression identified advanced age and alcohol consumption as independent risk factors for reduced peak O_2 pulse, while female sex was protective. Regarding blood pressure, unadjusted SBP increase correlated positively with peak O_2 pulse ratio and O_2 pulse relative increase, whereas MET-adjusted SBP increase showed a significant negative correlation with both. This inverse association suggests that an exaggerated blood pressure response per unit metabolic demand is linked to compromised cardiac pumping efficiency.

Conclusion: The negative correlation between Δ SBP/MET and O_2 pulse suggests that an exaggerated blood pressure response may come at the cost of compromised cardiac pumping efficiency. An excessively high Δ SBP/MET value often indicates more significant changes in the structure and function of the heart, and is an aspect that requires particular attention in the future.

Keywords: oxygen pulse, O_2 pulse, cardiopulmonary exercise testing, CPET, exaggerated blood pressure response, EBPR

Introduction

Exaggerated blood pressure response (EBPR) refers to an abnormally elevated blood pressure during physical exertion. This phenomenon is observed not only in patients with diagnosed hypertension but also in a considerable proportion of individuals with normal resting blood pressure, a population that faces a significantly increased risk of developing sustained hypertension and major adverse cardiovascular events in the future.^{1–4} Therefore, a deeper understanding of the hemodynamic mechanisms underlying EBPR is of great significance for elucidating the intrinsic nature of its adverse prognosis.

The cardiopulmonary exercise test (CPET) is the current gold standard for assessing cardiovascular responses to exercise. Oxygen pulse (O_2 pulse), defined as the ratio of oxygen uptake to heart rate, serves as a reliable indirect

indicator of stroke volume efficiency in the absence of severe anemia or metabolic abnormalities.^{5,6} Unlike assessments of cardiac function that rely solely on resting conditions, the trend of O_2 pulse during exercise can reflect, in real time, the heart's capacity to mobilize reserves during progressively increasing exercise workload.^{7,8} Previous studies have confirmed that an early plateau in the O_2 pulse curve is closely associated with impaired myocardial perfusion,^{9,10} suggesting that the morphological characteristics of O_2 pulse—rather than merely its peak absolute value—may provide incremental information for evaluating cardiac function. However, existing research on EBPR has predominantly focused on isolated factors such as sympathetic overactivation and vascular endothelial function, with few studies systematically investigating, from the perspective of O_2 pulse changes, the intrinsic relationship between blood pressure response patterns and cardiac work efficiency.^{11,12} Little is known about whether and how the intensity of blood pressure response, particularly when adjusted for metabolic demand, relates to the efficiency of cardiac pumping as reflected by O_2 pulse changes during exercise.

It is noteworthy that relying solely on absolute peak blood pressure values may introduce bias in assessing exercise-related risk. For instance, highly fit individuals can also achieve high peak systolic blood pressure during exercise. In such cases, adjusting for workload or metabolic equivalents (METs) allows for a more precise isolation of the impact of exercise intensity on cardiac output.^{13,14} Consequently, analyzing the correlation between MET-adjusted blood pressure increase and the trend of O_2 pulse may help clarify the hemodynamic essence of EBPR: whether it is predominantly characterized by an “excessive increase in cardiac output” or by “impaired cardiac pumping efficiency”.

Against this background, the present study adopted a cross-sectional design, using the trend of O_2 pulse during exercise as an entry point to systematically investigate the intrinsic relationship between the intensity of the exercise blood pressure response and cardiac work efficiency. We hypothesized that a higher MET-adjusted increase in systolic blood pressure (Δ SBP/MET) would be associated with a lower O_2 pulse relative increase and a reduced peak O_2 pulse ratio. Identifying such a hemodynamic pattern may improve early risk stratification for individuals with EBPR, especially those with normal resting blood pressure who are often overlooked in routine clinical practice. This study aims to investigate the impact of an exaggerated blood pressure response during exercise on peak O_2 pulse and its trend, thereby facilitating an earlier and more precise understanding of the masked threats associated with exertional hypertension.

Materials and Methods

Study Design and Participants

This cross-sectional study consecutively enrolled 480 patients who underwent CPET at RiZhao International Heart Hospital between March 2023 and March 2025 and demonstrated an EBPR was defined as peak systolic blood pressure ≥ 210 mmHg in men or ≥ 190 mmHg in women during exercise.² In accordance with the STROBE statement, 164 patients were excluded due to age >75 years, severe coronary artery disease without complete revascularization, hypertrophic cardiomyopathy, or severe heart failure (NYHA class III–IV). An additional 54 patients were excluded due to missing or duplicate data, resulting in a final analysis cohort of 262 patients with EBPR. Based on the percentage of predicted peak O_2 pulse achieved,^{15–17} patients were divided into two groups: the Normal O_2 pulse group (peak O_2 pulse $\geq 80\%$ of predicted value, $n=149$) and the Reduced O_2 pulse group (peak O_2 pulse $<80\%$ of predicted value, $n=113$). Detailed inclusion and exclusion criteria are presented in [Figure 1](#). The study was approved by the Ethics Committee of RiZhao International Heart Hospital (Approval No.: rzxzbyyl2021003) and was conducted in accordance with the Declaration of Helsinki. Written informed consent for the CPET procedure was obtained from all participants.

Inclusion Criteria: (1) Underwent CPET; (2) Increase in systolic blood pressure ≥ 20 mmHg per MET during exercise; (3) Peak systolic blood pressure during exercise met the criteria of ≥ 210 mmHg for men or ≥ 190 mmHg for women; (4) Complete clinical data available; (5) Provided informed consent.

Exclusion Criteria: (1) Age >75 years; (2) Severe coronary artery disease without complete revascularization (complete revascularization was defined as successful PCI or CABG for all stenoses $\geq 70\%$ in epicardial vessels ≥ 2.5 mm in diameter, with no residual stenosis $\geq 50\%$ post-procedure);¹⁸ (3) Hypertrophic cardiomyopathy; (4) Severe heart failure (NYHA functional class III–IV); (5) Pregnancy or gestational period; (6) Poor compliance due to mental illness; (7) Missing or duplicate clinical data.

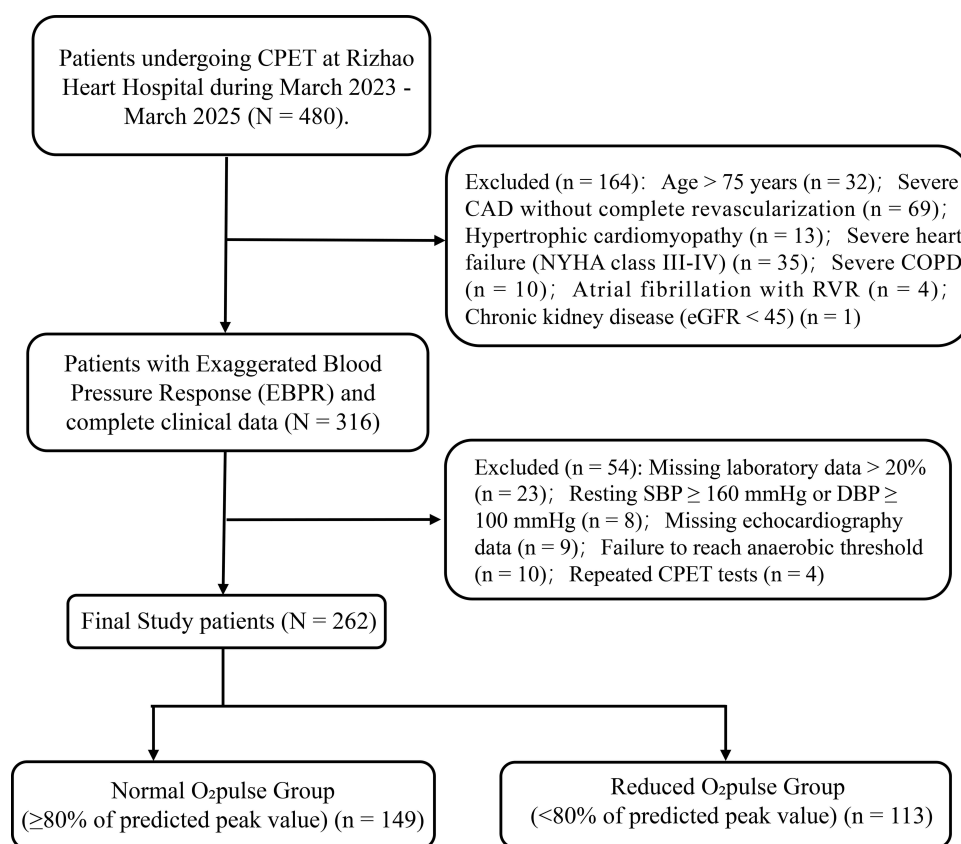


Figure 1 Flowchart of Patient Selection and Group Stratification.

CPET Protocol

CPET was performed using a Schiller CS-200 ergospirometry system (Schiller AG, Switzerland). The test was conducted by physicians/therapists with over one year of experience, following the guidelines of the American Heart Association and the American College of Sports Medicine.¹⁹ Participants were instructed to fast for at least 2 hours and avoid caffeine or tea prior to testing. A ramp protocol on a cycle ergometer was used for all tests. After at least 2 minutes of rest and 3 minutes of warm-up (0 W, 60 rpm), the workload increased incrementally each minute based on a pre-estimated ramp rate. The test was followed by a 5-minute recovery period. Indications for test termination included severe hypertension (SBP ≥ 250 mmHg and/or DBP ≥ 130 mmHg), significant ST-segment depression (≥ 0.1 mV) or elevation, new-onset severe arrhythmia, moderate-to-severe angina or dyspnea, leg weakness, dizziness, or extreme fatigue (Borg scale ≥ 18). In the absence of these criteria, patients were encouraged to exercise to maximal effort (respiratory exchange ratio, RER > 1.10).

Measurements and Data Analysis

Blood Pressure Measurement

Brachial blood pressure was measured and recorded every 2 minutes throughout the test. Resting blood pressure was defined as the value measured after at least 5 minutes of rest before CPET. Anaerobic threshold (AT) blood pressure was measured within 2 minutes of reaching the AT. Peak blood pressure was defined as the highest value recorded during the final 2 minutes of exercise.

Echocardiographic Measurements

All patients underwent transthoracic echocardiography within 24 hours before cardiopulmonary exercise testing, performed by the same experienced echocardiographer. Examinations were conducted using a Philips EPIQ 7C ultrasound

system equipped with an S5-1 transducer (1–5 MHz). Patients were placed in the left lateral decubitus position with simultaneous electrocardiographic monitoring, and images were acquired at end-expiration during quiet breathing. All measurements were averaged over three consecutive cardiac cycles.

MET Calculation

The blood pressure response per MET was calculated as the change in BP divided by the change in METs during specific phases. $\Delta\text{DBP}/\text{MET}$ (Rest-AT) and $\Delta\text{DBP}/\text{MET}$ (AT-Peak) were calculated similarly for diastolic BP. $\Delta\text{SBP}/\text{MET}$ (Rest-AT): $(\text{SBP}@AT - \text{SBP}@Rest) / (\text{METs}@AT - \text{METs}@Rest)$. $\Delta\text{SBP}/\text{MET}$ (AT-Peak): $(\text{SBP}@Peak - \text{SBP}@AT) / (\text{METs}@Peak - \text{METs}@AT)$.

CPET Parameters

Measured parameters included oxygen uptake (VO_2), O_2 pulse, metabolic equivalents (METs), minute ventilation (VE), the VE/ VCO_2 slope, end-tidal partial pressures of O_2 and CO_2 (PETO_2 and PETCO_2), work rate (WR), heart rate (HR), and breathing reserve. Peak VO_2 was defined as the average value during the last 15 seconds of exercise. The predicted percentage of peak VO_2 ($\text{VO}_{2\text{peak}}/\text{pred}$) and peak O_2 pulse ($\text{O}_{2\text{pulse}}/\text{pred}$) were calculated. The AT was determined using the V-slope method combined with ventilatory equivalents.

O_2 pulse Relative Increase Calculation

To quantitatively analyze the trend of the O_2 pulse curve, we defined the relative increase in two distinct phases segmented by the AT (Figure 2). The O_2 pulse relative increase from rest to AT was calculated as: $(\text{O}_2\text{pulse at AT} - \text{O}_2\text{pulse at Rest}) / \text{O}_2\text{pulse at Rest}$. The O_2 pulse relative increase from AT to peak exercise was calculated as: $(\text{O}_2\text{pulse at Peak} - \text{O}_2\text{pulse at AT}) / \text{O}_2\text{pulse at AT}$. This calculation represents the fractional increase of O_2 pulse relative to its value at the beginning of each exercise phase, providing a normalized measure of its growth pattern.

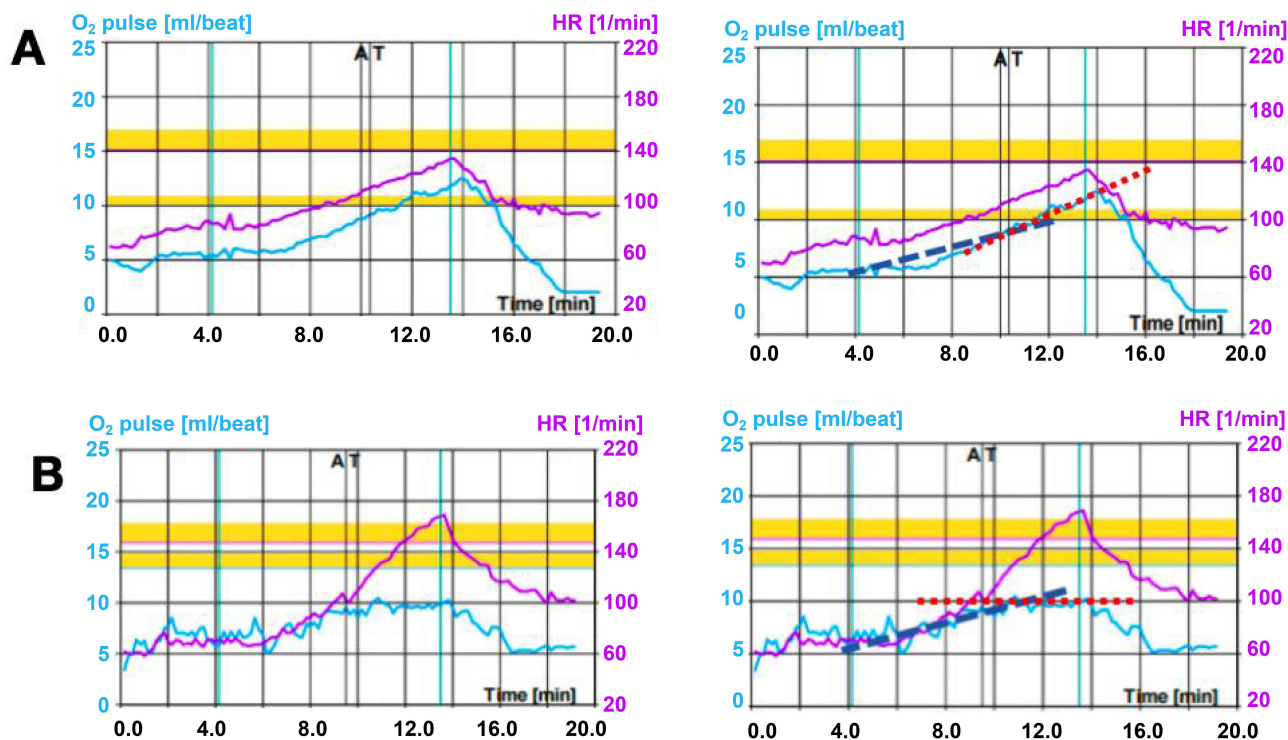


Figure 2 Pulse slope illustration.

Notes: Red dashed line indicates heart rate (HR); blue dashed line indicates oxygen pulse (O_2 pulse); (A) Normal oxygen pulse slope; (B) Early platform of oxygen pulse.

Statistical Analysis

Statistical analysis was performed using SPSS 20.0 software. For continuous variables, the Shapiro–Wilk test for normality was used. Quantitative variables conforming to a normal distribution were expressed as $\bar{x} \pm s$, and independent samples *t*-tests were used for comparisons between two groups. Quantitative variables not conforming to a normal distribution were expressed as M (inter quartiles), and Mann–Whitney *U*-tests were used for comparisons between two groups. Categorical variables were expressed as counts (%), and Fisher’s exact test (χ^2 -test) was used for comparisons. Binary logistic regression was used to analyze the risk factors for the peak proportion of O₂pulse, and multivariate linear regression was employed to screen the risk factors for the relative increase of O₂pulse, and to calculate OR and 95% CI. For binary logistic regression, univariate analysis was first performed, and variables with $P < 0.10$ in univariate analysis were entered into the multivariate model using the enter method. For multiple linear regression, all clinically relevant variables were simultaneously entered into the model using the enter method. The distribution of the dependent variable was tested for normality using the Shapiro–Wilk test. If significant deviation from normality was detected, logarithmic transformation or a generalized linear model with appropriate distribution family would be considered. Collinearity was assessed using variance inflation factors (VIF), and variables with VIF > 5 were not included simultaneously in the same model. The significance level α was set at 0.05, and $P < 0.05$ was considered statistically significant. Post-hoc power analysis was performed using GPower software (version 3.1). Assuming a medium effect size ($f^2 = 0.15$ for linear regression models, and an odds ratio of 1.5 for logistic regression models), a sample size of 262, a two-sided α of 0.05, and the number of predictors as in the final models (ranging from 4 to 6), the achieved power exceeded 0.90 for all regression analyses. This indicates that the study was adequately powered to detect clinically meaningful effect sizes.

Results

Baseline Clinical Characteristics

The O₂pulse trajectory throughout exercise, normalized to peak workload, is illustrated. The Reduced O₂pulse group demonstrated a flatter rise and lower peak value compared to the Normal group. Notably, the AT occurred earlier relative to peak workload in the Reduced group (Figure 3). The baseline characteristics of the 262 enrolled patients with EBPR are summarized in Table 1. Compared to the Normal O₂pulse group, the Reduced O₂pulse group was characterized by a higher proportion of males, a younger median age, a higher BMI, and a greater prevalence of smoking. Cr (Creatinine) and UA (Uric Acid) levels are higher, while HDL-C (High-Density Lipoprotein Cholesterol) level is lower ($P < 0.05$). It is noteworthy that 90 patients (34.35%) demonstrated an EBPR without

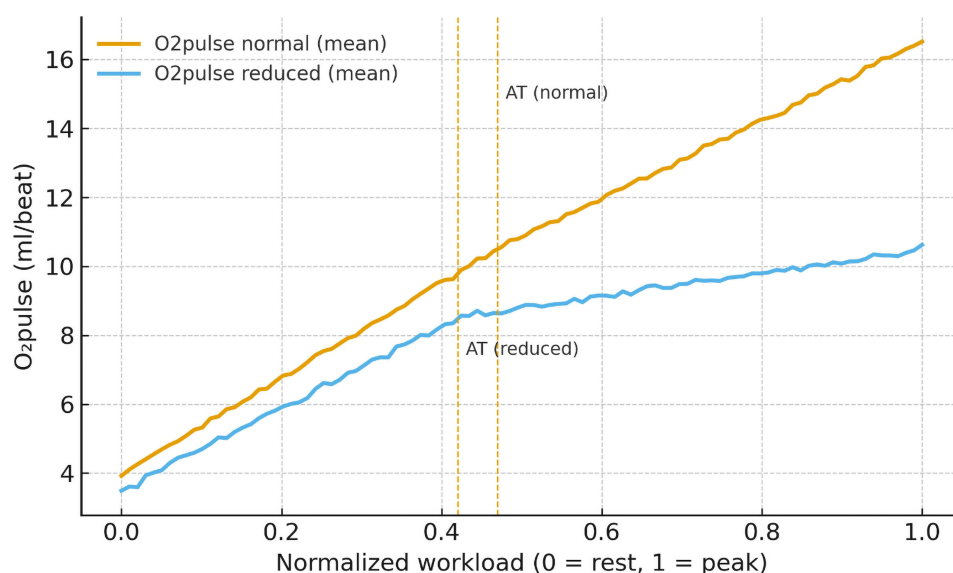


Figure 3 Exercise O₂pulse Trajectories Stratified by Peak Function.

Table 1 Baseline Characteristics and Laboratory Inspection Indicators

Characteristic	Reduced O ₂ pulse Group (n=113)	Normal O ₂ pulse Group (n=149)	χ^2/Z	P-value
Age [M (P ₂₅ , P ₇₅), years]	60.00 (53.00, 67.0)	62.00 (57.00, 68.00)	-2.142	0.032
Sex [n (%)]			40.734	<0.001
Male	92.00 (81.42)	63.00 (42.28)		
Female	21.00 (18.58)	86.00 (57.72)		
BMI [M (P ₂₅ , P ₇₅), kg/m ²]	27.80 (25.90, 29.60)	26.30 (24.60, 28.00)	-3.907	<0.001
Smoking History [n (%)]	55.00 (48.67)	31.00 (20.81)	22.633	<0.001
Alcohol Use [n (%)]	40.00 (35.40)	38.00 (25.50)	3.009	0.083
Hypertension [n (%)]	80.00 (70.80)	92.00 (61.74)	2.335	0.127
Diabetes [n (%)]	69.00 (61.06)	82.00 (55.03)	1.133	0.287
Coronary Artery Disease [n (%)]	28.00 (24.78)	43.00 (28.86)	0.542	0.462
Physical Activity Level [n (%)]			0.475	0.798
Light	60.00 (53.10)	74.00 (49.66)		
Moderate	32.00 (28.32)	48.00 (32.21)		
High	21.00 (18.58)	27.00 (18.12)		
BUN [M (P ₂₅ , P ₇₅), mmol/L]	5.50 (4.60, 6.30)	5.43 (4.70, 6.30)	-0.515	0.606
Cr [M (P ₂₅ , P ₇₅), μ mol/L]	71.70 (62.90, 78.80)	65.00 (54.10, 74.90)	-3.651	<0.001
UA [M (P ₂₅ , P ₇₅), μ mol/L]	359.00 (298.00, 413.00)	321.00 (259.50, 385.50)	-3.401	0.001
HDL-C [M (P ₂₅ , P ₇₅), mmol/L]	1.15 (1.00, 1.40)	1.27 (1.10, 1.50)	-2.713	0.007
LDL-C [M (P ₂₅ , P ₇₅), mmol/L]	2.43 (1.90, 3.10)	2.41 (1.70, 3.10)	-0.300	0.764
FBG [M (P ₂₅ , P ₇₅), mmol/L]	5.80 (5.10, 6.50)	5.90 (5.30, 6.70)	-1.295	0.195
TG [M (P ₂₅ , P ₇₅), mmol/L]	1.36 (1.00, 2.00)	1.32 (1.00, 1.90)	-0.835	0.403
TC [M (P ₂₅ , P ₇₅), mmol/L]	4.12 (3.40, 5.00)	4.41 (3.40, 5.20)	-0.635	0.526

Abbreviations: BMI, Body Mass Index; BUN, Blood Urea Nitrogen; Cr, Creatinine; UA, Uric Acid; HDL-C, High-Density Lipoprotein Cholesterol; LDL-C, Low-Density Lipoprotein Cholesterol; FBG, Fasting Blood Glucose; TG, Triglycerides.

a prior hypertension history. No significant intergroup differences were found in alcohol consumption, physical activity levels, or the prevalence of diabetes and coronary artery disease.

CPET Parameters

Comprehensive CPET parameters are detailed in Table 2. The analysis delineated a clear profile for the Reduced O₂pulse group, which was characterized by a consistent pattern of diminished cardiopulmonary functional reserve. This was evidenced by significantly lower values across all major aerobic capacity metrics, including VO₂ at AT, peak VO₂ (% predicted), peak METs, and peak WR (% predicted) ($P < 0.05$). Concurrently, this group exhibited a maladaptive hemodynamic profile, featuring an EBPR per metabolic equivalent (Δ SBP/MET and Δ DBP/MET) and higher HR both at the AT and at peak exercise ($P < 0.05$). To comprehensively present the study results, Figure 4 visually illustrates the trends of HR, SBP, and DBP at various time points. The results demonstrated that HR, SBP, and DBP in both groups exhibited an upward trajectory with increasing exercise workload. Specifically, no significant differences were observed in SBP between the two groups at any time point. For HR, no between-group difference was noted at rest; however, at the AT and peak exercise, HR was significantly higher in the Reduced O₂pulse Group than in the Normal O₂pulse Group (both $P < 0.05$). Regarding DBP, the Reduced O₂pulse Group showed significantly higher values at rest and peak exercise compared with the Normal O₂pulse Group (both $P < 0.05$).

Echocardiogram Comparison Results

The results showed that compared with the normal group, the LA (Left Atrial diameter), LVEDD (Left Ventricular End-Diastolic Diameter), EDV (Left Ventricular End-Diastolic Diameter), and LVSD (Left Ventricular End-Systolic Diameter) in the O₂pulse reduction group were all significantly increased (all $P < 0.05$). However, there was no statistically significant difference in left ventricular EF (Ejection Fraction) between the two groups ($P > 0.05$) (Figure 5).

Table 2 Comparison of CPET Parameters

Parameter	Reduced O ₂ pulse Group (n=113)	Normal O ₂ pulse Group (n=149)	Z	P-value
Rest				
HR (b/m)	72.00 (62.50, 82.00)	69.00 (61.0, 77.0)	-1.920	0.055
SBP (mmHg)	143.00 (131.50, 153.00)	143.00 (134.00, 151.00)	-0.104	0.917
DBP (mmHg)	89.00 (79.00, 93.00)	84.00 (76.50, 92.00)	-2.417	0.016
AT				
HR (b/m)	111.00 (103.00, 118.50)	105.00 (95.00, 113.00)	-3.750	0.000
SBP (mmHg)	169.00 (150.00, 184.00)	166.00 (152.00, 176.50)	-1.122	0.262
DBP (mmHg)	88.00 (81.00, 95.00)	85.00 (78.00, 93.00)	-1.754	0.079
VO ₂ (mL/Kg/min)	12.60 (10.90, 14.40)	13.30 (11.60, 15.40)	-2.495	0.013
VO ₂ /Pred (%)	50.00 (45.50, 56.00)	59.80 (53.80, 68.80)	-7.926	0.000
METs	3.60 (3.10, 4.10)	3.80 (3.30, 4.40)	-2.495	0.013
ΔSBP (Rest-AT) (mmHg)	27.00 (12.50, 40.00)	22.00 (11.00, 36.00)	-1.476	0.140
ΔDBP (Rest-AT) (mmHg)	1.00 (-3.50, 7.00)	1.00 (-4.00, 7.00)	-0.087	0.930
ΔSBP/MET (rest-AT)	17.31 (9.10, 25.40)	12.11 (6.30, 21.20)	-2.274	0.023
ΔDBP/MET (rest-AT)	0.77 (-2.40, 5.50)	0.69 (-2.40, 4.30)	-0.323	0.746
O ₂ pulse (Rest-AT) relative increase	0.49 (0.30, 0.70)	0.44 (0.30, 0.60)	-1.654	0.098
Peak				
HR (b/m)	136.00 (126.50, 148.00)	130.00 (118.00, 142.50)	-2.981	0.003
SBP (mmHg)	213.00 (200.50, 228.50)	213.00 (195.50, 226.00)	-0.964	0.335
DBP (mmHg)	104.00 (95.50, 113.00)	99.00 (90.50, 110.00)	-2.778	0.005
VO ₂ (mL/Kg/min)	18.40 (15.50, 20.90)	18.80 (16.60, 22.80)	-2.058	0.040
VO ₂ /Pred (%)	74.00 (65.00, 81.50)	87.00 (80.00, 98.00)	-8.568	0.000
METs	5.30 (4.50, 6.00)	5.40 (4.80, 6.50)	-2.054	0.040
ΔSBP (AT-peak) (mmHg)	43.00 (32.00, 58.00)	46.00 (34.00, 57.00)	-0.263	0.792
ΔDBP (AT-peak) (mmHg)	15.00 (9.00, 21.00)	12.00 (7.00, 20.50)	-1.452	0.147
ΔSBP/MET (AT-peak)	27.14 (21.70, 34.70)	25.91 (19.70, 34.30)	-1.123	0.262
ΔDBP/MET (AT-peak)	9.44 (5.90, 12.70)	7.20 (4.10, 10.80)	-2.917	0.004
O ₂ pulse (AT-Peak) relative increase	0.16 (0.10, 0.20)	0.17 (0.10, 0.30)	-0.528	0.598
Other				
BR@peak (%)	52.00 (40.00, 61.00)	51.00 (39.00, 58.00)	-1.093	0.274
WR@peak/pred (%)	74.00 (66.00, 83.50)	79.00 (69.00, 88.00)	-2.775	0.006
VE/VCO ₂ slope	24.37 (22.10, 28.10)	25.75 (22.80, 28.50)	-2.015	0.044
PETCO ₂ @rest (mmHg)	38.20 (35.50, 40.50)	37.50 (35.00, 40.10)	-1.199	0.230
PETCO ₂ increase (mmHg)	4.30 (1.20, 6.70)	3.80 (1.40, 3.80)	-0.896	0.370

Abbreviations: Rest, Resting state; HR, Heart rate; SBP, Systolic blood pressure; DBP, Diastolic blood pressure; AT, Anaerobic threshold; VO₂, Oxygen uptake; VO₂/Pred, Percentage of predicted oxygen uptake; MET, Metabolic equivalent of task; O₂pulse, Oxygen pulse; O₂pulse/pred, Percentage of predicted oxygen pulse; Rest-AT, from rest to anaerobic threshold; AT-Peak, from anaerobic threshold to peak; BR@peak, Breathing reserve at peak exercise; WR@peak/pred, Percentage of predicted work rate at peak; VE/VCO₂ slope, Ventilatory equivalent for carbon dioxide slope; PETCO₂@Rest, End-tidal carbon dioxide partial pressure at rest; PETCO₂ increase, Increase in end-tidal carbon dioxide partial pressure during exercise.

Factors Influencing O₂pulse Ratio

The key independent risk factor for reduced peak O₂pulse was advanced age, while female sex was protective. Using the presence of a reduced O₂pulse ratio as the dependent variable, demographic variables, resting blood pressure, peak blood pressure, and exercise-induced blood pressure increase were sequentially entered into the regression model. The results showed that advanced age was an independent risk factor for reduced peak O₂pulse (OR: 1.064, 95% CI: 1.016–1.114, $P=0.008$). Compared with males, female sex was a protective factor against reduced peak O₂pulse (OR: 0.038, 95% CI: 0.013–0.086, $P<0.001$). Individuals with a history of alcohol consumption had a significantly higher risk of reduced peak O₂pulse (OR: 1.766, 95% CI: 1.087–2.584, $P=0.002$). A greater increase in SBP from rest to peak ($\Delta\text{SBP}_{\text{Rest-Peak}}$) was

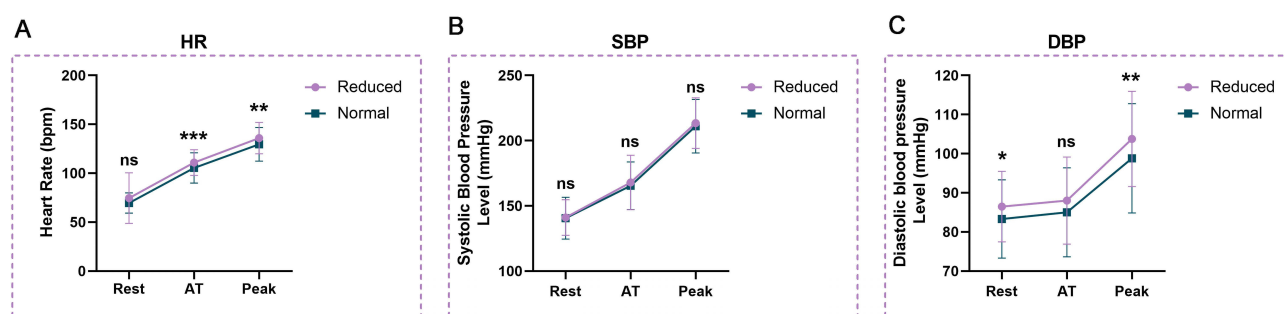


Figure 4 The changing trends of heart rate, systolic blood pressure and diastolic blood pressure of the two groups of patients at each time period.

Notes: * ($P < 0.05$), ** ($P < 0.01$), *** ($P < 0.001$); (A) Heart rate; (B) Systolic blood pressure; (C) Diastolic blood pressure.

Abbreviations: ns, not significant; Rest, Resting state; AT, Anaerobic threshold; Peak, Peak value.

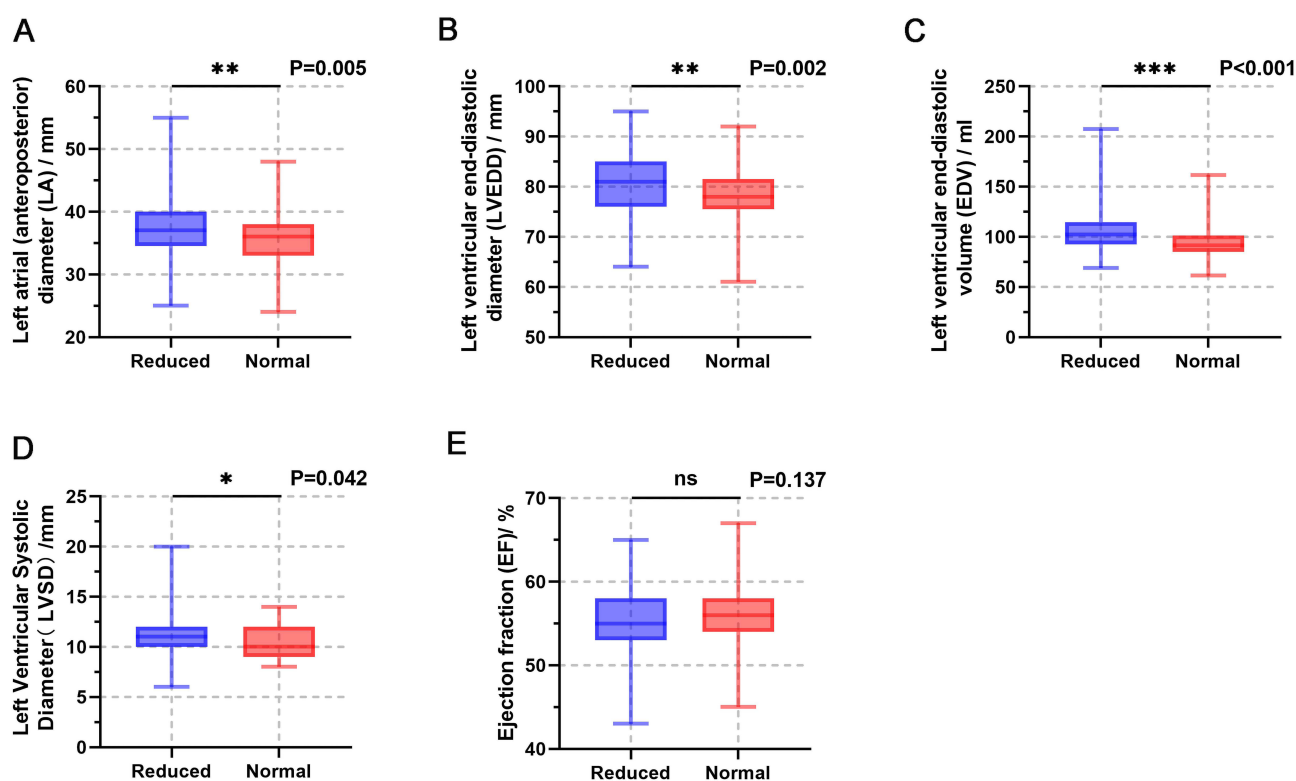


Figure 5 Comparison results of echocardiograms between the two groups of patients.

Notes: * ($P < 0.05$), ** ($P < 0.01$), *** ($P < 0.001$); (A) Left Atrial diameter; (B) Left Ventricular End-Diastolic Diameter; (C) Left Ventricular End-Diastolic Volume; (D) Left Ventricular End-Systolic Diameter; (E) Ejection Fraction.

Abbreviation: ns, not significant.

associated with an increased risk of reduced peak O_2 pulse (OR: 1.029, 95% CI: 1.011–1.048, $P = 0.002$). Conversely, a greater MET-adjusted increase in SBP ($\Delta SBP/MET_{Rest-Peak}$) was associated with a lower risk of reduced peak O_2 pulse (OR: 0.842, 95% CI: 0.794–0.893, $P < 0.001$). In addition, a higher peak $DBP@Peak$ level was associated with a lower risk of reduced peak O_2 pulse (OR: 0.960, 95% CI: 0.933–0.987, $P = 0.004$). In the logistic regression model, the VIF for all independent variables ranged from 1.053 to 1.538, all below the conventional threshold of 5, indicating no significant multicollinearity. Detailed results are presented in Table 3.

Table 3 Logistic Regression Analysis of Factors Influencing Peak O₂pulse Percentage

Variable	β	SE	OR	95% CI for OR	P-value	VIF
Age	0.062	0.023	1.064	1.016 ~ 1.914	0.008	1.053
Female	-3.403	0.486	0.038	0.013 ~ 0.086	0.000	1.172
Alcohol Use	0.569	0.361	1.766	1.087 ~ 2.584	0.002	1.392
Δ SBP (Rest-Peak)	0.029	0.009	1.029	1.011 ~ 1.648	0.002	1.099
Δ SBP/MET (Rest-Peak)	-0.172	0.030	0.842	0.794 ~ 1.893	0.000	1.538
DBP@Peak	-0.041	0.014	0.960	0.933 ~ 1.387	0.004	1.114

Abbreviations: Δ SBP, change in systolic blood pressure; Rest-Peak, from rest to peak exercise; DBP, diastolic blood pressure.

Table 4 Impact of Blood Pressure Increase on O₂pulse Relative Increase Before AT

Variable	β	SE	t	95% CI	P-value	VIF
Δ SBP (Rest-AT)	0.005	0.001	5.188	0.003 ~ 1.007	<0.001	1.078
Δ DBP (Rest-AT)	-0.003	0.003	-1.177	-0.009 ~ 0.502	0.240	1.143
Δ SBP/MET (Rest-AT)	-0.007	0.001	-7.248	-0.009 ~ -1.005	<0.001	1.423
Δ DBP/MET (Rest-AT)	0.005	0.003	1.605	-0.001 ~ 0.912	0.110	1.393

Abbreviations: Δ SBP, increase in systolic blood pressure; Δ DBP, increase in diastolic blood pressure; MET, metabolic equivalent; Rest-AT, from rest to anaerobic threshold.

Table 5 Impact of Blood Pressure Increase on O₂pulse Relative Increase After AT

Variable	β	SE	t	95% CI	P-value	VIF
Δ SBP (AT-peak)	0.004	0.001	6.575	0.003 ~ 0.505	<0.001	1.550
Δ DBP (AT-peak)	-0.003	0.001	-2.132	-0.306 ~ -0.000	0.034	2.310
Δ SBP/MET (AT-peak)	-0.004	0.001	-4.586	-0.006 ~ -0.802	<0.001	1.894
Δ DBP/MET (AT-peak)	0.000	0.002	0.254	-0.003 ~ 1.004	0.800	1.100

Abbreviations: Δ SBP, increase in systolic blood pressure; Δ DBP, increase in diastolic blood pressure; MET, metabolic equivalent; AT-Peak, from anaerobic threshold to peak exercise.

Factors Influencing the Relative Increase in O₂pulse

Because the relative increase in O₂pulse showed a skewed distribution, logarithmic transformation was applied before performing linear regression analysis. The core finding was that Δ SBP/MET was negatively correlated with the relative increase in O₂pulse both before and after AT, whereas unadjusted Δ SBP showed a positive correlation. The analysis revealed that both before and after the AT, the unadjusted increase in SBP (Δ SBP) was significantly positively correlated with the O₂pulse relative increase (pre-AT: $\beta=0.005$, 95% CI: 0.003–0.007, $P<0.001$; post-AT: $\beta=0.004$, 95% CI: 0.003–0.005, $P<0.001$). However, the MET-adjusted increase in SBP (Δ SBP/MET) was significantly negatively correlated with the O₂pulse relative increase (pre-AT: $\beta=-0.007$, 95% CI: -0.009 to -0.005, $P<0.001$; post-AT: $\beta=-0.004$, 95% CI: -0.006 to -0.002, $P<0.001$). The increase in DBP, both unadjusted and MET-adjusted, showed no consistent effect on the O₂pulse relative increase before or after the AT. In the linear regression models, the VIF for all independent variables ranged from 1.078 to 2.310, all below the threshold of 5, suggesting no significant multicollinearity. Detailed data are provided in Table 4 and Table 5. To assess the potential confounding effects of age and sex, we performed a sensitivity analysis by additionally including age and sex as covariates in the linear regression models. The results showed that the negative association between Δ SBP/MET and the relative increase in O₂pulse remained significant both before and after the AT. After adjustment, the β value was -0.006 (95% CI: -0.008 to -0.004, $P < 0.001$) for the rest-to-AT phase, and -0.004 (95% CI: -0.006 to -0.002, $P < 0.001$) for the AT-to-peak phase. Based on these tabulated data, scatter plots were constructed to visualize the relationship between changes in SBP and the O₂pulse relative increase during different exercise phases (Figure 6).

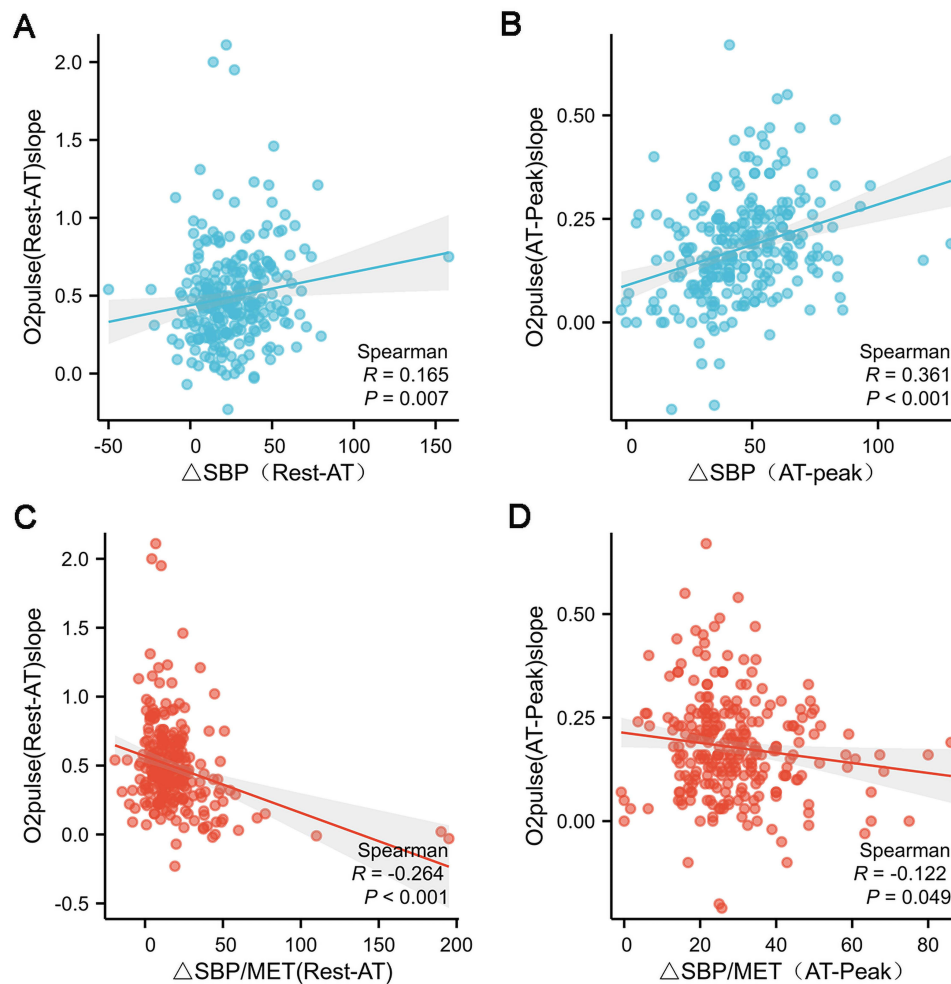


Figure 6 Correlation between systolic blood pressure changes and oxygen pulse relative increase across different exercise stages.

Notes: (A) Relationship between the increase in systolic blood pressure from rest to anaerobic threshold (Rest-AT) and the oxygen pulse relative increase; (B) Relationship between the increase in systolic blood pressure from anaerobic threshold to peak exercise (AT-peak) and the oxygen pulse relative increase; (C) Ratio of pre-anaerobic threshold systolic blood pressure increase to MET; (D) Ratio of post-anaerobic threshold systolic blood pressure increase to MET.

Abbreviations: Rest, Resting state; SBP, Systolic blood pressure; AT, Anaerobic threshold; MET, Metabolic equivalent of task.

Discussion

Although previous studies have largely attributed the pathophysiological mechanisms of an EBPR to sympathetic overactivation, inadequate reduction in peripheral vascular resistance, or vascular endothelial dysfunction,^{13,20} the intrinsic relationship between EBPR and cardiac work efficiency has not been systematically elucidated.¹⁴ To study this part, the present study introduced METs to standardize the increase in blood pressure during exercise testing, aiming to systematically evaluate the association between blood pressure response patterns and O_2 pulse from the perspective of cardiac pumping efficiency. The core finding of this study is that $\Delta SBP/MET$ is significantly negatively correlated with both the relative increase and the peak value of O_2 pulse. This result suggests that when the magnitude of the blood pressure rise exceeds the appropriate range corresponding to the body's current metabolic demand, the excessive hemodynamic response often comes at the cost of compromised cardiac pumping efficiency.^{21,22} In contrast, the unadjusted ΔSBP is positively correlated with O_2 pulse levels. The opposite directions of the ORs for reduced O_2 pulse observed in regression analyses are not a statistical contradiction but rather reflect distinct pathophysiological meanings: the unadjusted ΔSBP mainly increases with exercise workload, and its elevation may be matched by higher metabolic demand and compensatory cardiac output, thus showing a positive association with O_2 pulse in cross-sectional data.¹⁴ In contrast, $\Delta SBP/MET$, by removing the interference of metabolic demand, more precisely captures the cardiovascular

dysregulation implied by “an excessive blood pressure rise per unit metabolic load”. Therefore, the true masked cardiovascular risk does not originate from the simple elevation of blood pressure values, but rather from the decreased cardiac work efficiency that becomes evident after metabolic standardization.^{14,23}

Echocardiography showed that in EBPR patients with reduced O₂pulse, although resting LVEF remained normal, left atrial diameter, left ventricular end-diastolic diameter, and left ventricular end-diastolic volume were significantly increased. This suggests that a chronically “high energy consumption, low efficiency” loading state may have triggered compensatory structural remodeling; such subclinical changes may represent an anatomical basis for future adverse outcomes such as heart failure.^{24–26} Laboratory findings also revealed that this patient group concurrently exhibited elevated serum uric acid levels and decreased HDL-C levels. Elevated uric acid is not only a marker of endothelial dysfunction but may also directly interfere with myocardial energy metabolism, while decreased HDL-C compromises cardiovascular protective mechanisms.^{27,28} Together, these factors constitute a metabolic microenvironment associated with reduced O₂pulse efficiency, further indicating that EBPR may be a systemic risk network involving structural, functional, and metabolic dimensions.

Furthermore, 34.35% of EBPR patients in this study had completely normal resting blood pressure, a proportion significantly higher than previously reported in the literature.²⁹ This finding suggests that reliance solely on office resting blood pressure monitoring is prone to miss many cases of masked exercise-induced hypertension. These individuals appear healthy under resting conditions but reveal hemodynamic dysregulation under stress. Therefore, clinical assessment paradigms need to be extended from static to dynamic conditions, and from focusing merely on blood pressure values to an in-depth evaluation of cardiac work efficiency, in order to achieve earlier risk identification. Another noteworthy paradox is that univariate analysis showed a younger median age in the reduced O₂pulse group, yet multivariate logistic regression identified advanced age as an independent risk factor (OR = 1.064). This phenomenon may be explained by the compositional characteristics of the reduced O₂pulse group: this group had a higher proportion of males and a higher BMI, both of which are positively associated with higher absolute O₂pulse values. In the univariate comparison, the “positive” effects of these factors masked the true effect of age, resulting in a reduced O₂pulse despite a younger age in this group. After adjusting for sex and BMI in the regression model, the true effect of age became apparent.

This study has several limitations. First, as a cross-sectional study, we can only reveal associations between blood pressure response patterns and O₂pulse efficiency, but cannot establish causality. Whether the EBPR during exercise is a cause, a consequence, or both of decreased cardiac pump efficiency requires further validation through longitudinal follow-up or interventional studies. Second, the enrolled population exhibited a relatively wide age range, although the majority of patients were distributed between 46 and 74 years. Age remains a strong determinant of blood pressure, cardiac function, and arterial stiffness; therefore, further studies should refine the influence of age stratification on blood pressure and cardiopulmonary parameters. Third, detailed statistical analysis of medication regimens—particularly antihypertensive agents, statins, and beta-blockers—was not performed for all patients in the cohort, precluding precise identification of drug-related effects on O₂pulse changes. Moreover, this was a single-center study, which may introduce selection bias and limit generalizability. The lack of systematic medication records further compounds this limitation, as we could not adjust for potential confounding by these drugs. Fourth, We only used a simplified relative increase metric and did not analyze plateau or inflection points of the O₂pulse curve. Future studies employing more detailed morphological analysis may provide additional insights. Fifth, O₂pulse is an indirect surrogate for stroke volume and may be influenced by factors other than cardiac function. Although we excluded patients with severe anemia or metabolic abnormalities, this inherent limitation should be acknowledged.

Conclusion

In summary, by revealing the intrinsic association between an excessive rise in systolic blood pressure per unit metabolic load and a decrease in O₂pulse efficiency, this study suggests that the hemodynamic essence of EBPR may be a “high energy consumption, low efficiency” cardiovascular response pattern. By focusing on Δ SBP/MET, it may be possible to use Δ SBP/MET to differentiate, from among individuals with seemingly ordinary blood pressure elevation, those whose hearts are already in a compensatory state of “high workload, low efficiency”. This finding offers a potential

physiological perspective for understanding the masked threats of exertional hypertension, and provides potential considerations for subsequent risk stratification and optimization of intervention strategies.

Ethics Statement

This study was approved by the Ethics Committee of RiZhao International Heart Hospital (Approval No. rzzxbyyl2021003) and was conducted in accordance with the Declaration of Helsinki. All participants provided written informed consent prior to undergoing cardiopulmonary exercise testing.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The research was carried out without any financial or commercial ties that might be seen as a potential conflict of interest, according to the authors.

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