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Exercise heart rates determined by a ventilatory threshold vs. standardized equation methods in individuals with metabolic syndrome

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This study aimed to compare the target heart rate (THR) for aerobic exercise based on standardized physiological maximum value percentages with the first-ventilatory-threshold heart rate (HR_{VT1}) in individuals with metabolic syndrome. Three HR_{max} prediction equations were used to calculate the THR as 35%, 40% and 45% of the heart rate reserve (HRR) and 55%, 60% and 65% of the HR_{max}, and the results were compared with the HR_{VT1}. The HR_{VT1} was measured through a CPET that complied with current guidelines and laboratory standards. In addition, the THRs calculated by combining the HR_{max}-measured values with standardized methods were compared with those of HR_{VT1} as a supplement for situations where HR_{max}-measured values can be evaluated but gas exchange analysis cannot be performed. According to the Fox equation, the difference between the HR_{VT1} and 35% HRR was not statistically significant ($t = -0.528$, $P = 0.600$). Bland–Altman analysis indicated that the mean difference between the two values was −0.350, which was close to the 0th line (SD: ±4.595; 95% CI −1.684–0.984), with 95% limits of agreement ranging from −9.356 to 8.656; the interclass correlation coefficient (ICC) was 0.862 ($P < 0.001$, 95% CI 0.766–0.920), indicating high reliability. Regarding the results, the measured values indicate that 40% HRR and 70% HR_{Peak} showed good reliability with HR_{VT1} (ICC: 0.850, 95% CI 0.747–0.913; and ICC: 0.719, 95% CI 0.551–0.832, respectively). Among Chinese patients with MetS, the THR calculated by combining the standardized 35% HRR method with the Fox equation shows excellent agreement with the HR_{VT1} obtained from the CPET. When the HR_{Peak} can be obtained, the THR calculated from the 40% HRR and 70% HR_{Peak} can better estimate the HR_{VT1}. The above results can be used to guide patients to gradually start exercise training near the VT1 in cases where CPET data cannot be obtained.

Keywords Aerobic exercise, Maximum physiological value, First ventilatory threshold, Bland-Altman analysis, Interclass correlation coefficient

Metabolic syndrome (MetS) is a constellation of interrelated metabolic risk factors with complex pathogenic mechanisms involving genetic and epigenetic factors and unhealthy lifestyles (such as a lack of physical activity, overeating and an imbalanced diet)[1], which significantly increase the risk of diabetes and cardiovascular disease (CVD)[2]. As CVD is currently the main cause of death and low quality of life among the elderly population worldwide, it is important to study MetS prevention and treatment to reduce the risk of CVD progression[3].

Exercise prescription can improve protective factors against CVD, such as cardiorespiratory fitness and increased muscle mass. Aerobic exercise is the foundation for the treatment of and recovery from MetS[4–7]. However, there is significant heterogeneity in the post-training response to aerobic exercise among both healthy individuals and patients with MetS[8–10], which is caused by factors such as individual biological differences and methodological variations in exercise prescriptions, including modifications to exercise intensity, frequency, duration, and mode[11]. As a modifiable approach to reduce post-training response heterogeneity, methods for determining exercise intensity play crucial roles in practical applications.

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Two related studies in 2020[12,13] reported poor agreement between the traditional standardized methods for determining exercise intensity on the basis of maximum physiological parameters (constant percentage) and the exercise intensity domains in which the body performs metabolism during practical exercise; standardized methods cannot control metabolic stimulation well. Among various individuals, the first ventilatory threshold (VT1) may correspond to different peak effort percentage intervals (%HR_{Peak}, %VO_{2Peak}, etc.), which correspond to various guideline-based exercise intensity domains[14–16].

Prior to that, Peter Hofmann et al.[17] had already pointed out that the method used to determine the physiological threshold is rarely mentioned in the relevant cardiac rehabilitation guidelines, and the target heart rate (THR) for prescribed exercise in individuals with disease and apparently healthy individuals should not be estimated only by relevant parameters of the maximum physiological value. In 2013, the European Association for Cardiovascular Prevention and Rehabilitation (EACPR), the American Association of Cardiovascular and Pulmonary Rehabilitation (AACVPR) and the Canadian Association of Cardiac Rehabilitation (CACR) released a joint position statement in which a method for prescribing exercise intensity on the basis of a physiological metabolic threshold was introduced to maximize the benefits of aerobic exercise in patients undergoing cardiac rehabilitation[18]. Subsequent studies showed that, compared with standardized exercise intensity prescriptions, physiological metabolic threshold-based exercise intensity prescriptions yielded a 100% response rate to maximum oxygen uptake in sedentary people[19–23] and performed better at improving MetS severity[24]. In 2022, the European Association of Preventive Cardiology (EAPC) released a position statement that set the VT based on a cardiopulmonary exercise test (CPET) as the gold standard for determining aerobic exercise intensity[25]. By mainly using CPETs to evaluate VT1, VT2 and peak oxygen uptake, a system based on the physiological metabolic threshold classified exercise intensity into four levels. Although there is currently no consensus on the range of exercise intensity defined above[26], the intensity range around VT1 is usually regarded as the "lower limit of moderate intensity"[27,28]. Patients with MetS are at high risk for CVD, including those who have recovered from a previous cardiovascular event. Therefore, VT1 can serve as a good initial marker for determining the actual exercise intensity of patients. Starting training near this point and then gradually increasing the exercise intensity to VT2 can ensure appropriate training benefits and prevent negative impacts on the heart and other metabolic indices[29].

Despite existing problems, standardized methods are still irreplaceable because of their convenience and affordability. For patients with MetS, starting with low- to moderate-intensity exercise, with an intensity based on a fixed percentage range of heart rate reserve (e.g., 40–59% HRR), is usually recommended[30]. However, this range is relatively broad and does not fully consider the pathological features of MetS, such as insulin resistance and chronic inflammation[3]. These features lead to cardiovascular dysfunction during exercise in this group. Specifically, patients with MetS often have an imbalance in the autonomic nervous system, manifested as excessive sympathetic nerve activity at rest, impaired parasympathetic regulation of the heart, and a higher resting heart rate than healthy individuals[31]. During incremental load exercise, the ability of the heart to adjust its rate to meet the oxygen demand of the muscles is impaired, which in turn leads to a lower maximum heart rate (HR_{max})[32]. With the progression of MetS components such as hypertension and hyperlipidemia, these adverse changes may lead to cardiac structural remodeling[33], such as left ventricular hypertrophy and myocardial fibrosis, which in turn affect diastolic filling and reduce cardiac output during exercise. For many patients who are sedentary and have other unhealthy behaviors, their physical function further deteriorates, manifesting as reduced skeletal muscle mass, decreased mitochondrial function[34], a low lactate clearance rate, and an earlier-onset anaerobic threshold[35]. These physiological disorders ultimately result in significantly lower exercise tolerance and cardiopulmonary fitness levels[36,37].

We speculate that the above factors may lead to the HRR and HR_{max} in patients with MetS being lower than the predicted values. When HR_{max} prediction equations and fixed percentage ranges applicable to healthy individuals are used, the THR of patients with MetS may deviate from the individual's true lower limit of moderate-intensity exercise (VT1).

Therefore, on the basis of the fixed percentages indicating low and moderate exercise intensity domains in the existing guidelines, we selected several potentially reasonable percentages for this study, aiming to compare the THR for aerobic exercise determined by standardized methods with the HR_{VT1} measured via the CPET to determine a safe, effective and simple way to guide patients with MetS in performing aerobic exercise when CPET data are not available.

Materials and methods

Materials

From November 2022 to June 2023, a total of 56 participants were consecutively enrolled through advertising at local hospitals, doctor recommendations, and health lectures. This study combined a single-center, cross-sectional observational study with a method comparison. The potential subjects underwent screening at Taiyuan Central Hospital within a 48-h period. The data that could be included in the final analysis were then determined.

The inclusion criteria were as follows: ① Patients aged 18 to 65 years with a sedentary lifestyle and a confirmed diagnosis of MetS (the diagnostic criteria released by the Chinese Diabetes Society were adopted in this research)[38]. Patients who had three or more of the following five symptoms met the diagnostic criteria: abdominal obesity, defined as an abdominal perimeter equal to or greater than 90 cm in males and equal to or greater than 85 cm in females; hyperglycemia, defined as a fasting blood glucose level equal to or greater than 6.1 mmol/L, a blood glucose level equal to or greater than 7.8 mmol/L two hours after glucose loading or a diabetes diagnosis; hypertension, defined as blood pressure equal to or greater than 130/85 mmHg or a hypertension diagnosis; a fasting triglyceride level equal to or greater than 1.70 mmol/L; and fasting high-density lipoprotein cholesterol lower than 1.04 mmol/L; ② patients who did not use beta blockers or other drugs that could impact their heart rate or exercise tolerance; and ③ patients who signed the informed consent form.

The exclusion criteria were as follows: absolute exercise contraindications, including the acute stage of various diseases, lower limb fracture, organ system failure, tumors, the acute phase of myocardial infarction, cardiac insufficiency, myocarditis, or chronic lung disease.

The shedding and rejection criteria were as follows: ① poor compliance; ② a CPET peak respiratory exchange ratio (RER_{peak}) lower than 1.10; and ③ unable to sustain 60 r/min during power cycling while following the metronome during the CPET.

All procedures performed in studies involving human participants were conducted in accordance with the ethical standards of the institutional and national research committees and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This research was reviewed and approved by the Taiyuan Central Hospital Ethics Committee (No. 2022026). All study participants signed informed consent forms.

Testing scheme

The study participants underwent medical body composition analysis (770, InBody, Seoul, Korea), abdominal perimeter measurements, and blood draws to screen indices such as fasting blood glucose and blood lipid levels at Taiyuan Central Hospital one day before the start of the CPET. Those who met the inclusion criteria and did not meet any of the exclusion criteria were invited by phone to participate in the subsequent testing.

On the testing day, the premeasured weight and other data of the patients were input into the CPET operation system (CPX-770, HeartGym, Beijing, China). Gas and volume calibrations were conducted according to the manufacturer's instructions, and the environmental temperature was maintained between 19 and 21 °C. Before the formal test, patients sat on the chair silently for 5 min, with their back against the chair, their feet on the floor, and their arms supported at heart level. An automatic upper arm sphygmomanometer (M5 professional, Omron, Mannheim, Germany) was used to measure the resting heart rate and blood pressure[30]. Within the doctor ward, a 12-lead electrocardiogram (ECG) system (EC-12S, Labtech, Debrecen, Hungary) was connected to continuously monitor the ECG and blood pressure during the exercise test period. Patients rested for 3 min before power cycling (Ergoselect 100, Ergoline, Germany) and then performed a 3-min zero-load warm-up at 60 r/min. According to sex and age, a proper incremental power (8–30 W/min) was chosen to ensure that the patients reached symptom-limited peak exercise within 6–10 minutes[39]. Then, the patients could rest and recover for 5–10 min, after which the test ended. All patients were encouraged to reach their maximum effort level.

Determination of the testing data

Determination of VT1

VT1 was jointly determined by three verified methods[28] in the operation system. These three methods include the V-slope method (the comparatively increased slope inflection point of the VCO_2 in comparison with the VO_2 during the test), the VE/VO_2 method, and the end-expiratory O_2 pressure method. The V-slope method was the main calibration method, whereas the other two methods were used for validation to exclude V-slope inflection points caused by nonphysiological hyperventilation[40]. The data were evaluated by two professional cardiac rehabilitation physicians, and the corresponding heart rate of VT1 determined in the system was considered HR_{VT1}. When the patient's VT1 could not be effectively determined, the researchers jointly reviewed the case and determined the cause. If the cause was a human factor that could be corrected, the patient was retested with their consent.

Standardized HRR% method and HR_{max}% method

The HRR% method recommended by the American College of Sports Medicine (THR = (HR_{max}—resting heart rate) × exercise intensity percentage + resting heart rate) was used[30], and the Fox equation (HR_{max} = 220—age), Miller equation ($HR_{max} = 200 - 0.48 \times age$) and Tanaka equation ($HR_{max} = 208 - 0.7 \times age$) were applied to calculate the HR_{max}. The THR of the 35% HRR, 40% HRR, and 45% HRR and the 55% HR_{max}, 60% HR_{max}, and 65% HR_{max} were calculated separately. Additionally, since the HR_{max} of the patients was measured during the CPET (HR_{Peak}), standardized method calculation results were also used for agreement testing in this case.

Statistical analysis

The data were processed with SPSS 27.0 (IBM, Armonk, NY, USA), and the SPSSAU data analysis platform (https://spssau.com/) was used to construct the diagrams. The data are presented as the mean and standard deviation (SD). The Kolmogorov-Smirnov test for normality was performed, and the significance level α was equal to 0.05. The paired-sample t test was used for preliminary testing of differences. The Bland-Altman test and the interclass correlation coefficient (ICC) were used for further agreement testing to ensure that the results had the highest reliability and validity[41]. The ICC model selected was a two-way random effects model.

Results

Clinical characteristics

Among the 56 screened participants, 8 were excluded (5 due to the use of beta-blockers and 3 for an RER_{peak} lower than 1.10). A total of 48 patients with MetS were ultimately included in the final analysis, including 32 males and 16 females aged 24–64 years (44.3 ± 10.6 years). In the CPET used in this study, all patients terminated the test because of muscle fatigue, resulting in the inability to maintain a power cycling rate of 60 r/min. Table 1 presents the basic clinical characteristics and physiological variables of the patients.

Characteristics	Patients (n = 48)
Demographics	
Age (years)	44.3 ± 10.6
Female, n (%)	16 (33.3%)
Male, n (%)	32 (66.7%)
Anthropometrics	
Body weight (kg)	87.3 ± 14.2
Body mass index (kg/m^2)	30.69 ± 4.06
Waist circumference (cm)	104.5 ± 12.1
Body fat percentage (%)	33.38 ± 5.84%
Cardiopulmonary exercise test results	
Resting heart rate (bpm)	80 ± 9
VO_2 at VT1 (ml/kg/min)	13.22 ± 1.93
HR_{VT1}	113.2 ± 9.2
PeakVO_2 (ml/kg/min)	24.31 ± 4.51
HR_{Peak} (bpm)	164 ± 14
RER_{peak}	1.15 ± 0.05
Clinical measurements	
Triglycerides (mmol/L)	2.43 ± 1.11
Total cholesterol (mmol/L)	4.69 ± 1.05
Low density lipoprotein (mmol/L)	2.99 ± 0.9
High density lipoprotein (mmol/L)	1.07 ± 0.15
Systolic blood pressure (mmHg)	134 ± 10
Diastolic blood pressure (mmHg)	86 ± 8
Underlying diseases	
Dyslipidemia, n (%)	43 (89.6%)
Hypertension, n (%)	32 (66.7%)
Type 2 diabetes, n (%)	30 (62.5%)

Table 1. Basic information of the study group. Abbreviations: VO_2 at VT1 = first ventilatory threshold oxygen uptake; HR_{VT1} = heart rate of VT1; PeakVO_2 = peak oxygen uptake; RER_{peak} = peak respiratory exchange ratio.

Comparison of the % HRR standardized method and the HR_{VT1}

The THRs calculated by combining the 40% HRR or 45% HRR with any prediction equation were greater than the HR_{VT1} ($P < 0.001$), whereas there were no statistically significant differences between any of the calculated results of the 35% HRR and HR_{VT1} values ($P > 0.05$) (Table 2). Compared with that of the other equations, the THR calculated by combining the 35% HRR with the Fox equation resulted in the smallest significant difference compared with the HR_{VT1} (t = − 0.528, $P = 0.600$). The results of the Bland-Altman agreement test revealed that the mean difference between the 35% HRR determined by the Fox equation and the HR_{VT1} was -0.350, which was close to the 0th line (SD: ± 4.595; 95% CI − 1.684–0.984), with 95% limits of agreement ranging from − 9.356 to 8.656 (Fig. 1a). After considering the results of the ICC test (0.862; 95% CI 0.766–0.920) (Table 3), the combination of the 35% HRR and the Fox equation showed good reliability and excellent agreement with the HR_{VT1}.

Comparison of the % HR_{max} standardized method and the HR_{VT1}

The THRs calculated by combining the 55% HR_{max} or 60% HR_{max} with any prediction equation were lower than the HR_{VT1} ($P < 0.001$) (Table 2). For the 65% HR_{max}, only the difference between the THR calculated with the Miller equation and that calculated with the HR_{VT1} was significant (t = − 2.764, $P = 0.008$), whereas the difference in the THR calculated with the Fox equation was the smallest (t = − 0.994, $P = 0.326$). The results of the Bland-Altman agreement test revealed that the mean difference between the 65% HR_{max} determined by the Fox equation and the HR_{VT1} was -0.989, which was close to the 0th line (SD: ± 6.894; 95% CI − 2.990–1.013), with 95% limits of agreement ranging from − 14.500 to 12.523 (Fig. 2c). After including the ICC results (0.639; 95% CI 0.435–0.780) (Table 4), the combination of the 65% HR_{max} and the Fox equation had only moderate reliability and moderate agreement with the HR_{VT1}.

Comparison of the HR_{VT1} and THR obtained by combining the measured HR_{max} with the standardized method

After the THR was calculated by combining the measured values with the %HRR, the results revealed that the 40% HRR had the greatest reliability and greatest agreement with the HR_{VT1}; that is, the mean difference between the two was -0.421, which was close to the 0th line (SD: ± 5.184; 95% CI − 1.926–1.084), with 95% limits of agreement ranging from − 10.581 to 9.739 (Fig. 3b), as demonstrated by the Bland-Altman agreement test. The ICC was 0.850 (95% CI 0.747–0.913) (Table 3). The results also indicated good agreement between the other

Predicted values (bpm)		Mean ± SD	Mean of difference	95% CI	*P* value
Fox[a]	35% HRR	113.6 ± 8.2	−0.4	−1.7–1.0	0.600
	40% HRR	118.4 ± 8.0	−5.2	−6.6–−3.9	< 0.001
	45% HRR	123.3 ± 8.3	−10.1	−11.4–−8.7	< 0.001
	55% HR_{max}	96.6 ± 5.8	16.6	14.6–18.6	< 0.001
	60% HR_{max}	105.4 ± 6.4	7.8	5.8–9.8	< 0.001
	65% HR_{max}	114.2 ± 6.9	−1.0	−3.0–1.0	0.326
Miller[b]	35% HRR	114.7 ± 6.8	−1.5	−3.0–0.0	0.051
	40% HRR	119.6 ± 6.5	−6.4	−7.9–−4.9	< 0.001
	45% HRR	124.5 ± 6.4	−11.3	−12.8–−9.9	< 0.001
	55% HR_{max}	98.3 ± 2.8	14.9	12.7–17.1	< 0.001
	60% HR_{max}	107.2 ± 3.1	6.0	3.8–8.1	< 0.001
	65% HR_{max}	116.2 ± 3.3	−3.0	−5.1–−0.8	0.008
Tanaka[c]	35% HRR	114.1 ± 7.3	−0.9	−2.3–0.5	0.200
	40% HRR	119.0 ± 7.1	−5.7	−7.1–−4.4	< 0.001
	45% HRR	123.8 ± 6.9	−10.6	−12.0–−9.2	< 0.001
	55% HR_{max}	97.3 ± 4.1	15.9	13.8–17.9	< 0.001
	60% HR_{max}	106.2 ± 4.5	7.0	5.0–9.1	< 0.001
	65% HR_{max}	115.0 ± 4.8	−1.8	−3.9–0.2	0.075
Measured values (bpm)					
35% HRR		109.5 ± 9.5	3.7	2.3–5.2	< 0.001
40% HRR		113.6 ± 9.6	−0.4	−1.9–1.1	0.576
45% HRR		117.8 ± 9.9	−4.6	−6.1–−3.0	< 0.001
65% HR_{Peak}		106.4 ± 9.2	6.8	4.9–8.8	< 0.001
70% HR_{Peak}		114.6 ± 9.9	−1.4	−3.4–0.7	0.191
75% HR_{Peak}		122.7 ± 10.6	−9.5	−11.7–−7.4	< 0.001

Table 2. Target heart rate values calculated from various maximum heart rate prediction equations and the CPET measurements, as well as the differences between these values and HR_{VT1}. a. Data calculated with the Fox equation; b. data calculated with the Miller equation; c. data calculated with the Tanaka equation. Abbreviations: HRR = heart rate reserve; HR_{max} = maximum heart rate; HR_{Peak} = the maximum heart rate measured in the CPET.

%HRRs (35% and 45%) and the HR_{VT1} (ICC: 0.787, 95% CI 0.659–0.873; and ICC: 0.757, 95% CI 0.619–0.853, respectively) (Table 3). This may indicate the heterogeneity of HR_{VT1} among individuals with MetS.

According to the CPET results in this study, which revealed that patients typically did not reach their predicted HR_{max}, the HR_{Peak} percentages were increased. The results revealed that 70% HR_{Peak} had the smallest statistical difference with the HR_{VT1} (t = −1.328, P = 0.191), while 65% HR_{Peak} was significantly lower than HR_{VT1}, and 75% HR_{Peak} was significantly higher than HR_{VT1} (Table 2). The results of the Bland-Altman agreement test revealed that the mean difference between the 70% HR_{Peak} and HR_{VT1} was −1.358, which was close to the 0th line (SD: ± 7.086; 95% CI −3.416–0.699), with 95% limits of agreement ranging from −15.246 to 12.529 (Fig. 3e), and the ICC was 0.719 (95% CI 0.551–0.832) (Table 4).

Discussion

The cardiopulmonary endurance levels of the patients in this study were lower than those of the MetS population in previous studies and the healthy population[36], with lower VT1 (13.22 ± 1.93 ml/kg/min) and HR_{Peak} (164 ± 14 bpm) values and a higher resting heart rate (80 ± 9 bpm). All the agreement test results indicated that regardless of which HR_{max} prediction equation was used, the 35% HRR had excellent agreement with the HR_{VT1}, whereas the 40% HRR had only moderate agreement and significant differences with the HR_{VT1}. Although the Bland–Altman test indicated good agreement between the 65% HR_{max} (Fox equation) and HR_{VT1}, the ICC analysis showed relatively poor reliability of the %HR_{max} method in practical applications. This is likely due to the inherent mathematical error of the %HR_{max} method[16]. When the intercept correction is not used and the HR_{max} predicted value is used, the higher the HR_{VT1} of an individual is, the lower the HR_{VT1} calculated by a fixed %HR_{max}; the opposite is true for a lower HR_{VT1}. This also explains the asymmetry of the error distribution shown in Fig. 2 in this study, where there are more negative errors at lower HR values and more positive errors at higher HR values. At the macro level, this may be related to the mismatch between HR and workload in incremental exercise, which is caused by poor heart rate dynamics in some patients with MetS[32,42]. In fact, as early as 1978, researchers questioned the method of determining exercise intensity on the basis of the HR_{max} percentage[43]. The HR is a poor VT1 indicator, and it is necessary to use the external load power and other indicators. In a

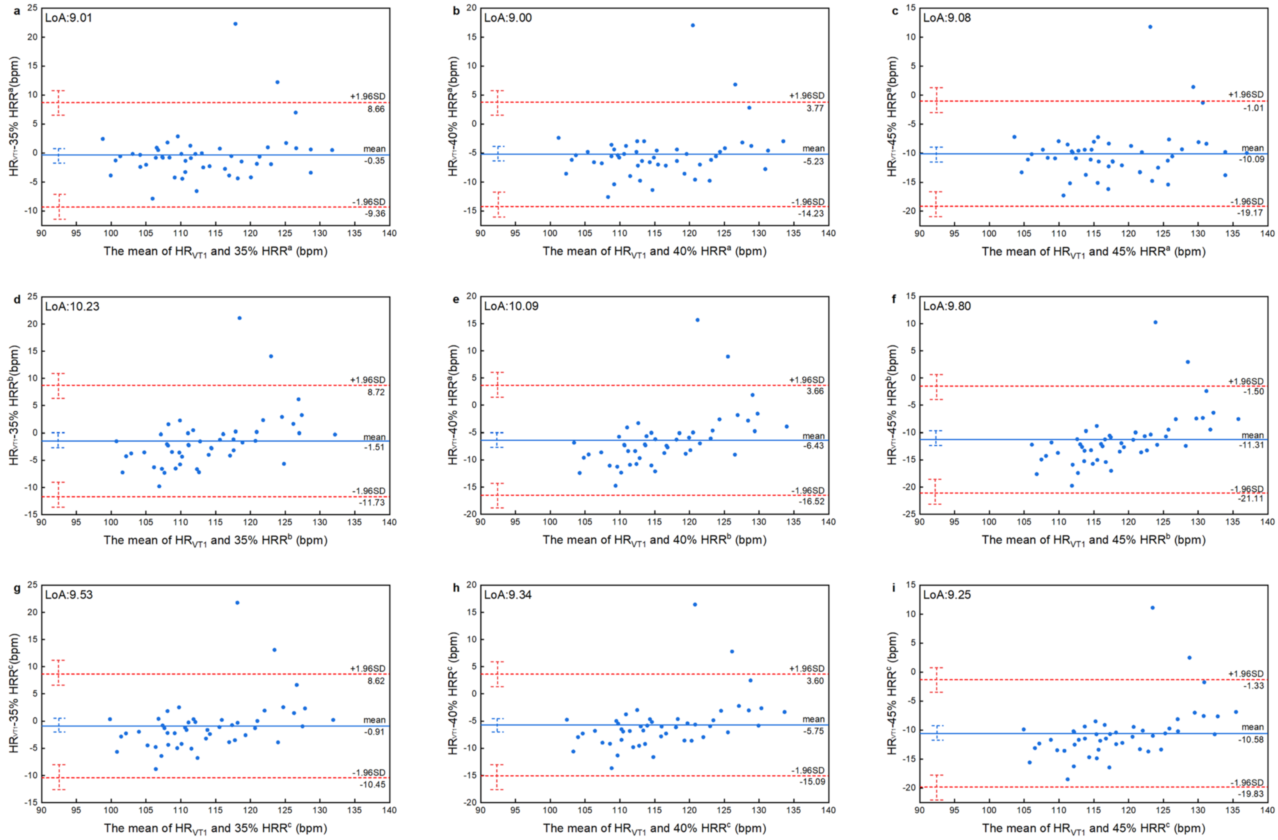

Fig. 1. Bland-Altman agreement tests between the HR_{VT1} and %HRR calculated by the prediction equations. (**a**) Data calculated with the Fox equation; (**b**) data calculated with the Miller equation; (**c**) data calculated with the Tanaka equation. Abbreviations: HRR = heart rate reserve; HR_{VT1} = heart rate of VT1.

			95% Confidence interval		
	Exercise intensity Percentage	**ICC value**	**Lower limit**	**Upper limit**	***P* value**
Fox[a]	35% HRR	0.862**	0.766	0.920	< 0.001
	40% HRR	0.726*	0.573	0.833	< 0.001
	45% HRR	0.504*	− 0.087	0.817	< 0.001
Miller[b]	35% HRR	0.780**	0.636	0.871	< 0.001
	40% HRR	0.597*	0.373	0.755	< 0.001
	45% HRR	0.394	− 0.031	0.707	< 0.001
Tanaka[c]	35% HRR	0.825**	0.709	0.898	< 0.001
	40% HRR	0.669*	0.486	0.797	< 0.001
	45% HRR	0.451	0.024	0.729	< 0.001
CPET[d]	35% HRR	0.787**	0.659	0.873	< 0.001
	40% HRR	0.850**	0.747	0.913	< 0.001
	45% HRR	0.757**	0.619	0.853	< 0.001

Table 3. ICC analysis of the THR determined by the standardized reserve heart rate method and the HR_{VT1} (n = 48). 0.9 > **ICC > 0.75, 0.75 > *ICC > 0.5 a. Data calculated with the Fox equation; b. data calculated with the Miller equation; c. data calculated with the Tanaka equation; d. data calculated with the peak heart rate measured by the CPET. Abbreviation: HRR = heart rate reserve.

recent study, it was also confirmed that the %HRR method performs better than the $\%HR_{max}$ method in terms of measurement quality and agreement with the HR_{VT1}[44].

In the exercise intensity domain, which is divided on the basis of the maximum physiological value percentage, the 35% HRR is in the light intensity zone. When the HR_{max} prediction equations are used, the previous moderate intensity zone of the 40–59% HRR[30] or the 40–69% HRR[25], which is based on the maximum physiological value percentage, results in an increase in the actual exercise intensity for patients with MetS to

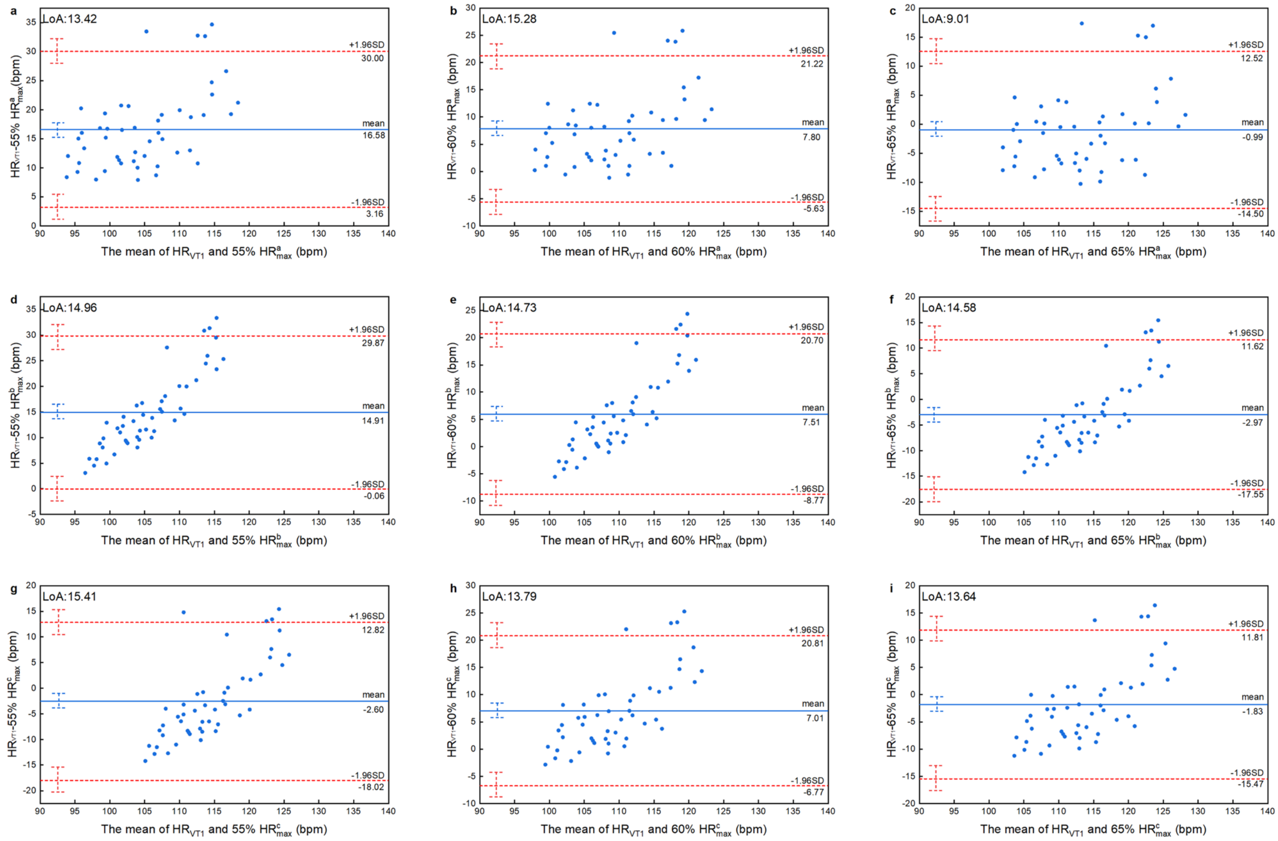

Fig. 2. Bland-Altman agreement tests between the HR_{VT1} and % HR_{max} calculated by the prediction equations. (**a**) Data calculated with the Fox equation; (**b**) data calculated with the Miller equation; (**c**) data calculated with the Tanaka equation. Abbreviations: HR_{max} = maximum heart rate; HR_{VT1} = heart rate of VT1.

			95% Confidence interval		
	Exercise intensity Percentage	ICC value	Lower limit	Upper limit	*P* value
Fox[a]	55% HR_{max}	0.181	−0.065	0.505	< 0.001
	60% HR_{max}	0.421	−0.068	0.712	< 0.001
	65% HR_{max}	0.639*	0.437	0.780	< 0.001
Miller[b]	55% HR_{max}	0.107	−0.070	0.343	0.005
	60% HR_{max}	0.288	−0.022	0.543	0.003
	65% HR_{max}	0.386	0.124	0.599	< 0.001
Tanaka[c]	55% HR_{max}	0.142	−0.068	0.426	< 0.001
	60% HR_{max}	0.357	−0.049	0.638	< 0.001
	65% HR_{max}	0.537*	0.304	0.710	< 0.001
CPET[d]	65% HR_{max}	0.570*	0.359	0.730	< 0.001
	70% HR_{max}	0.719*	0.551	0.832	< 0.001
	75% HR_{max}	0.491	0.216	0.691	< 0.001

Table 4. ICC analysis of the THR determined by the standardized maximum heart rate method and the HR_{VT1} (n = 48). 0.9 > **ICC > 0.75, 0.75 > *ICC > 0.5. a. Data calculated with the Fox equation; b. data calculated with the Miller equation; c. data calculated with the Tanaka equation; d. data calculated with the peak heart rate measured by the CPET. Abbreviation: HR_{max}=maximum heart rate.

levels greater than the VT1. In fact, the guidelines for exercise testing and exercise prescription by the American College of Sports Medicine already recommend that unhealthy people carry out exercise at 30 ~ 39% HRR or VO_2R[30], which is basically consistent with the results of this research. However, when the measured HR_{max} is used, the lowest value in the moderate exercise intensity domain (40% HRR) may still be applicable, whereas the baseline value of the 65% HR_{Peak} may underestimate the HR_{VT1} of patients with MetS. The 70% HR_{Peak} may be a better choice for estimating the HR_{VT1}.

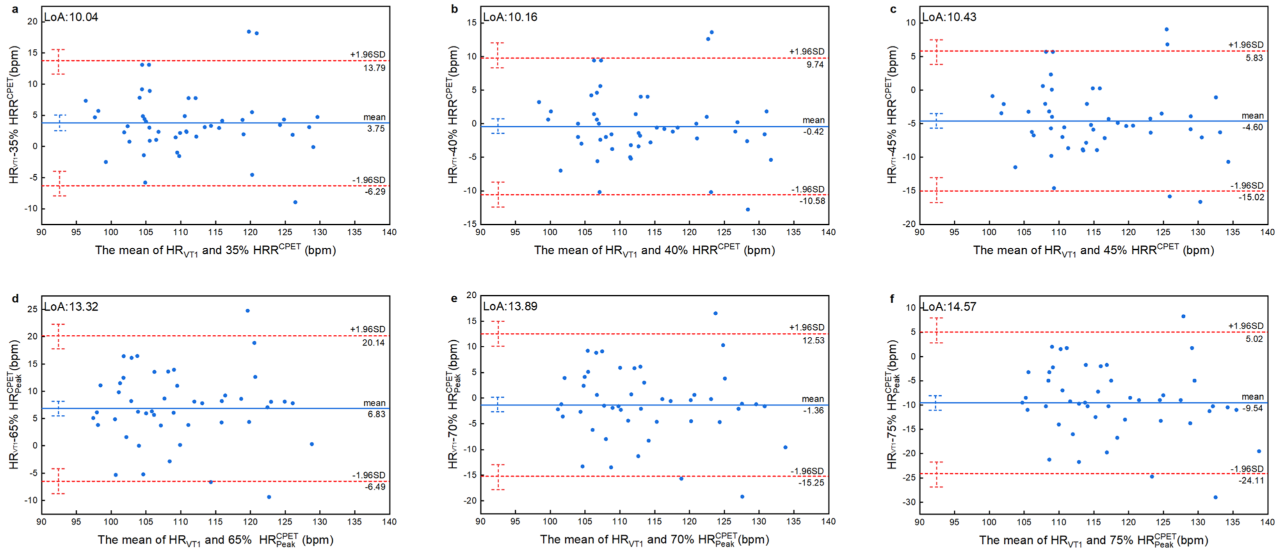

Fig. 3. Bland-Altman agreement tests between HR_{VT1} and THRs calculated from measured heart rate values and standardized methods. Abbreviations: CPET = cardiopulmonary exercise test; HR_{Peak} = actual maximum heart rate measured in the CPET.

The widely promoted and applied Fox equation and Tanaka Eq. [45] were used in this research. Because the average body fat percentage of the participants in this study was greater than 30%, the Miller equation, which is recommended for overweight people with sedentary lifestyles, was also tested[46]. Many improved equations are suitable for different individuals[30], but an HR_{max} prediction equation that is suitable for patients with MetS has yet to be developed. The purpose of this study was not to develop HR_{max} prediction equations. The three HR_{max} prediction equations were used only to test the corresponding standardized exercise intensity in the VT1 exercise intensity domain in patients with MetS. Compared with the other two HR_{max} prediction equations, the 35% HRR (113.56 ± 8.20) values calculated by the Fox equation showed the highest agreement with the $HR_{VT1,}$ which might be due to the average age of the participants in this study being 40–50 years[47]. Additionally, the HR_{max} predicted by the Fox equation decreases rapidly with increasing age, so it can be underestimated in healthy individuals[48]; however, it might conform to the situation where the HR_{max} of patients with MetS is generally lower than in healthy populations.

There are significant differences in physiological responses among individuals during exercise, and even with the use of measured values, this difference still exists. This once again indicates that an objective physical exercise ability assessment for patients with MetS is necessary for developing personalized exercise prescriptions[49]. We believe that even in situations where gas exchange analysis is not available, it is still necessary for patients to perform a treadmill exercise test (or other ergometric test) to obtain a measured HR_{max} value for calculating the optimal exercise intensity. Although this study included a standardized exercise domain with high agreement with the VT1, it should serve only as a reference when the CPET cannot be obtained, and it should be the minimum exercise intensity for patients with MetS undergoing rehabilitation. In practical applications, subjective methods of setting the exercise intensity, such as the talk test and Borg scale, should be used to continuously adjust the exercise prescriptions to meet the needs of patients[16].

Limitations

The limitations of this research include the small sample size and wide age range. Future studies should validate our findings by expanding the sample size with a detailed differentiation by age group and sex. Owing to the limited sample size, we did not conduct any subgroup analyses with patients with MetS as the reference. We excluded patients with MetS who were using drugs that could impact their heart rate, which may limit the applicability of the results. In addition, no equations for predicting the HR_{max} of the MetS population were developed in this study, and only the Fox equation was used as a substitute.

Perspective

The first ventilatory threshold is the baseline for moderate-intensity continuous exercise, and most exercise prescriptions require a gradual increase in exercise intensity and volume in practical applications. Our study provides a way to approximate the VT1 in the CPET in patients with metabolic syndrome using traditional exercise intensity determination methods. Without CPET equipment and related technical operators, patients with MetS can start effective and safe endurance training in this exercise intensity domain on the basis of our results, and guardians should use subjective methods for monitoring the exercise intensity at any time. The consistency between the exercise intensity determined by the 35% HRR calculated by the Fox equation and the exercise intensity determined by the VT1 in the practical application of exercise prescriptions for improving cardiovascular risk factors and cardiovascular fitness in patients with MetS needs to be verified. By verifying the consistency of the two methods for determining the exercise intensity in practical applications, it may be possible to further refine the percentage of the HRR corresponding to VT1, which is suitable for patients with MetS. In addition, an HR_{max} prediction equation suitable for adult patients with MetS needs to be developed, and given the heterogeneity of the MetS clinical cohort, individuals using β-blockers should be evaluated separately from those who do not[50].

Conclusion

In the field of clinical rehabilitation medicine, the method of prescribing exercise intensity based on the percentage of maximum physiological values has been gradually replaced by a method based on thresholds; however, when guiding patients with MetS to exercise without obtaining CPET, it is still necessary to use the 35% HRR standardization method combined with the Fox equation to estimate the HR_{VT1} or to use the 40% HRR and 70% HR_{Peak} when the measured HR_{max} can be obtained, but gas exchange analysis cannot be performed.

Data availability

The data that support the findings of this study are available from the authors（Both the first author or corresponding author can be contacted to obtain the data for this study） but restrictions apply to the availability of these data, which were used under license from the Peking University First Hospital Taiyuan Hospital ethics committee for the current study, and so are not publicly available. Data are, however, available from the authors upon reasonable request and with permission from the Centre for Heart Rehabilitation at the Peking University First Hospital Taiyuan Hospital.

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Author contributions
LRJ designed the research, collected the data and wrote the paper. QJM participated in the research proposition, method construction and data analysis revision. WF was involved in the data collection. XWZ and ZHH helped to enroll people in the study and to revise the data analysis. All the authors have read and approved the final version of the paper and agreed to the presentation sequence.

Declarations

Competing interest
The authors declare no competing interests.

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