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Old and new equations for maximal and anaerobic threshold heart rate prediction in coronary heart disease in Chinese population

Leilei Wang^{1†}, Zihao Huang^{2†}, Luxia Gao¹, Xi Chen¹, Deming Deng¹, Meiming Lin^{1*} and Xiuyu Leng^{3*}

Abstract

Background The prediction of maximal heart rate (MHR) and anaerobic threshold heart rate (HRAT) in patients with coronary heart disease (CHD), particularly among the Chinese population, remains a significant challenge. Existing equations for MHR prediction are primarily designed for healthy individuals not on medication for optimized β -blocker (BB) therapy, showing limited efficacy for individuals on various drug regimens. Moreover, the prediction of HRAT lacks established formulas. This study aims to develop equations for MHR and HRAT, assess the accuracy of historical MHR formulas, and examine their correlation with HR measurements at the anaerobic threshold (AT).

Methods Among 2021 to 2023, 170 CHD patients were recruited. Patients were categorized into groups based on BB usage. BB dose was transformed into carvedilol dose. Multiple linear stepwise regression analysis was employed to identify predictors of MHR and HRAT, incorporating key patient variables according to prior studies (age, sex, height, weight, carvedilol dose, HRrest). The mean absolute percentage errors (MAPEs) were calculated and compared among abovementioned MHR and HRAT prediction formulas. Besides, the percentages of MHR in predicting HRAT among different formulas were calculated.

Results For the patients with BB medication, the simplified equations derived for MHR and HRAT were $176 - 1.2 * \text{age} + 0.7 * \text{HRrest} - 0.4 * \text{weight}$ and $98 - 0.6 * \text{age} + 0.7 * \text{HRrest} - 0.3 * \text{weight}$, respectively. For those without BB medication, the derived equations for MHR and HRAT were $200 - 1.1 * \text{age}$ and $91 - 0.5 * \text{age} + 0.5 * \text{HRrest}$, respectively. There are significant differences between the results predicted by the new formula and the prior formulas. The new formulas are helpful for predicting the MHR of patients during exercise more accurately and guiding exercise training more scientifically.

Conclusions The new equations for estimating MHR and HRAT in CHD patients enhance the accuracy of prior formulas. Given the BB impact on sympathetic nerve activity, the predictive formulas for MHR and HRAT were significantly improved.

Keywords Heart rate prediction formulas, Cardiac rehabilitation, Chinese/East Asian population, Coronary heart disease, Cardiopulmonary exercise test, β -blocker

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Background

In 2019, cardiovascular diseases (CVD) accounted for 32% of global mortality, culminating in approximately 17.9 million deaths worldwide [1]. In China, the prevalence of CVD reached an alarming 330 million cases, including 11.39 million instances of coronary heart disease (CHD), which contributed to over one million deaths annually [2]. To mitigate the mortality and hospitalization risks associated with CHD, the 2021 European Society of Cardiology (ESC) guidelines advocated individuals with CHD to participate in 75–150 min of exercise weekly in moderate-to-vigorous intensity [3]. Physiologically, the determination of exercise intensity hinges on two critical metrics: the maximum heart rate (MHR) and the anaerobic threshold heart rate (HRAT). Consequently, assessing MHR and HRAT is pivotal in devising tailored exercise protocols for individuals with CHD.

Currently, the measurement of MHR and HRAT predominantly relies on cardiopulmonary exercise test (CPET) which may be time-consuming and less accessible for the individuals. These limitations underscore the clinical importance of predicting MHR and HRAT based on individual characteristics. Existing prediction models, such as the FOX [4], Tanaka [5], and Fairbairn [6] equations, estimate MHR primarily through age. However, these formulas were developed based on data from healthy, medication-free individuals and have shown limited efficacy in the context of exercise-based cardiac rehabilitation. The formulas proposed by Keteyian et al. [7] and Damiano et al. [8] for heart failure (HF) patients under β -blocker (BB) treatment do not encompass the East Asian demographic. To date, CHD is considered a prior stage of HF, but predicting MHR for individuals with CHD was still understudied, especially in East Asian population. Furthermore, HRAT is commonly estimated as a percentage of the predicted MHR, a method that potentially amplifies the margin of error in HRAT prediction.

Therefore, this study was to develop equations for predicting MHR and HRAT among individuals with CHD in East Asian population and compare the accuracy of the new formulas against the existing models in predicting MHR and HRAT.

Methods

Study population

We retrospectively analyzed a total of 210 patients with CHD of Cardiac Rehabilitation Department of First Affiliated Hospital of Sun Yat-sen University in our study from 2022.01 to 2023.08. The inclusion criteria were: (1) confirmed diagnosis of CHD by coronary computed tomography angiography (CTA) or coronary

arteriography (CAG) whatever the treatment of percutaneous coronary intervention, (2) age not younger than 40 years old with no limit of gender, (3) NYHA class I-III, (4) optimal medical therapy recommended by guidelines, (5) CPET with ergometer. Exclusion criteria included, (1) complication with sick sinus syndrome or II-degree or higher atrioventricular block or uncontrolled arrhythmia, (2) scheduled preoperative assessment for left ventricular assisted device implantation or surgery, (3) peak respiratory exchange ratio (RER) <1.1 , (4) unidentified HRAT, (5) other drugs (e.g. ivabradine, digoxin) affecting HR. 170 people met the above criteria. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and was approved by the Medical Ethical Committee of Clinical Research and Animal Trials of the First Affiliated Hospital of Sun Yat-sen University. (Application ID: [2023]004).

β -blockers medication

According to the intake of BB, those who met the criteria above were divided into two groups: with BB group and without BB group regardless of age, sex and complications. To avoid the possible heterogeneous outcomes because of different types of BB, the doses were converted to an equivalent dose of carvedilol. The daily dosages in those who took atenolol, metoprolol, or metoprolol sustained release tablets were divided by four, whereas the doses for bisoprolol were multiplied by five [9].

Cardiopulmonary exercise testing

A maximal, symptom-limited CPET was performed on an ergometer (Ergoline) with a facemask (COSMED K4B2, Italy) collecting and measuring the cardiopulmonary metabolic variables breath by breath. A personalized Raise, Activate, Mobilise, Potentiate (Ramp) exercise protocol was chosen, aiming at a test duration of 10 ± 2 min [10, 11]. For patients with $RER \geq 1.1$ included in our study, the exercise duration was not regarded as an exclusion criterion.

The scheme of CPET included four phases: (1) resting for 1 min to relieve the patient's tension; (2) warming up for 3 min with load-free cycling (no resistance on the pedals); (3) exercising for 5–12 min with increasing resistance of 8–25 W/min increment on the pedals until maximal exertion or symptom limitation; (4) recovering for 6 min which included a load-free cycling for the first 3 min and sitting still for the rest 3 min [12].

A 12-lead electrocardiogram (ECG), heart rate (HR), and blood pressure (BP) were also recorded. Exercise duration, peak oxygen uptake (VO_{2peak}), oxygen uptake at anaerobic threshold (VO_{2AT}), oxygen uptake at rest (VO_{2rest}), metabolic equivalent (METs), RER and other indicators were calculated. AT was determined using

the V-slope method by an advanced cardiologist with over 10-year working experience [13, 14].

Classification of the exercise-induced HR response

Baseline HR (HR_{rest}), peak HR (HR_{peak}), and HRAT were collected during CPETs. HR_{rest} was measured at 1 min sitting on the ergometer after a 15-minute rest. Different MHR predicting formulas were included in the study. HR_{peak} were analyzed as the percentage of MHR based on different formulas as followed:

$$\%MHR, \text{ FOX} = \left[\text{HR}_{\text{peak}} / (220 - \text{age}) \right] \times 100$$

$$\%MHR, \text{ TANAKA} = \left[\text{HR}_{\text{peak}} / (208 - 0.7 * \text{age}) \right] \times 100$$

$$\%MHR, \text{ FAIRBARN} = \left[\text{HR}_{\text{peak}} / (201 - 0.63 * \text{age}) \right] \times 100$$

$$\%MHR, \text{ KETEYIAN} = \left[\text{HR}_{\text{peak}} / (114 + 0.5 * \text{HR}_{\text{rest}} - 0.5 * \text{age}) \right] \times 100$$

Statistical analysis

The Shapiro–Wilk test was used to test normality. Comparisons were conducted according to BB medication (with BB and without BB groups). Unless otherwise indicated, all continuous variables were expressed as mean ± standard deviation (SD), and compared by the independent t-test. Data with skewed distribution were given as median and interquartile range, and compared by Mann-Whitney U test. Categorical variables were expressed in numbers and percentages, and compared by Chi-square test.

Pearson correlation was employed to assess the correlation between variables. Multiple linear stepwise regression analysis was performed to evaluate the predictors for MHR and HRAT by including the main variables of the patients (age, gender, height, weight, carvedilol dose, HR_{rest}). The higher correlation variables ($P < 0.05$) and their coefficients were obtained to fit the possible predicting formula. All independent variables included in the new MHR and HRAT predicting formula had a partial $R^2 \geq 0.01$. A Subgroup analysis was conducted by stratifying NYHA class.

The mean absolute percentage errors (MAPEs) = (average absolute percent error for each time period – actual values) / actual values were calculated and compared among abovementioned MHR and HRAT prediction formulas. Besides, the percentages of MHR in predicting HRAT among different formulas were calculated.

Statistical analyses were performed using IBM SPSS 19.0 and R v4.2.3 [9].

Results

Demographic and clinical characteristics

The baseline clinical patients' characteristics were shown in Table 1. A total of 170 CHD who completed CPET were enrolled, including 145 (85.3%) males, mean (SD) aged at 57.6 (9.2) years. Compared to the non-BB group, patients in the BB group had lower HR_{rest} (71.7 versus 78.3 bpm), lower HR_{peak} (122.9 versus 140.3 bpm), lower VO_{2peak} (17.0 versus 19.2), shorter exercise duration (386.7 versus 425.2) seconds and higher proportion of hypertension of (26.2% versus 17.9%). No significant differences were observed between BB and non-BB groups in other variables.

In another way, statistical analysis with basic characteristics stratified by NYHA status was conducted (Table S1). Compared to the NYHA I group, patients in NYHA II/III group were older, had lower HR_{rest}, lower HRAT, lower HR_{peak}, lower VO_{2peak}, lower exercise capacity, shorter exercise duration seconds and higher proportion of BB.

For BB group, the independent influencing factors of MHR and HRAT are all including age, HR_{rest} and weight. The new formula for MHR was $176 - 1.2 * \text{age} + 0.7 * \text{HR}_{\text{rest}} - 0.4 * \text{weight}$. And the new formula for HRAT was $98 - 0.6 * \text{age} + 0.7 * \text{HR}_{\text{rest}} - 0.3 * \text{weight}$ (Table 2).

The MAPEs of new MHR and HRAT formulas are 9.4% and 7.3% respectively. Compared with the Fox/Tanaka/Fairbarn formulas, the new MHR formula showed a significantly lower MAPE. And it showed an approximate equality performance with the Keteyian formula (9.4 vs. 8.7). The new HRAT formula showed a satisfactory effect with the MAPE of 7.3% (Table 3).

Similar predictive values for MHR and HRAT were observed when stratifying the individuals by NYHA. HR_{peak} and HRAT in the test are expressed as percentages of MHR according different equations. For HR_{peak}, the new MHR formula all show nearly 20% higher %MHR compared with the Fox/Tanaka/Fairbarn formulas respectively, and a little lower %MHR compared with the Keteyian formula (95.6 vs. 101.6). The same result could be observed for HRAT (Fig. 1A / Table S3).

Figure 1A is for BB group. For HRAT, %MHRs are respectively 57.0%, 55.1%, 56.1% and 76.3% to the Fox/Tanaka/Fairbarn/Keteyian formulas and 71.8% for the new formula. For HR_{peak}, %MHRs are respectively 75.9%, 73.4%, 74.7% and 101.6% to the Fox/Tanaka/Fairbarn/Keteyian formulas and 95.6% to the new formula.

Figure 1B is for Non-BB group. For HRAT, %MHRs are respectively 62.4%, 60.5%, 61.6% and 81.6% to the

Table 1 Basic characteristics of the study population, M (SD)

	Overall, n = 170	BB, n = 103	Non-BB, n = 67	P-value
Age, years	57.6 (9.2)	58.3 (8.7)	56.5 (9.8)	0.231
Male (%)	145(85.3)	91 (88.3)	55 (82.1)	0.380
Height, cm	167.3 (6.6)	166.9 (6.8)	167.8 (6.3)	0.420
Weight, kg	68.9 (6.6)	69.3 (11.9)	68.2 (8.2)	0.525
BMI, kg/m ²	24.5 (2.9)	24.7 (3.2)	24.2 (2.4)	0.248
SBP rest, mmHg	111.6 (16.3)	109.1 (16.1)	115.4 (16.1)	0.014
DBP rest, mmHg	70.6 (10.1)	68.6 (9.5)	73.7 (10.3)	0.001
HRrest, bpm	74.3 (10.7)	71.7 (10.8)	78.3 (9.3)	<0.001
HRAT, bpm	96.1 (13.3)	92.3 (12.6)	101.9 (7.7)	<0.001
HRpeak, bpm	129.8 (19.6)	122.9 (17.8)	140.3 (17.6)	<0.001
VO ₂ AT, ml/min/kg	11.5 (3.0)	11.2 (2.9)	12.0 (3.1)	0.079
VO ₂ peak, ml/min/kg	17.8 (4.0)	17.0 (3.6)	19.2 (4.3)	<0.001
Metabolic equivalent, MET	5.1 (1.2)	4.8 (1.1)	5.5 (1.2)	<0.001
Duration, s	401.7 (84.5)	386.7 (74.6)	425.2 (93.8)	0.004
RER	1.2 (0.10)	1.2 (0.08)	1.2 (0.12)	0.108
Carvedilol dose equivalent, mg, MD [IQR]	6.25 [0-12.5]	12.5 [6.25-12.50]	0 [0]	<0.001
Diabetes mellitus, n (%)	25 (14.7)	16 (15.5)	9 (13.4)	0.826
Hypertension, n (%)	39 (22.9)	27 (26.2)	12 (17.9)	0.263
NYHA, n (%)				0.001
I	147 (86.5)	82 (79.6)	65 (97.0)	
II/III	23 (13.5)	21 (20.4)	2 (3.0)	

BMI Body mass index, *SBP rest* Systolic blood pressure at rest, *DBP rest* Diastolic blood pressure at rest, *HRrest* Heart rate at rest, *HRAT* Heart rate at anaerobic threshold, *HRpeak* Heart rate at peak exercise, *VO₂AT* Oxygen uptake at anaerobic threshold, *VO₂peak* Peak oxygen uptake, *MET* Metabolic equivalent, *RER* Respiratory exchange ratio, *BB* β -blocker, *NYHA* New York Heart Association

Table 2 Main clinical variables independently associated at HRpeak and HRAT in the patients stratified by BB medication

	With BB			Without BB		
	Beta	P values	Partial R ²	Beta	P values	Partial R ²
HRpeak						
Intercept	175.67	<0.001		200.12	<0.001	
Age	-1.24	<0.001	0.332	-1.06	<0.001	0.349
Weight	-0.39	0.003	0.088	-	-	-
HR _{rest}	0.65	<0.001	0.228	-	-	-
HRAT						
Intercept	97.91			91.38	<0.001	
Age	-0.60	<0.001	0.193	-0.48	0.001	0.168
Weight	-0.27	0.004	0.083	-	-	-
HRrest	0.67	<0.001	0.389	0.48	0.001	0.156

BB β -blocker, *HRpeak* Heart rate at peak exercise, *HRrest* Heart rate at rest, *HRAT* Heart rate at anaerobic threshold

Fox/Tanaka/Fairbarn/Keteyian formulas and 74.1% for the new formula. For HRpeak, %MHRs are respectively 85.8%, 83.2%, 74.7% and 112.4% to the Fox/Tanaka/Fairbarn/Keteyian formulas and 101.9% to the new formula.

The new formula also shows a 15% higher cut-off value to identify AT intensity domain than the Fox/Tanaka/Fairbarn formulas and a 5% lower cut-off value than the Keteyian formula (Table 4).

For non-BB group, the independent influencing factor of MHR only includes age. And the new formula of

Table 3 Historical and new equations for estimating MHR and new equations for estimating HRAT and related accuracy data for patients with BB

Formula	Equations	R ²	SSE, bpm	MAPE, %		
				Overall	NYHA I	NYHA II/III
MHR, Historical equations						
FOX	220–age	0.303	14.83	33.8	32.2	40.2
TANAKA	208–0.7*age	0.303	14.83	38.5	36.5	46.3
Fairbarn	201–0.63*age	0.303	14.83	36.1	34.1	44.0
KETEVIAN	114 + (0.5*HRrest) – (0.5*age)	0.437	13.32	8.7	8.5	9.2
MHR and HRAT New equation						
MHR	176 – 1.2*age + 0.7*HRrest – 0.4*weight	0.495	12.62	9.4	9.1	10.3
HRAT	98 – 0.6*age + 0.7*HRrest – 0.3*weight	0.510	8.80	7.3	10.5	6.9

MHR Maximal heart rate, HRAT Heart rate at anaerobic threshold, HRrest Heart rate at rest, BB β-blocker

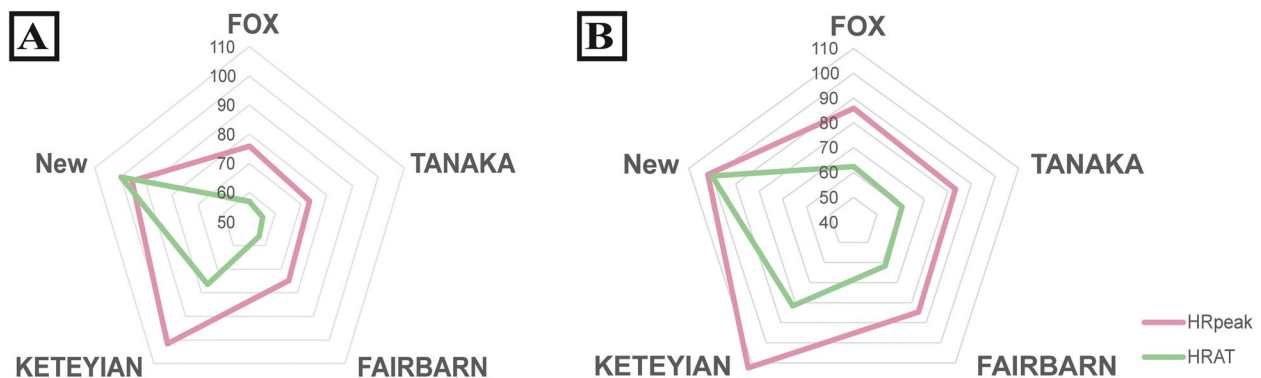


Fig. 1 HRpeak and HRAT are expressed as percentages of MHR

Table 4 Possible cut-off values to identify the AT intensity domain and related accuracy data, with BB

Formula	Percentage	MAPE, %		
		Overall	NYHA grade I	NYHA grade II/III
FOX	55%	13.3	13.5	12.5
	60%	9.7	9.8	9.6
	65%	11.3	11.3	11.4
TANAKA	55%	11.5	11.8	10.4
	60%	9.7	9.8	9.3
	65%	13.6	13.3	14.7
Fairbarn	55%	12.3	12.7	11.0
	60%	9.6	9.7	9.1
	65%	12.5	12.3	13.2
KETEVIAN	75%	9.8	9.9	9.3
	80%	7.7	7.7	7.9
	85%	9.6	9.7	9.4
New formula	70%	10.6	10.5	11.0
	75%	7.9	7.7	8.6
	80%	9.1	9.1	9.0

AT Anaerobic threshold, BB β-blocker

MHR was $200 - 1.1 \cdot \text{age}$. Whereas for HRAT, despite age, HRrest is another influence factor. The new formula for HRAT was $91 - 0.5 \cdot \text{age} + 0.5 \cdot \text{HRrest}$ (Table 2). The MAPEs of new MHR and HRAT formulas are 8.2% and 7.6% respectively. Compared with the Fox/Tanaka/Fairbarn formulas, the new MHR formula showed a significantly lower MAPE. And it also showed a much lower MAPE compared with the Keteyian formula (8.2 vs. 12.5). The new HRAT formula showed a satisfactory effect with the MAPR of 7.6% (Table S2). Also in non-BB group, HRpeak and HRAT in the test are expressed as percentages of MHR according to different equations. For HRpeak, the new MHR formula shows 16.1%, 18.7% and 17.2% higher %MHR compared with the Fox/Tanaka/Fairbarn formulas respectively and show a more satisfactory %MHR compared with the Keteyian formula (101.9 vs. 112.4). For HRAT, the new MHR formula shows 11.7%, 13.6% and 12.5% higher %MHR compared with the Fox/Tanaka/Fairbarn formulas respectively, and shows 7.5% lower %MHR compared with the Keteyian formula. The new HRAT formula shows a satisfactory %HRAT of 100.1% (Fig. 1B / Table S4). The new formula

also shows a 15% higher cut-off value to identify the anaerobic threshold (AT) intensity domain than the Fox/Tanaka/Fairbairn formulas and a 5% lower cut-off value than the Keteyian formula (Table S5).

Discussion

This study was a retrospective study on MHR and HRAT predicting for CHD patients. For the patients with BB, the main influencing factors of MHR include age, HRrest and weight, whereas for those without BB, the influencing factor of MHR only include age. For the subgroup analysis of NYHA grade, no new formula was established for the small sample size. The MHR and HRAT formulas established in the present study may be more accuracy than prior formula which included weight only.

Demographic characteristics displayed variation among different ethnicities (i.e., height, weight, heart rate recovery and body mass index) [15–17]. Most studies recruited Americans or Europeans for developing and/or validating MHR formulas, so developed universal formulas may be difficult to predict the MHR in Asians [18]. Park et al., cross validated MHR prediction formulas among healthy Koreans of 7–55 years old and found that there were significant differences between the formula predicted age and the actual MHR [18]. There is a lack of research on East Asian population especially in CHD.

Recent research has challenged traditional views of heart rate dynamics during incremental exercise by revealing that the heart rate performance curve (HRPC) is non-linear and non-uniform [19]. This finding underscores the importance of considering HRPC deflection when setting %MHR targets for exercise prescription [19]. The progression of HR with increasing exercise intensity is best described as an S-shaped curve, a concept previously introduced by Brooke and Hamley [20]. The formula proposed by Fox et al. in 1971, $HR_{max} = 220 - \text{age}$, remains the most prevalently utilized method for predicting MHR. However, this equation has been critiqued for its broad standard deviation, and for its tendency to overestimate MHR in younger adults while underestimating it in older individuals [5, 21, 22]. Alternative formulas, such as those by Tanaka et al. and Fairbairn et al., have demonstrated similar levels of accuracy. Both FOX and Tanaka formulas tended to overestimate the MHR for males and females over 15 years old, and the two universal equations were not suitable to predict the MHR of Koreans except for children aged from 7 to 14 [18]. Yet, these models were primarily developed from data involving healthy, non-medicated individuals and exhibit limited applicability for patients in exercise-based cardiac rehabilitation, particularly those on BB medication. Existing formulas, including those tailored for HF patients on BB by Keteyian et al. and Damiano

et al., also do not accommodate the East Asian demographics, highlighting a significant gap in current HR prediction models.

Our study highlights the relationship between MHR, HRAT, age, body weight, and HRrest in CHD patients, with a distinction between those with BB and those without. For CHD patients with BB, MHR and HRAT correlate with age, HRrest, and weight, suggesting the effects of BB dosage may be indirectly accounted for by these variables. Conversely, for those without BB, MHR is only age-dependent, while HRAT also depends on HRrest. This indicates the need for personalized HR predictions in CHD patients, emphasizing the interplay between medication and physiological factors in exercise prescription. Our findings advocate for a nuanced approach to cardiac rehabilitation, underscoring the differential impact of BB therapy on HR predictions.

The specific mechanisms for the result were understudied. Studies have shown that intrinsic pacemaker rate declines linearly from birth at a rate of ~ 0.8 bpm/year in humans and ~ 4 bpm/month in mice [23]. The slowdown of the intrinsic pacemaker rate is the main cause for the accompanying decline in MHR, playing a significant role in the loss of aerobic capacity in older adults [24]. This is consistent with the negative correlation of age. HRAT was related to HRrest which may be explained by the relationship between sympathetic and parasympathetic nervous systems [25]. For CHD patients without BB, HRrest is generally low and sympathetic nerves are at a relatively low level. As exercise increases, sympathetic nerves activate and parasympathetic nerves are suppressed, resulting in increased HR. At AT, the relationship between sympathetic and parasympathetic nerves is shown as HRAT, and the cardiopulmonary function reflects the aerobic exercise capacity of the body. HRrest represents the role of parasympathetic nerve at AT in the HRAT formula. As exercise continues, the sympathetic nerves activate to the top at which HR is almost entirely influenced by the sympathetic nerves, resulting in the MHR formula being only age-dependent. For CHD patients with BB, their HRrest was usually higher than those without BB, which indirectly implied that the sympathetic nerves in this group were relatively higher than the without BB group. The inhibitory effect of BB on sympathetic nerves was reflected in the difference between HRrest and basal HR, which was directly related to drug dose. And due to the fat-solubility characteristics of the drug, the individual effect of BB was related to individual body weight. The effects of BB dosage on HR during exercise are indirectly accounted for by HRrest and weight. Because of the effect of BB on sympathetic nerves [26], the MHR during exercise is also suppressed

to varying degrees. The MHR of the patients with BB was not only related to age, but also related to resting HR and body weight.

This study has remarkable clinical implications:

Firstly, the HRAT and MHR prediction formula may be used more scientifically and accurately in clinical work in Chinese population.

Secondly, exercise prescriptions for CHD patients in future clinical trials on remote or home-based cardiac rehabilitation may refer to the present formulas, which may ultimately guiding optimal exercise training in a more effective way.

In addition, the prediction formulas were separately provided according to whether patients were under BB medication or not to help patients or medical staff individualize exercise HR.

This study has several strengths including the subjects of East Asian and subgroup analyses according to whether they were taking BB or not which may indicate more accurate of the formulas.

Nevertheless, there are also some limitations in this study:

Firstly, the study is a single-center retrospective study with a small sample size. The generalization of the results is limited for the lack of external verification.

Secondly, the CHD patients included in this study were able to finish CPET with RER not less than 1.1. As such, the study's conclusions may not apply to CHD patients with multiple comorbidities, a bedridden status, or a poor exercise capacity who cannot tolerate the exercise with RER over 1.1.

Thirdly, this study is an observational study, and the included variables refer to previous studies. Some unknown confounders may be unadjusted.

Finally, this study only examined the MHR and HRAT using cycling, which may limit the generalization of the formula to treadmill-based CPET. However, previous meta-analysis reported a non-significant difference of age-predicted MHR by treadmill compared to cycling ergometers [6].

Conclusions

Among individuals with CHD, the maximum heart rates were lower than estimated due to the disease nature and medications. BB could reduce the HR by inhibiting sympathetic activity. The MHR and HRAT could be estimated by comprehensively considering the indicators including age, HR_{rest}, weight and the BB blockers. This may promote the effectiveness in the clinical practice of cardiac rehabilitation.

Abbreviations

MHR	Maximal heart rate
HRAT	Anaerobic threshold heart rate
CHD	Coronary heart disease
AT	Anaerobic threshold
RER	Respiratory exchange ratio
MAPEs	the mean absolute percentage errors
CVD	Cardiovascular diseases
ESC	European Society of Cardiology
CPET	Cardiopulmonary exercise test
BB	β-blockers
HF	Heart failure
CTA	Computed tomography angiography
CAG	Coronary arteriography
ECG	Electrocardiogram
HR	Heart rate
BP	Blood pressure
VO ₂ peak	Peak oxygen uptake
VO ₂ AT	Oxygen uptake at anaerobic threshold
VO ₂ rest	Oxygen uptake at rest
METs	Metabolic equivalent
RER	Respiratory exchange rate
HRPC	Heart rate performance curve

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12872-024-04307-x>.

Supplementary Material 1.

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Authors' contributions

LL, LX and XC contributed to the data collation. LL, ZH, DM contributed to the analysis and interpretation of data for the work. ZH, MM and XY contributed to the design of the paper. LL and ZH drafted the manuscript. MM and XY critically revised the manuscript. All authors reviewed the manuscript. All gave final approval and agreed to be accountable for all aspects of work ensuring integrity and accuracy.

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Data availability

Data could be shared by reasonable request to the corresponding authors.

Declarations

Ethics approval and consent to participate

The data in this research was medical record data and informed consent was not required. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and was approved by the Medical Ethical Committee of Clinical Research and Animal Trials of the First Affiliated Hospital of Sun Yat-sen University. (Application ID: [2023]004).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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References

- World health statistics 2021: monitoring health for the SDGs, sustainable development goals. Geneva: World Health Organization; 2021. Licence: CC BY-NC-SA 3.0 IGO.
- Writing committee of the report on cardiovascular health and diseases in china. Report on Cardiovascular Health and Diseases in China 2021: An Updated Summary. *Biomed Environ Sci*. 2022;35(7):573–603. doi: 10.3967/bes2022.079. PMID: 35945174.
- Pelliccia A, Sharma S, Gati S, Bäck M, Börjesson M, Caselli S, ESC Scientific Document Group. 2020 ESC Guidelines on sports cardiology and exercise in patients with cardiovascular disease. *Eur Heart J*. 2021;42(1):17–96. <https://doi.org/10.1093/eurheartj/ehaa605>. Erratum in: *Eur Heart J*. 2021;42(5):548–549. PMID: 32860412.
- Fox SM 3rd, Naughton JP, Haskell WL. Physical activity and the prevention of coronary heart disease. *Ann Clin Res*. 1971;3(6):404–32.
- Tanaka H, Monahan KD, Seals DR. Age-predicted maximal heart rate revisited. *J Am Coll Cardiol*. 2001;37:153–6.
- Fairbairn MS, Blackie SP, McElvaney NG, Wiggins BR, Paré PD, Pardy RL. Prediction of heart rate and oxygen uptake during incremental and maximal exercise in healthy adults. *Chest*. 1994;105(5):1365–9.
- Kezeyian SJ, Kitzman D, Zannad F, Landzberg J, Arnold JM, Brubaker P, et al. Predicting maximal HR in heart failure patients on β -blockade therapy. *Med Sci Sports Exerc*. 2012;44(3):371–6. <https://doi.org/10.1249/MSS.0b013e318234316f>. PMID: 21900844; PMCID: PMC3755356.
- Magri D, Piepoli M, Gallo G, Corrà U, Metra M, Paolillo S, et al. Old and new equations for maximal heart rate prediction in patients with heart failure and reduced ejection fraction on beta-blockers treatment: results from the MECKI score data set. *Eur J Prev Cardiol*. 2022;29(12):1680–8. <https://doi.org/10.1093/eurjpc/zwac099>. Erratum in: *Eur J Prev Cardiol*. 2023 Dec 22; PMID: 35578814.
- Paolillo S, Mapelli M, Bonomi A, Corrà U, Piepoli M, Veglia F, et al. Prognostic role of β -blocker selectivity and dosage regimens in heart failure patients. Insights from the MECKI score database. *Eur J Heart Fail*. 2017;19(7):904–14. <https://doi.org/10.1002/ehf.775>. Epub 2017 Feb 24. PMID: 28233458.
- Agostoni P, Dumitrescu D. How to perform and report a cardiopulmonary exercise test in patients with chronic heart failure. *Int J Cardiol*. 2019;288:107–13. <https://doi.org/10.1016/j.ijcard.2019.04.053>. Epub 2019 Apr 18. PMID: 31047701.
- Task Force of the Italian Working Group on Cardiac Rehabilitation Prevention; Working Group on Cardiac Rehabilitation and Exercise Physiology of the European Society of Cardiology; Piepoli MF, Corrà U, Agostoni PG, Belardinelli R, Cohen-Solal A, Hambrecht R, et al. Statement on cardiopulmonary exercise testing in chronic heart failure due to left ventricular dysfunction: recommendations for performance and interpretation. Part I: definition of cardiopulmonary exercise testing parameters for appropriate use in chronic heart failure. *Eur J Cardiovasc Prev Rehabil*. 2006;13(2):150–64. <https://doi.org/10.1097/01.hjr.0000209812.05573.04>. PMID: 16575267.
- Huang F, Leng X, Kasukurthi MV, Huang Y, Li D, Tan S, et al. Utilizing machine learning techniques to predict the efficacy of Aerobic Exercise intervention on young hypertensive patients based on cardiopulmonary Exercise Testing. *J Healthc Eng*. 2021;2021:6633832. <https://doi.org/10.1155/2021/6633832>. PMID: 33968353; PMCID: PMC8084649.
- Yang H, Song L, Ning X, Ma Y, Xue A, Zhao H, et al. Enhanced external counterpulsation ameliorates endothelial dysfunction and elevates exercise tolerance in patients with coronary artery disease. *Front Cardiovasc Med*. 2022;9:997109. <https://doi.org/10.3389/fcvm.2022.997109>.
- Carriere C, Corrà U, Piepoli M, Bonomi A, Merlo M, Barbieri S, et al. Anaerobic threshold and respiratory compensation point identification during cardiopulmonary exercise tests in chronic heart failure. *Chest*. 2019;156(2):338–47. <https://doi.org/10.1016/j.chest.2019.03.013>. Epub 2019 Mar 27. PMID: 30926397.
- Esco MR, Williford HN. Race influences the relationship between aerobic power and heart rate recovery. *J Sports Med Phys Fitness*. 2013;53(6):583–7 PMID: 24247181.
- O'Neal WT, Alam AB, Sandesara PB, Claxton JS, MacLehose RF, Chen LY, et al. Sex and racial differences in cardiovascular disease risk in patients with atrial fibrillation. *PLoS ONE*. 2019;14:e0222147. <https://doi.org/10.1371/journal.pone.0222147>.
- Egan KJ, Knutson KL, Pereira AC, von Schantz M. The role of race and ethnicity in sleep, circadian rhythms and cardiovascular health. *Sleep Med Rev*. 2017;33:70–8. <https://doi.org/10.1016/j.smrv.2016.05.004>.
- Park JH, Jung HC, Jung YS, Song JK, Lee JM. Re-visiting maximal heart rate prediction using cross-validation in population aged 7–55 years. *Int J Environ Res Public Health*. 2022;19(14):8509. <https://doi.org/10.3390/ijerph19148509>. PMID: 35886359; PMCID: PMC9320369.
- Hofmann P, Pokan R, von Duvillard SP, Seibert FJ, Zweiker R, Schmid P. Heart rate performance curve during incremental cycle ergometer exercise in healthy young male subjects. *Med Sci Sports Exerc*. 1997;29:762–8. <https://doi.org/10.1097/00005768-199706000-00005>.
- Brooke JD, Hamley EJ. The heart-rate–physical work curve analysis for the prediction of exhausting work ability. *Med Sci Sports*. 1972;4:23–6.
- Pollock ML, Franklin BA, Balady GJ, Chaitman BL, Fleg JL, Fletcher B, et al. AHA science advisory. resistance exercise in individuals with and without cardiovascular disease: benefits, rationale, safety, and prescription: an advisory from the committee on exercise, rehabilitation, and prevention, council on clinical cardiology, american heart association; position paper endorsed by the american college of sports medicine. *Circulation*. 2000;101(7):828–33. <https://doi.org/10.1161/01.cir.101.7.828>. PMID: 10683360.
- Gellish RL, Goslin BR, Olson RE, McDonald A, Russi GD, Moudgil VK. Longitudinal modeling of the relationship between age and maximal heart rate. *Med Sci Sports Exerc*. 2007;39(5):822–9. <https://doi.org/10.1097/mss.0b013e31803349c6>. PMID: 17468581.
- Larson ED, St Clair JR, Sumner WA, Bannister RA, Proenza C. Depressed pacemaker activity of sinoatrial node myocytes contributes to the age-dependent decline in maximum heart rate. *Proc Natl Acad Sci U S A*. 2013;110(44):18011–6. <https://doi.org/10.1073/pnas.1308477110>.
- Choi S, Baudot M, Vivas O, Moreno CM. Slowing down as we age: aging of the cardiac pacemaker's neural control. *Geroscience*. 2022;44(1):1–17. <https://doi.org/10.1007/s11357-021-00420-3>. Epub 2021 Jul 22. PMID: 34292477; PMCID: PMC8811107.
- Kawada T, Sugimachi M, Shishido T, Miyano H, Sato T, Yoshimura R, Miyashita H, Nakahara T, Alexander J Jr, Sunagawa K. Simultaneous identification of static and dynamic vagosympathetic interactions in regulating heart rate. *Am J Physiol*. 1999;276(3):R782–9. <https://doi.org/10.1152/ajpregu.1999.276.3.R782>. PMID: 10070139.
- Andersen S, Andersen A, de Man FS, Nielsen-Kudsk JE. Sympathetic nervous system activation and β -adrenoceptor blockade in right heart failure. *Eur J Heart Fail*. 2015;17(4):358–66. <https://doi.org/10.1002/ehf.253>. Epub 2015 Feb 22. PMID: 25704592.

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