ORIGINAL ARTICLE

Mechanisms of adaptations in cardiorespiratory fitness with exercise prescriptions differing in volume and intensity in middle-age men

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ABSTRACT

Background: To examine the mechanisms of adaptations in cardiorespiratory fitness with different dose of amount and intensity exercise training in middle-aged men. Methods: A total of 67 sedentary subjects aged 40-49 yr were assigned to participate for 12 weeks in a control group or in one of three exercise groups: 1) low volume/moderate intensity 2) low volume/vigorous intensity and 3) high volume/vigorous intensity. They were tested for VO_{2max}, cardiac output (Q) and stroke volume (SV) before and after training and maximal arterial-venous oxygen difference ($a\text{-}vO_{2diff}$) calculated by the Fick Equation. Results: Contrasted to control group, VO_{2max} increased similar in both LVVI and HVVI groups after 12 weeks; It indicated that the intensity of exercise appears to make a greater benefit than the amount of exercise on VO_{2max}. However, Maximal cardiac output (Q_{max}) and $a\text{-}vO_{2diff}$ contributed to increase VO_{2max} were differences in both of vigorous intensity groups. In LVVI group, Q_{max} together with maximal $a\text{-}vO_{2diff}$ contributed to the greater VO_{2max}; in HVVI group, the majority of the increment in VO_{2max} was relied on larger Q_{max} whereas a widened $a\text{-}vO_{2diff}$. Conclusion: It is appropriate to recommend vigorous intensity exercise to improve cardiorespiratory fitness and encourage higher amount to confer additional benefit for Q_{max}.

Keywords: Sport medicine, Cardiorespiratory fitness, Maximal oxygen uptake, Cardiac output, Arterial-venous oxygen difference.

Cite this article as:
Lin, J., Huang, Q., Zhong, X., Zhang, A., & Lin, P. (2025). Mechanisms of adaptations in cardiorespiratory fitness with exercise prescriptions differing in volume and intensity in middle-age men. *Journal of Human Sport and Exercise, 20*(1), 130-143. https://doi.org/10.55860/qmfy7d62

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Submitted for publication July 13, 2024.
Accepted for publication August 26, 2024.
Published October 15, 2024.
Journal of Human Sport and Exercise. ISSN 1988-5202.

doi: https://doi.org/10.55860/qmfy7d62

INTRODUCTION

There is accumulating evidence that cardiorespiratory fitness, represented by maximal oxygen uptake (VO_{2max}) (Åstrand,2003), is important for the prevention of many lifestyle-related diseases in epidemiological (Laukkanen et al., 2010) observational (Lee et al., 2014; Steell et al., 2019; Sui et al., 2017) and randomized studies (Nordby et al., 2012); moreover, some studies (Tarp et al., 2021; Farrell et al., 2010) indicate that higher levels of cardiorespiratory fitness are associated with lower risks for poorer health. Kokkinos pointed out in another study of 20,950 American veterans that each 1-MET increment in CRF confers an 15% decree in mortal up to 10 METs beyond which the additional survivor benefits largely plateau (Kokkinos et al., 2017).

ACSM's Guidelines for Exercise Testing and Prescription clearly demonstrate that exercise of the intensity, duration, and frequency recommended results in improvements in VO_{2max}, it is important to beg the question of what the effect of exercise training on cardiorespiratory fitness is. In recent years, studies appear to provide conflicting recommendations regarding the relationship between exercise amount and intensity on increases in VO_{2max}. Current guidelines suggest that changes in cardiorespiratory fitness are similar in high and moderate intensity interventions of longer duration if the energy cost of exercise is similar. O'Donovan reported that among 63,591 adult liability participants, those who performed less than 150 minutes of moderate physical activity per week or less than 75 minutes of heavy physical activity per week had a similar risk of cardiovascular disease reduction compared with those who performed more than 150 minutes of moderate physical activity per week or at least 75 minutes of heavy physical activity per week (O'Donovan et al., 2017). In contrast, vigorous exercise provides greater CVD benefits than moderate PA with equal energy expenditure (Franklin et al., 2023). Min concluded that individuals who performed vigorous PA had a significantly lower risk of all-cause and cause-specific death compared with patients who performed only mild/moderate PA (Zhao et al., 2019). Briefly, data regarding the specific quantity and quality of exercise for the attainment of the VO_{2max} are less clear.

In accordance with a derivation of the Fick equation (Yamabe et al., 1997), VO_{2max} is typically due to both maximal cardiac output (Q_{max}) and the maximal arterial-venous oxygen difference (a-vO_{2diff}). However, there is limited data available on the parameters of proportion contributions of Q_{max} and a-vO_{2diff} underlying the increases in VO_{2max} in different dose of exercise, while some studies (Murias et al., 2010; Dogra et al.) have demonstrated the proportion contributions in different ages. For instance, Murias JM investigated the time-course and mechanisms of adaptation of cardiorespiratory fitness in older and young men with a short-term (12wk) endurance training, the results showed that the majority of the increase in VO_{2max} was attributed to an increased Q_{max}(~69%) with the remaining ~31% to a widened a-vO_{2diff} in older men; and 56% of the increase in VO_{2max} explained by a greater Q_{max} and 44% by a widened a-vO_{2diff} in young. Thus, there is clear need for a randomized, controlled trial that address the mechanisms of adaptations in different amounts and intensities of exercise training. The mainly purpose of this study was to investigate which parameters, central or peripheral, are responsible for greater VO_{2max} in a short-term (12wk) different dose of volume and intensity exercise. We hypothesized that 1) the intensity of exercise would be more important than volume for improving VO_{2max}; 2) A greater VO_{2max} is majority due to a higher Q_{max} compared to peripheral widened a-vO_{2diff}.

METHODS

Study design

A complete description of the STRRIDE study design has been published elsewhere (Kraus et al., 2001). The research protocol was reviewed and approved by the relevant institutional review boards, and all subjects provided written, informed consent.

Subjects

Sedentary male volunteers (n = 67), aged 40-49 yr were recruited from the local community to participate in this study. A letter was sent to male soliciting their interest in taking part in a 12-wk study of the mechanisms of adaptations in cardiorespiratory fitness with different dose of amount and intensity exercise training. This letter stated that eligible men were nonsmokers or ex-smokers with at least 2 yr of abstinence. A history of recreational drugs or had significant chronic medical problems were screened with an International Physical Activity Questionnaire (IPAQ) (https://www.academia.edu/5346814), and volunteers were excluded if the questionnaire revealed any participation in very hard activities or exercise for >30min/day on two or more occasions per week. Volunteers were examined by a cardiologist and were excluded if there was evidence of cardiovascular disease.

Exercise training protocols

After screening, subjects were randomized via computer program into one of four groups differing in exercise intensity and amount. The 12 weeks exercise training programs were as follows: 1) low-volume/moderate intensity, LVMI, the caloric equivalent of working approximately 19 km/wk, 1,200 kcal/wk at 40-55%VO_{2max}; 2) low-volume/vigorous intensity, LVVI, jogging approximately 19 km/wk, 1,200 kcal/wk at 65-80% VO_{2max}; 3) high-volume/vigorous intensity, HVVI, jogging approximately 32 km/wk, 2,000 kcal/wk at 65-80% VO_{2max}; 4) a non-exercising control group. The specific training regimens were chosen to compare different dose/volume of exercise (1,200 vs.2,000 kcal/wk) in groups exposed to the same intensities of training (65-80% VO_{2max}) and different dose/intensities (40-55 vs. 65-80%VO_{2max}) in groups with the same exercise volume (1,200 kcal/wk). The exercise volume (1,200 and 2,000 kcal/wk) were consistent with recommendations of the Surgeon General's report (US Department of Health & Human Services Centers for Disease Control (CDC) 200 Independence Avenue, 1996). The 65-80% VO_{2max} level was chosen because this is the traditional exercise intensity prescribed for cardiovascular fitness benefits (American College of Sports Medicine). The lower training intensity (40-55% VO_{2max}) approximated brisk walking or moderate-intensity exercise as advised in health guidelines (Pate et al.1995). Once the exercise volume (kcal/kg/wk) was calculated, subjects selected, with the assistance of an exercise physiologist, an appropriate exercise frequency and duration to achieve their weekly dose.

Exercise training monitor

All exercise sessions were verified by direct supervision and use of a heart rate monitor (Polar Electro, RS600, Finland) and tri-axial RT3 accelerometer (Stayhealthy, Inc., Monrovia, CA) that provided recorded data. Subjects were instructed to wear the device during the exercise time as described in a previous study (Hollowell et al., 2009), physical activity energy expenditure (PAEE) determined via the RT3 accelerometer has been shown to consistent with the Prescribed volume (kcal/wk). Adherence was calculated weekly as a percent, equal to the actual number of exercise minutes completed each week at the appropriate intensity, divided by the total number of minutes prescribed. Subjects were counselled to maintain baseline body weight and the goal of the intervention was not weight loss.

All of groups were provides with the IPAQ to record in arbitrary units any additional physical activity or exercise that was above the prescribed program. On entering the study participants were asked to complete a typical retrospective week of the same questionnaire. This was to ensure that all individuals from groups participated in similar amounts of physical activity or exercise at baseline. The control group was offered the intervention at the end of the trial.

Cardiorespiratory fitness measurements

Cardiorespiratory fitness (CRF) was indexed by VO_{2max} using a graded maximal bicycle ergometer test. Briefly, an initial test was performed to screen for underlying cardiovascular disease and to acclimate the

subject. If no evidence for cardiovascular disease was detected, a second test was conducted to determine the pretraining VO_{2max}. Additional VO_{2max} test were performed after the ramp period and periodically during training in order to modify the exercise workload to maintain the weekly caloric expenditure prescription. Finally, VO_{2max} was also determined after the final week of training.

The initial workload of 25W was increased every 2-min by 25W until volitional exhaustion. Participants were required to meet three of the four following criteria for having achieved VO_{2max}: heart rate ≥ age-predicted maximum heart rate [220-age (yr)], respiratory exchange ratio ≥ 1.15, rating of perceived exertion ≥ 19, or an increment in VO_2 ≤ 2 ml/kg/min in response to an increased gradient. During the test, HR was measured by electrocardiographically at the same times, while blood pressure was measured by auscultation. Respiratory data through breath-by-breath analysis were continuously measured (Cortex MetaMax II; Cortex, Leipzig, Germany). These measurements were corrected to standard conditions and used to determine VO_2 at 20-s intervals throughout the test. VO_{2max} was determined by averaging values over the final minute of testing.

Maximal cardiac output measurements

Participants performed a standard echocardiographic assessment system (Vivid 7, GE Vingmed, Horten, Norway) for Maximal cardiac output (Q_{max}) determination during the ramp incremental exercise to volitional fatigue. That is, when the participant indicated that they felt they could only sustain exercise for one more minute, the Q_{max} measures were initiated. Peak blood velocity across the mitral valve (E-wave) was measured by pulse wave Doppler echocardiography form an apical four-chamber view at the tips of open mitral valve leaflets using a 2.5-MHz transducer. Myocardial longitudinal velocities at the lateral aspect of the mitral valve annulus were recorded by pulse wave tissue Doppler imagine using the same transducer in the apical four-chamber view. This protocol was performed to not only confirm the attainment of VO_{2max} and for determination of Q_{max}, but also to be highly reliable (T. Rowland & Whatley Blum, 2000), Further, this method compares well to other techniques and provides values that reliable at maximum exercise (T. W. Rowland & Willers, 2010).

Subjects pedalled to exhaustion in the upright sitting position at a cadence of 60 revolutions per minute on a mechanically braked cycle ergometer (Monark model 818, Varberg, Sweden). During data acquisition, the transducer beam was aligned as closely as possible with the cardiac longitudinal axis. These measurements were performed by one operator adjusting and fixing the transducer position on the subject's chest while the other researcher operated the echocardiographic controls. Subjects were asked to limit body motion, what is avoid exaggerated swinging or leaning forward over the handlebars but were not otherwise constrained. All echocardiographic measures were obtained during spontaneous breathing.

Q_{max} was calculated as the product of stroke volume and HR, Q_{max} and stroke volume were both indexed to body surface area (BSA). Arterial venous oxygen difference ($a\text{-}vO_{2diff}$) was calculated from the Fick equation as: $a\text{-}vO_{2diff}$ (ml O_2/100 ml blood) = VO_2 (l/min)/Q (l/min) × 100.

Statistical analysis

All tabular data are presented as means ± SD, and all data in Figure 1 are presented as mean ± SE. Analysis of variance with Bonferroni *post hoc* testing was used to test for demographic difference between groups. Paired *t* tests were used to compare intragroup differences between baseline and after training. Analysis of variance with Bonferroni *post hoc* testing was used to test relative (percentage) change scores between groups. To determine whether there were significant differences between groups, data were analysed using one-way ANOVA by SPSS version 12.0 (SPSS, Chicago, IL). Statistical significance was denoted at the $p < .05$ level.

RESULTS

Subjects

Initially, 67subjects were randomly assigned to one of four groups; data are presented from the 58 subjects who completed the training/testing (randomized/completed: control group, 16/15; low-volume/moderate intensity group, 16/14; low-volume/vigorous intensity group, 18/16; high-volume/vigorous intensity group, 17/13). Dropout was similar in all of exercise groups, the main reasons discontinued intervention were moved away, especially on a business trip, and change physical activity. There were no within-group differences observed between dropouts and men who finished the intervention.

Exercise training

Characteristics for subjects that completed the exercise training were presented in Table 1. There were no significant differences between the groups in age, height and Weight. The rate of adherence was significantly ($p < .05$) lower in the HVVI group compared with the LVVI group. As expected, all of the exercise groups achieve the prescribed volume (1155.8 ± 204.3, 1196.2 ± 281.5 vs 2034.9 ± 445.4 kcal/wk, respectively), and HVVI group exercise for significantly greater volume (km/wk) and time (min/wk) than the low volume groups. The actual exercise time was approximately 2.5 h/wk for the low volume groups and 3 h/wk for the HVVI group. Weekly training volume averaged ~16 km/wk or ~134 min/wk in LVVI group; this volume was obtained with three or four exercise sessions per week of ~5 km or ~40-min duration in contrast to the LVMI group, which consisted of ~4 km or ~40-min duration. Caloric intake (calculated by IPAQ) measured before and after intervention, did not change significantly in any exercise group or in the control group (data not shown).The exercise frequency chosen to attain 3-4 time/wk dosage was not significantly among any exercise groups.

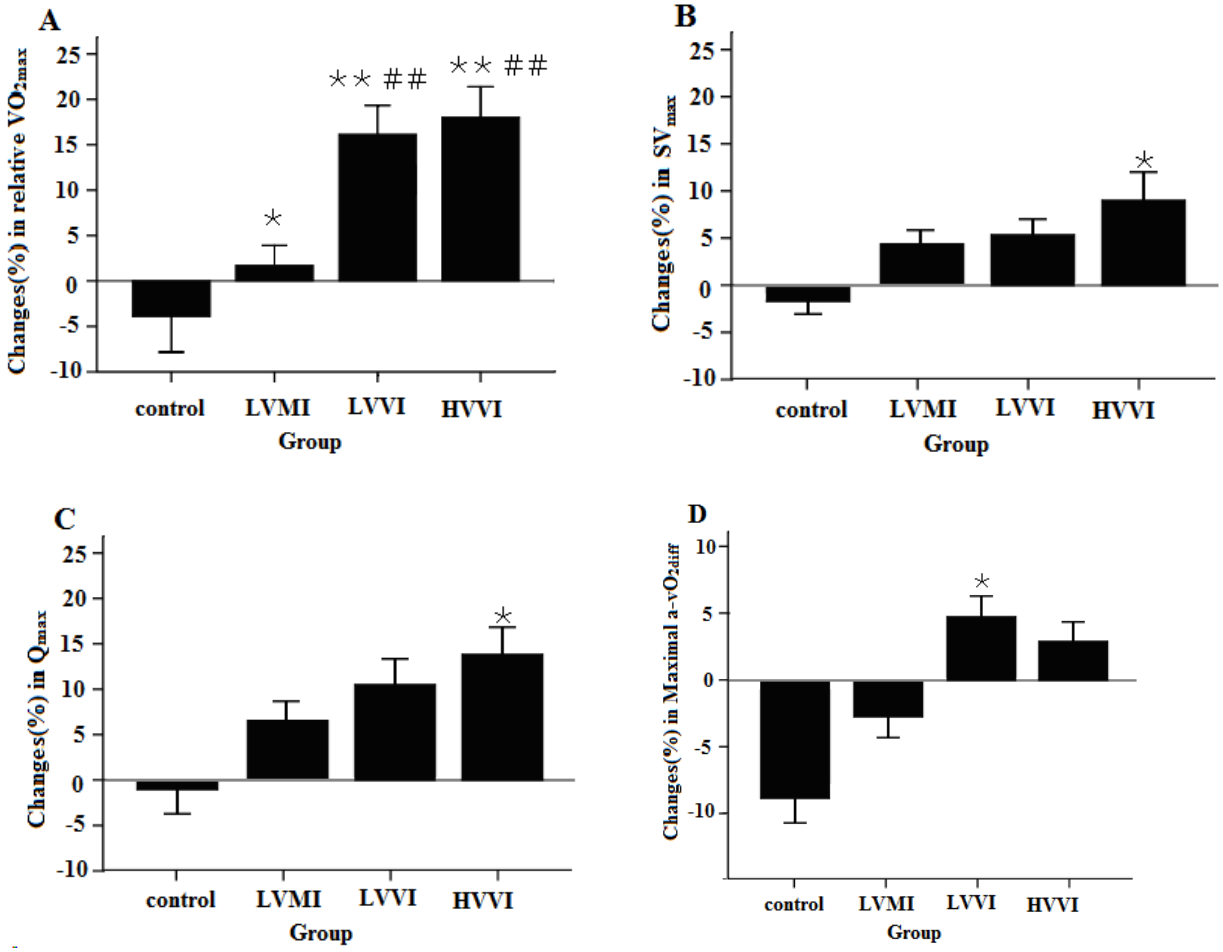
Table 1. Baseline characteristics of the subjects who completed post-training testing.

	Control	**LVMI**	**LVVI**	**HVVI**
Variable	(n = 15)	(n = 14)	(n = 16)	(n = 13)
Age, yr	44.3 ± 3.4	43.8 ± 4.0	45.4 ± 2.1	45.3 ± 4.8
Height, cm	171.2 ± 5.4	171.2 ± 5.7	169.6 ± 4.0	173.5 ± 3.1
Weight, kg	75.3 ± 10.4	73.9 ± 8.6	71.5 ± 11.9	73.4 ± 5.2
Exercise prescription				
Prescribed intensity, $\%VO_{2max}$	/	40-50	65-80	65-80
Prescribed volume, kcal/wk	/	1200	1200	2000
Prescribed volume, km/wk #	/	19	19	32
Prescribed time, min/wk	/	173.5 ± 55.3	140.5 ± 40.4	208.8 ± 57.4
Actual exercise dose				
Adherence %		88.2 ± 8.6	93.7 ± 11.3	84.6 ± 12.8@
Actual volume, kcal/wk	/	1155.8 ± 204.3	1196.2 ± 281.5	2034.9 ± 445.4
Actual volume, km/wk	/	14.8 ± 4.4	16.3 ± 4.9	20.5 ± 4.0&
Actual time, min/wk§	/	148.9 ± 57.3	133.5 ± 47.8	182.5 ± 70.3※
Frequency, sessions/wk	/	3.7 ± 0.9	3.4 ± 0.5	4.2 ± 1.4

Note. Values are presented as mean ± SD, # values are the approximate number of km per week that are calorie equivalent to the prescribed 14 kcal/kg/wk for the moderate intensity group and 23 kcal/kg/wk for the vigorous intensity groups. Adherence was calculated as a percent by dividing the time spent exercising by the time needed the defined exercise prescription. § Values are the prescribed time multiplied by the rate of adherence for each subject. @Significantly different (p < .05) from the low-volume/vigorous intensity group; & Significantly different (p < .05) from the low-volume/moderate intensity group; ※Significantly different (p < .05) from low-volume groups.

Cardiorespiratory fitness

Table 2 depicts the within-group changes of absolute maximal oxygen uptake, relative maximal oxygen uptake, peak power output, maximal heart rate and exercise time to exhaustion between groups following exercise training. After 12 weeks, there were only differing slightly changes for absolute VO_{2max} in control and LVMI groups, but the changes in vigorous intensity groups were higher compared to the control group (p < .05), which increased by 0.2 ± 0.3 L/min in the LVVI group and 0.3 ± 0.2 L/min in the HVVI group, respectively (Table 3). When expressed relative to body weight, relative VO_{2max} increased to a greater extent in the vigorous intensity groups than in the control and moderate intensity groups (p < .01), which increased by 4.6 ± 3.0 mL/kg/min in the LVVI group and 5.4 ± 2.7 mL/kg/min in the HVVI group (both p < .01 vs. control and LVMI groups). More interestingly, peak power output and exercise time to exhaustion, as measured for a surrogate marker of aerobic fitness, were similar to relative VO_{2max}, increased significantly in both of vigorous intensity groups (p < .01). There was no difference change within-group for maximal heart rate following exercise training. The percent change in VO_{2max} from baseline was similar to both vigorous intensity groups (LVVI, 16.3 ± 3.1% vs. HVVI, 17.8 ± 2.8%; p < .01) respectively (Figure 1A).



A: relative VO_{2max} (** p < .01, control vs LVVI and HVVI, # # p < .01, LVMI vs LVVI and HVVI). B: SV_{max} (* p < .05, control vs HVVI). C: Q_{max} (* p < .05, control vs HVVI). D: Maximal a-vO_{2diff} (* p < .05, control vs LVVI).

Figure 1. Percentage changes between groups from before exercise to after training (mean ± SE).

Table 2. Effects of the volume and intensity of exercise on cardiorespiratory fitness.

	Control (n = 15)		**LVMI (n = 16)**	
Variable	Baseline	12 wk	Baseline	12 wk
VO_{2max} (L/min)	2.2 ± 0.4	2.0 ± 0.3	2.4 ± 0.5	2.4 ± 0.4
VO_{2max} (mL/kg/min)	28.5 ± 3.7	27.0 ± 2.8	28.8 ± 3.5	29.0 ± 3.0
PO_{peak} (W)	168 ± 31	155 ± 23	155 ± 19	168 ± 23※
HR_{max} (bpm)	157 ± 19	158 ± 16	157 ± 17	163 ± 13
TTE (s)	738 ± 144	697 ± 115	713 ± 101	765 ± 104
	LVVI (n = 14)		**HVVI (n = 13)**	
Variable	Baseline	12 wk	Baseline	12 wk
VO_{2max} (L/min)	2.1 ± 0.3	2.4 ± 0.4※	2.1 ± 0.3	2.4 ± 0.4※
VO_{2max} (mL/kg/min)	29.3 ± 3.4	34.0 ± 3.7※※	29.3 ± 3.4	34.0 ± 3.7※※
PO_{peak} (W)	157 ± 25	180 ± 15※※	157 ± 25	180 ± 15※※
HR_{max} (bpm)	165 ± 14	175 ± 10	165 ± 14	175 ± 10
TTE (s)	675 ± 109	793 ± 72※※	675 ± 109	793 ± 72※※

Note. Values are presented as mean ± SD, VO_{2max}, maximal oxygen uptake; HR_{max}, maximal heart rate; PO_{peak}, peak power output; TTE, exercise time to exhaustion; Within-group change is significantly different from baseline, ※ p < .05, ※※ p < .01.

Table 3. Change from baseline in cardiorespiratory fitness characteristics of each group.

Variable	**Control (n = 15)**	**LVMI (n = 16)**	**LVVI (n = 14)**	**HVVI (n = 13)**
VO_{2max} (l/min)	-0.1 ± 0.3	0.0 ± 0.3	0.2 ± 0.3	0.3 ± 0.2
VO_{2max} (ml/kg/min)	-1.5 ± 2.0	0.2 ± 2.0	4.6 ± 3.0**##	5.4 ± 2.7**##
PO_{peak} (W)	-12.5 ± 17.7	13.6 ± 17.2**	22.7 ± 20.8**	25.0 ± 15.8**
HR_{max} (bpm)	1.2 ± 7.8	6.6 ± 10.3	8.1 ± 8.9*	6.2 ± 10.1
TTE (s)	-41 ± 76	52 ± 83*	117 ± 75**	119 ± 110**

*Note. Groups compared using one-way ANOVA, values are presented as mean ± SD, VO_{2max}, maximal oxygen uptake; HR_{max}, maximal heart rate; PO_{peak}, peak power output; TTE, exercise time to exhaustion; Change from baseline is significantly different from control group, * p < .05, ** p < .01; Change from baseline is significantly different from low-volume/moderate intensity group, # p < .05, ## p < .01.*

Maximal cardiac output

Table 4 summarizes the values which maximal SV_{max}, Q_{max}, and maximal a-vO_{2diff} in response to training from pre to post-training. SV_{max} and Q_{max} increased from baseline to post-training in each exercise group, a higher SV_{max} and Q_{max} were observed in HVVI group after 12 weeks (p < .05) when compared with the baseline. However, the maximal a-vO_{2diff} from baseline to after 12 weeks was did not significantly affect by training in any exercise group. A similar SV_{max} change was observed in the same exercise volume groups (LVMI, 4.8 ± 8.5 mL/beat vs LVVI, 5 ± 8.1 mL/beat,); more interestingly, with further increases in SV_{max} (8.4 ± 9.6 mL/beat, p < .01) and Q_{max} (2.2 ± 1.1 L/min, p < .05) seen in the high-volume exercise group when compared with control group (Table 5).

As observed in Figure 1B, the percent changes in SV_{max} were 4.8 ± 1.7, 5.1 ± 1.9, and 9.0 ± 2.2% (p < .01) for the LVMI, LVVI, and HVVI groups, respectively; Which in Q_{max} in response to training improve constantly, values were 6.1 ± 2.3, 10.8 ± 3.3, and 14.6 ± 3.7% (p < .01) (Figure 1C). Although the maximal a-vO_{2diff}

increases in the vigorous intensity groups, only the LVVI group remained significantly increase (4.8 ± 1.3%, $p < .05$), HVVI group widened slightly (3.0 ± 1.0%, $p > .05$) (Figure 1D).

Table 4. Effects of the volume and intensity of exercise on cardiac output.

	Control (n = 15)		**LVMI (n = 16)**	
Variable	Baseline	12 wk	Baseline	12 wk
SV_{max}(ml/beat)	90 ± 20.3	88 ± 24.4	93.6 ± 11.5	97.4 ± 17.6
Q_{max}(l/min)	14.1 ± 1.1	13.9 ± 4.6	14.7 ± 1.5	15.6 ± 2.9
Maximal a-vO_{2diff} (ml O_2/100ml blood)	21.4 ± 1.3	19.5 ± 4.0	19.1 ± 2.4	18.6 ± 3.9
	LVVI (n = 14)		**HVVI (n = 13)**	
Variable	Baseline	12 wk	Baseline	12 wk
SV_{max}(ml/beat)	94.8 ± 17.4	98.8 ± 16.5	94.8 ± 17.4	98.8 ± 16.5
Q_{max}(l/min)	15.8 ± 2.7	17.5 ± 3.3*	15.8 ± 2.7	17.5 ± 3.3*
Maximal a-vO_{2diff} (ml O_2/100ml blood)	18.6 ± 5.0	19.5 ± 4.4	18.6 ± 5.0	19.5 ± 4.4

*Note. Values are presented as mean ± SD. SV_{max}, maximal stroke volume; Q_{max}, maximal cardiac output; Maximal a-vO_{2diff}, maximal arterial-venous O_2 difference; Within-group change is significantly different from baseline, * $p < .05$.*

Table 5. Change from baseline in cardiac output characteristics of each group.

Variable	**Control (n = 15)**	**LVMI (n = 16)**	**LVVI (n = 14)**	**HVVI (n = 13)**
SV_{max}(ml/beat)	-2 ± 10.6	4.8 ± 8.5	5 ± 8.1	8.4 ± 9.6**
Q^{max}(l/min)	-0.2 ± 2.9	1 ± 1.8	1.7 ± 2.5	2.2 ± 1.1*
Maximal a-vO_{2diff} (ml O_2/100ml blood)	-2 ± 1.9	-0.6 ± 1.3	1 ± 4.3*	0.6 ± 1.5

*Note. Groups compared using one-way ANOVA, values are presented as mean ± SD. SV_{max}, maximal stroke volume; Q_{max}, maximal cardiac output; Maximal a-vO_{2diff}, maximal arterial-venous O_2 difference; Change from baseline is significantly different from control group, * $p < .05$, ** $p < .01$.*

In order to describe the relative contribution of Q_{max} and maximal a-vO_{2diff} to the increase in VO_{2max}, the percentage was calculated as the percent change in Q_{max} (or maximal a-vO_{2diff}) divided by the total percent change in VO_{2max}. In LVVI group, ~66% of the change in VO_{2max} from pre-training to post-training was explained by the increase in Q_{max}, whereas the remaining ~34% was explained by an improved maximal a-vO_{2diff}. In HVVI group, ~82% of the improvement in VO_{2max} was attributed to a higher Q_{max}, and only ~18% was attributed to a widened maximal a-vO_{2diff}. Collectively, the contribution percentage reflected the remainder of the change in VO_{2max} mostly reliance on Q_{max} in contrast to maximal a-vO_{2diff} in different dose of exercise training.

DISCUSSION AND CONCLUSIONS

This study examined the central and peripheral mechanisms contributing to adaptations in cardiorespiratory fitness in response to a 12 weeks endurance training program in difference dose of exercise. The primary findings were as follows: (1) the percent change in VO_{2max} was similar to the both vigorous intensity groups, while 12 weeks of low-volume/ vigorous-intensity exercise, at a volume calorically equivalent to walking approximately 16 km over an average of 134 minutes per week, will be enough to improve VO_{2max} significantly. (2) A trend toward both a separate and combined effect of exercise volume and intensity on increasing VO_{2max} does exist, while the intensity of exercise appears to be more effective in increasing VO_{2max} than volume; this conclusion is drawn from our data showing that increasing the volume from 1200 to 2000

kcal/week (with the same intensity of 65-80%VO_{2max}) did not significantly improve VO_{2max}; however, increasing the intensity from 40-55% to 65-80 %VO_{2max} (with the same exercise volume of 1200 kcal/week) did improve VO_{2max} significantly. (3) The central and peripheral mechanisms contributed to increase VO_{2max} were differences in vigorous intensity groups. The majority of the improvement of VO_{2max} was attributed to significantly higher Q_{max} (~82% of the improvement) with a widened a-vO_{2diff} (~18%) in high-volume/vigorous-intensity group; whereas in low-volume/vigorous-intensity group, Q_{max} (~66%) together with maximal a-vO_{2diff} (~34%) contributed to the greater VO_{2max}.

The duration of the exercise prescriptions keeping only 12 weeks, which different from the 24 weeks designed by the Studies of Targeted Risk Reduction Interventions through Defined Exercise (STRRIDE),was consisted with the 12 wk endurance training program (Lee et al,2014). In this study, 16.3% and 17.8% increasing in VO_{2max} in both of vigorous intensity groups, which agreement with those of Gossard D (Gossard et al., 1986), VO_{2max} increased by 8% in the low intensity group (42-60% VO_{2max}) and by 17% in the high intensity group (63-81% VO_{2max}) after 12 weeks. Moreover, the vigorous intensity groups had similar increases in VO_{2max} when compared to the 6-mo intervention (16.3% and 17.8% vs 16.7% and 17.8%) (Kraus William E. et al., 2002). Thus, it concluded that in the short term, higher intensity exercise training is more beneficial than moderate intensity exercise training, while in the long term high or moderate intensity exercise training is equally effective (Van Ryckeghem et al., 2022). Hansen et al. (Hansen et al., 2009) reported that there was a significant interaction effect (exercise training × intensity) for the changes in VO_{2max} after 2 months of exercise training, which increased to a greater extent in the high intensity (75%VO_{2max}) group than in the group following the moderate intensity (55%VO_{2max}) (16 ± 2% vs 9 ± 2%, respectively; $p < .05$); More interestingly, there were no interactions about the percent change of VO_{2max} observed within from 2- to 6-mo (16 ± 4%). It is applying that 12 weeks exercise project enough to improve VO_{2max}, continuous exercise training does not further augment VO_{2max}. It is noteworthy that the values of VO_{2max} during the 12 wk exercise would be no further improvement whereas an additional 12 wk of progressive exercises training. This study contributes to a growing body of evidence concerning the beneficial effects of short-term (12wk) improvements in VO_{2max}.

The beneficial effects of regular exercise on cardiorespiratory fitness are well documented (Sagelv et al., 2019; Tari et al., 2019). However, the previous studies did not include detailed information on the preferred exercise modalities that should be implemented to maximize the VO_{2max}. In the present study, common components of exercise prescriptions which improve in VO_{2max} were volume and intensity. In our date, the LVVI group (expended 1200 kcal/wk at 40-55% of VO_{2max}) and HVVI group (expended 2000 kcal/wk at 65-80% of VO_{2max}) had similar increases in VO_{2max} (16.3% and 17.8%, both $p < .001$ vs controls), without further changes in VO_{2max} despite the progressive increase in training volume, which indicated that increasing the volume from 1200 kcal/week to 2000 kcal/week, at a controlled intensity of 65 to 80% VO_{2max}, is not a strong stimulus to significantly improve VO_{2max}. However, the additional intensity of exercise (40-55% vs 65-80% VO_{2max}) prescribed in the LVMI and LVVI groups with the same volume of exercise did result in a significant increase in VO_{2max}. It suggests that the intensity of exercise is more important than the volume of exercise in terms of increasing the level of VO_{2max} Talsnes (Talsnes et al., 2022) argues that even though both low and high intensity improve maximal oxygen uptake capacity of exercise, high intensity training is more sufficient to elicit better maximal oxygen uptake adaptations, which is consistent with our view. Although it is often suggested that the genetic component of physical fitness undermines its prognostic power, genetic differences explain only 25-47% of the individual variation in VO_{2max} (Bouchard et al., 1999). However, there were high and low responders, vigorous exercise (75% of VO_{2max}) has been shown to increase cardiorespiratory fitness by 20% in sedentary individuals, regardless of age, gender, race, and initial fitness level (Skinner et al., 2001). Storen (Støren et al., 2017) reported an increase in VO_{2max} of approximately 9%-

13% in adults between the ages of 20 and 80 years after completion of post-8 HIIT, which was a significant inverse relationship between baseline fitness (expressed as a percentage of mean maximal aerobic capacity at pre-training age) and the percentage increase in "*maximal aerobic capacity*" (r = -0.66).In conclusion, these findings taken together suggest that exercise intensity may be a critical factor to consider when designing exercise prescriptions to optimize the persistence of the training-induced improvement in VO_{2max}.

The concept that cardiorespiratory fitness, a physiological characteristic that quantifies the ability of the body to transport and use oxygen at the working muscle and is dependent primarily on maximal cardiac output, maximal arterial-venous oxygen difference, and efficient shunting of blood to working skeletal muscle. In the resting state, the body's O_2 uptake ($\dot{V}O_{2max}$) is 3.5ml^{-1}kg^{-1}min^{-1}, with only a small fraction consumed by skeletal muscle. However, during incremental exercise, lung $\dot{V}O_2$ increases progressively and, depending on gender, age, body weight, genetics, training status, and fitness, reaches approximately 90 ml^{-1}kg^{-1}min^{-1} maximum ($\dot{V}O_{2max}$) (Joyner & Casey, 2015; Bouchard et al., 2011). An early study by Murias JM et al. assessed the interplay of central vs. peripheral mechanisms explaining the adaptations involving improvements in VO_{2max} in older (68 ± 7 yr) and young (23 ± 5 yr) with the training protocol performed on a cycle ergometer three times per week for 45 min (135 min/wk) at ~70% VO_{2max}. this study demonstrated that In older, 69% of the increase in VO_{2max} was explained by an increased Q_{max} with the remaining 31% explained by a widened a-vO_{2diff}, while 56% attributed to a greater Q_{max} and 44% to a widened a-vO_{2diff} in young Ekblom et al (Ekblom et al., 1968). found that 16 wk of physical training increased VO_{2max} from 3.15 to 3.68 L/min. this improvement in VO_{2max} resulted from an 8.0% increase in cardiac output (from 22.4 to 24.2 L/min) and a 3.6% increase in a-vO_{2diff} (from 138 to 143 mL/L). These findings are in keeping with the present study, given that ~66% of the increase in VO_{2max} was attributed to larger Q_{max} and ~34% to a widened maximal a-vO_{2diff} in LVVI group for adult. However, in HVVI group, the majority of the increment in VO_{2max} was relied on larger Q_{max} (~82%) whereas widened a-vO_{2diff} (~18%). It is wonder why VO_{2max} increase similarly in those groups but with different changed in Q_{max} and maximal a-vO_{2diff}; moreover, with the additional increases in exercise volume, the proportion of Q_{max} contributed more important than maximal a-vO_{2diff}. Increase in VO_{2max} after short-term, high-intensity interval training may be due to central haemodynamic (Gibala & MacInnis, 2022). Mandić studied a 10-minute exercise programme in which participants were healthy men and women who would perform all-out cycle sprints of 30s three times a week. Q_{max}, measured after training using the inert gas rebreathing method (Bostad et al., 2021), was found to increase Q_{max} by 9 per cent, with similarities to a 10 per cent increase in VO_{2max}. The authors also reported training-induced increases in plasma volume (8%), blood volume (7%) and haemoglobin volume (6%) (Mandić et al., 2022). Considering that the overall HR_{max} response was changed not significantly from baseline to 12 weeks. Thus, the majority of the improvement in Q_{max} was a consequence of a larger SV_{max} which indicate that volume of exercise is an important marker for improving SV_{max} (Nottin et al., 2012). it is possible that when increase volume in the vigorous intensity, metabolic style would change from aerobic to anaerobic, the function of body's ability to deliver and extract oxygen to meet the metabolic demands of vigorous exercise is limited (Gordon et al., 2015), which induce the relative O_2 extraction at vigorous intensity exercise was smaller and diminish oxidative capacity. Taken together, the majority of the increase in VO_{2max} observed in this study was explained by central adaptations.

In conclusion, we demonstrated that the training-induced improvement in VO_{2max} is dependent on the nature of the original exercise intensity with VO_{2max} improvements similar to both vigorous intensity groups. However, the central and peripheral mechanisms contributed to increase VO_{2max} were differences in vigorous intensity groups. In low-volume/vigorous-intensity group, Q_{max} (~66%) together with maximal a-vO_{2diff} (~34% of the improvement) contributed to the greater VO_{2max}. However, in high-volume/vigorous-intensity group, the majority of the increment in VO_{2max} was relied on larger Q_{max} (~82%) whereas widened a-vO_{2diff} (~18%). It

was a trend toward that higher volume exercise might confer additional benefit for Q_{max}, but the "*ceiling effect*" would be expected with further research such as long-term endurance training.

AUTHOR CONTRIBUTIONS

LJ and HQ designed the study, wrote the initial draft, and made revisions, managed data, conducted surveys, formulated methods, created visualizations, supervised, and managed the project. ZX participated in software, data curation, formal analysis, visualization, and manuscript revision. ZA and LP conducted formal analysis, supervision, validation and revision. All authors have contributed to the manuscript, approved the final version for submission, and consent to its publication in JHSE.

SUPPORTING AGENCIES

This study was supported by the key projects in the National Science &Technology Pillar Program during the Eleventh (2006BAK33B02) and Twelfth Five-year Plan Period (2012BAK21B02). Additional support was provided by National Natural Science Foundation of China (31401017) and the Ministry of Education of Humanities and Social Science, project grant (Number: 20YJA890014)

DISCLOSURE STATEMENT

No potential conflict of interest was reported by the authors.

ETHICS STATEMENT

The studies involving humans were approved by Ethics Committee of Jimei University. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/Supplementary Material and further inquiries can be directed to the corresponding author.

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