High-intensity Interval Training Enhances Hypoxia-mediated Right Cardiac Mechanics in Sedentary Men

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Abstract

Purpose: Hypoxic exposure increases right ventricular (RV) afterload by triggering pulmonary hypertension, with consequent effects on the structure and function of the right ventricle. Improved myocardial contractility is a critical circulatory adaptation to exercise training. However, the types of exercise that enhance right cardiac mechanics during hypoxic stress have not yet been identified. This study investigated how high-intensity interval training (HIIT) and moderate-intensity continuous training (MICT) influence right cardiac mechanics during hypoxic exercise (HE).

Methods: A total of 54 young and healthy sedentary males were randomly selected to engage in either HIIT (3-min intervals at 40% and 80% of VO_{2max}, n = 18) or MICT (sustained 60% of VO_{2max}, n = 18) for 30 min/day and 5 days/week for 6 weeks or were included in a control group (CTL, n = 18) that did not engage in any exercise. Right cardiac mechanics during semiupright bicycle exercise tests under hypoxic conditions (i.e., 50 watts under 12% FIO_2 for 3 min) were measured using two-dimensional speckle-tracking echocardiography.

Results: After 6 weeks of training, HIIT was superior to MICT in improving VO_{2max}. Furthermore, the HIIT group showed reduced pulmonary vascular resistance (PVR) as well as an elevated RV ejection fraction (RVEF) under hypoxia, coupled with a significant enhancement of the right atrial (RA) reservoir and conduit functions. HIIT is superior to MICT in dilating the right ventricle and ameliorating radial strain rate but reducing radial strain in either systole or diastole. In the correlation analysis, the changes in RVEF were directly associated with improved RA reservoir and conduit functions but inversely associated with the change in radial RV strain caused by HIIT.

Conclusion: HIIT is superior to MICT in improving right cardiac mechanics by simultaneously increasing RA reservoir and conduit functions and decreasing PVR during HE.

Introduction

According to the Frank–Starling mechanism, the ventricle is able to increase its force of contraction and therefore stroke volume in response to increases in venous return and hence preload. Perturbations in afterload or inotropy move the Frank–Starling curve up or down. [1] Hypoxic exposure induces pulmonary vasoconstriction and hypertension, increases right ventricular (RV) afterload, and induces changes in RV function and dimension [2,3]; consequently, it limits physical performance during exercise in healthy individuals and patients with respiratory diseases [4,5]. In this study, we used a novel methodology combining both acute hypoxic exposure and exercise stress to generate perturbations to the right ventricle.

Conventionally, it was considered that the right ventricle is exposed to volume overload only due to increased cardiac output during exercise; nevertheless, a recent study further demonstrated the presence of significant pressure overload [6,7]. Furthermore, significant volume overload may cause enlargement of

the right ventricle and right atrium [8,9] with a relatively enhanced longitudinal function in the right ventricle [10], whereas RV pressure overload primarily affects radial shortening and induces changes in fiber orientation in the right ventricle [11-13]. Although most studies have focused on the longitudinal motion of the right ventricle, current data suggest that radial motion seems to be a key indicator to assess RV pump function as well [13]. In the concept of mixed hemodynamic RV overload in exercise, these effects can be distinct in different exercise regimens and may also induce functional remodeling. However, few studies have elucidated the distinct effects of different training regimens on radial or longitudinal RV mechanics.

Endurance training is a valuable approach to the management of pulmonary-related disease by augmenting pulmonary vasodilatation [14]. High-intensity interval training (HIIT) has recently been demonstrated to significantly attenuate RV dysfunction and reverse RV hypertrophy in a rat model of pulmonary hypertension [15]. However, although several human studies have focused on the left heart, only a few studies have focused on the right heart in association with endurance exercise. Moreover, an effective training strategy that enhances right cardiac mechanics during hypoxic exercise (HE) has not yet been established.

Typically, right cardiac performance is assessed by echocardiography under normoxic environments, which only displays chamber size and wall motion by speckle-tracking echocardiography (STE) with normal estimated pulmonary vascular resistance (PVR) [16]. To comprehensively explore the distinctive mechanical responses to mixed hemodynamic RV overload following various exercise interventions, exercise stress echocardiography (ESE) [17] with STE was performed in a 12% FiO_2 hypoxic environment.

In this study, we hypothesize that acute HE would provoke volume load to enhance RV contractility in longitudinal motion, whereas after 6 weeks of interventions, HIIT, resulting in a significantly dilated right ventricle, would be superior to MICT in diminishing PVR and enhancing RA functions, which further affects the right ventricle in both radial and longitudinal motions. This study aimed to compare the effectiveness of HIIT and MICT in improving right cardiac mechanics during HE. It comprehensively clarified how HIIT (3-min intervals at 40% and 80% of maximal O_2 consumption (VO_{2max}) or MICT (sustained 60% of VO_{2max}) for 6 weeks affected right cardiac mechanics at rest or during HE in sedentary men using STE-ESE.

Results

Cardiopulmonary fitness in normoxia

No significant difference in anthropometric parameters or functional capacity among the three groups was found at the onset of the study (Table 1). After the six-week interventions, either HIIT or MICT significantly increased stroke volume (SV) and decreased mean arterial pressure (MAP) and total peripheral resistance (TPR) at rest in normoxic conditions ($P < 0.05$, Table 1). Moreover, these two exercise groups demonstrated improved cardiopulmonary fitness by increased work rates, V_E, and VO_2 at the ventilation threshold and peak exercise performance ($P < 0.05$, Table 1). However, HIIT led to a greater

improvement in aerobic capacity (VO_{2max}) than MICT ($P < 0.05$, Table 1). No significant changes in cardiopulmonary responses to CPET were observed after 6 weeks in the CTL group (Table 1).

Conventional echocardiographic parameters in hypoxia

Under hypoxic conditions, both HIIT and MICT simultaneously lowered TPR and PVR at rest; moreover, only HIIT further decreased RV afterload, PVR_{ex} and $RVSP_{ex}$ during HE ($P < 0.05$, Table 2). Although both types of training augmented the tricuspid E wave, HIIT was superior to MICT. Furthermore, only HIIT significantly elevated RVEF ($P < 0.05$, Table 2). No significant changes in echocardiographic parameters were observed after 6 weeks in the CTL group (Table 2).

RA functions

Before interventions, acute HE increased reservoir and conduit volumes and decreased the booster volume in the right atrium ($P < 0.05$, Fig. 1A-1C). Following the 6-week interventions, HIIT induced increases in RA reservoir (Fig. 1A) and conduit volumes (Fig. 1A and 1B), while MICT ameliorated only RA reservoir volume during HE. No changes in RA volumes occurred at rest or during HE after 6 weeks in the CTL group.

Area and dimensions of the right ventricle under hypoxia

A bout of acute HE augmented RV FAC% by reducing the systolic RV area (Fig. 1E-1F) in RVD3 (longitudinal) (Fig. 2G-2I). Following the 6-week intervention, HIIT was superior to MICT in enhancing FAC% by a greater diastolic RV area (Fig. 1D and 1F). Figure 2 further shows details of the dimensions of the right ventricle at rest and during HE. A significantly enlarged right ventricle was observed in the HIIT group, as demonstrated by a longer diastole of RVD1 (basal) and RVD2 (middle), when compared to the MICT and CTL groups (Fig. 2A and 2D). Moreover, compared with no exercise, HIIT led to shorter systoles in both RVD2 and RVD3 during HE ($P < 0.05$, Fig. 2D and 2G).

Strain and strain rate (SR) in the right atrium and right ventricle under hypoxia

Before the interventions, acute HE enhanced both RV longitudinal strain and SR while reducing radial strain ($P < 0.05$, Table 4). In addition, in the right atrium, both radial and longitudinal strain and SR were increased under HE ($P < 0.05$, Table 3). Following the 6-week interventions, both HIIT and MICT augmented RA radial strain and systolic/diastolic SR at rest or during HE, whereas only HIIT increased RA longitudinal strain and systolic SR during HE ($P < 0.05$, Table 3). On the other hand, although HIIT, but not MICT, decreased RV radial strain, the systolic/diastolic SR was ameliorated ($P < 0.05$, Table 4). Moreover, no significant changes were found in radial/longitudinal strain and systolic/diastolic SR in the right atrium or right ventricle at rest or during HE after 6 weeks in the CTL group ($P < 0.05$, Tables 3 and 4).

Relationship between HE-induced changes in right cardiac mechanical variables following interventions

Here, the change indicates the difference between pretraining and posttraining. No significant resting relationship was observed between RA volumes and RVEF following either intervention (Fig. 3A to 3C). However, HE-induced changes in the RA reservoir (Fig. 3A; r = 0.60, $P < 0.05$) and conduit volumes (Fig. 3B; r = 0.64, $P < 0.01$) were positively associated with RVEF after HIIT. Furthermore, the HE-induced change in RV radial strain was negatively correlated with the RVEF change in the HIIT group (Fig. 3D; r = −0.70, $P < 0.01$). Additionally, in the HIIT group, both resting (Fig. 3F; r = −0.77, $P < 0.01$) and HE-induced changes in PVR (Fig. 3F; r = −0.70, $P < 0.01$) were inversely associated with RVEF. However, no significant correlations were found between HE-induced changes in RVEF and RV longitudinal strain following HIIT (Fig. 3E). In contrast to the HIIT group, no significant correlations were observed among RA reservoir, conduit, and booster pump functions; radial/longitudinal strains and SRs in the right ventricle; and PVR at rest or during HE in the MICT or CTL groups (Fig. 3).

Test-retest reliability

The intraobserver ICC and CV% were 0.89 (0.74~0.95) and 7.9 (7.6–8.2), respectively, for radial strain, whereas they were 0.93 (.83~0.97) and 5.7 (5.2–6.2), respectively, for longitudinal data (see Supplementary Fig. S1 online). In addition, the Cronbach alpha value was 0.94 for radial motion and 0.95 for longitudinal motion. Supplementary Fig. S2 shows the Bland-Altman plots and correlation dot plots for descriptive purposes.

Discussion

This is the first investigation to clarify the effects of various exercise regimens on right cardiac mechanics during HE using 2D-STE technology. Both HIIT and MICT improve RA reservoir function, while only HIIT enhances RA conduit function to reinforce RV preload. Therefore, HIIT is more efficient than MICT in dilating the chamber of the right ventricle by ameliorating radial SR but reducing radial strain in either systole or diastole. Although both interventions lessen resting RV afterload, PVR and RVSP, only HIIT further diminishes PVR under HE. Notably, the correlation analysis further demonstrated that an augmented RVEF is significantly associated with greater RA reservoir and conduit functions and lower PVR following HIIT.

The atrium tends to dilate in response to greater venous return or chronic elevations in ventricular filling pressure when exercising [18]. However, the elevated RA afterload caused by acute hypoxic exposure may cause the ratio of passive reservoir to active contraction to decline [19]. In our longitudinal study, both HIIT and MICT for 6 weeks enhanced reservoir function even during HE to accommodate more venous return. These results correspond with a cross-sectional investigation, i.e., highly dynamic athletes had larger RA reservoir functions for venous return and more blood filling into the right ventricle than less dynamic athletes [20]. As the enhanced tricuspid E wave represented, the ameliorated conduit function in HIIT accelerated RV early filling and enhanced RV preload even under hypoxic stress [21].

Because of the higher cardiac output demand in the HIIT, volume load-related remodeling may be increased in the HIIT group compared with that in the MICT group [22]. Although most studies have focused on longitudinal motion to generate RV ejection, our study further confirmed that RV dilation primarily occurred in the radial direction instead of the longitudinal direction. Elevated radial motion influences systolic function via the bellows effect because the free wall of the right ventricle has a larger surface than the tricuspid annular cross-sectional area [23]. Therefore, we speculated that the improvement of ejection fraction during HE is related with not only longitudinal but also radial motion.

Interestingly, suppressed RV radial strain at the onset of HE and following HIIT was noticed. This is in contrast to the traditional viewpoint of enhancing longitudinal strain as the key contributor to overall RV contractility under RV overloading [12]. Regarding RV dilation, the reduced radial strain is considered to further increase wall tension. In this case, we believe that the significantly reduced HE-related PVR and dilated right ventricle in HIIT are accommodations to overcome this situation. Briefly, these findings may represent a consequence of RV remodeling rather than dysfunction in healthy young men. In fact, our findings are partly similar to athletes' heart characteristics, with a relative decrease in radial shortening with greater RV enlargement and better RVEF [24,25].

The augmented RV radial strain rate (SR) in the HIIT group may indicate a greater RV contractile efficiency by homeometric autoregulation in response to the decreased radial strain. SR is relatively more independent of HR, structure, and loading conditions than strain and diameter [26]. Hence, SR might better reflect the training responses and appears to be the more accurate parameter in myocardial contractility, especially during exercise [27]. In addition to the context of loading and structure, in some hypoxia-susceptible patients, RV dysfunction has been suggested to be caused by a direct negative inotropic effect of hypoxia on cardiac myocytes and decreased oxygenation [28]. Although the comparison of effects of normoxia and hypoxia on cardiac mechanics is not the main aim of this study, we focused on the fact that both RV diastolic and systolic functions were augmented when facing both exercise and loading stresses after 6 weeks of exercise training.

An elevated PVR is a well-known physiological response to hypoxia [29]. In this investigation, both HIIT and MICT reduced PVR and subsequently decreased RV afterload, thereby improving RVEF in resting conditions. The PVR and RVSP were further reduced during HE in HIIT, thus additionally lowering the afterload when the right ventricle contracted. Previous studies demonstrated that exercise training upregulated endothelial eNOS expression in the pulmonary vasculum [30]. Hassel et al. further revealed that HIIT reduced the muscularization of pulmonary vessels and subsequently attenuated RV dysfunction in COPD mice [15].

The fixed absolute exercise intensity used in HE is due to the concern about the influence of HE on an altered loading state by the different VO_{2max} after training. Therefore, our intention is to compare the relative change before and after the intervention rather than the absolute data. In addition, our previous study demonstrated that this protocol is feasible to clarify the LV mechanics during HIIT and MICT [31].

Limitations Of The Study

As observed in other investigations, the number of men who are young, healthy, and sedentary is limited. Thus, additional clinical evidence is required to extrapolate the present results to patients with abnormal cardiovascular systems, such as those with pulmonary hypertension or right HF, and to analyze potential sex differences [32].

Because of the thin walls of the right ventricle, the image quality might have highly influenced the accuracy of our detection. Although our test-retest reliability indicates good imaging quality, it is still important to note the limitations of 2D-STE [33].

The noninvasive estimation of PVR might not have obtained true absolute data. However, it has been reported that the estimate has an error margin of < 10% relative to the real pressure [34]. Furthermore, using noninvasive echocardiography is more ethical than using invasive catheterization under dynamic conditions, with a much lower risk for the study participants [35].

The MICT exercise volume is speculated to have been too low to exert a positive effect on cardiac hemodynamic adaptation. The plurality of the positive MICT results suggested that exercise training at least 5 days weekly up to six times daily for a period of at least 12 weeks is necessary [36].

Conclusion

Typically, right cardiac performance is assessed by echocardiography under normoxic environments, which displays only the chamber size and myocardial motion with a normal PVR. This study further contributes to a greater understanding of RV and RA mechanical responses to hypoxic stress following various exercise interventions by using STE-ESE. The experimental results clearly demonstrate that HIIT with a dilated right ventricle enhances RVEF by increasing the RA reservoir and conduit functions, enhancing RV radial strain rate and decreasing PVR. These findings provide novel insights into the superior effects of HIIT on contractile efficiency of the right heart during HE by simultaneously increasing preload and decreasing afterload, which might have important implications for exercise training in cardiopulmonary rehabilitation.

Methods

Subjects

The investigation was performed in accordance with the principles of the Declaration of Helsinki and was approved by the Institutional Review Board of the Chang Gung Memorial Hospital in Taiwan. A total of 54 sedentary males were recruited. We recruited males who were nonsmokers; did not take medications or vitamins; did not have any cardiopulmonary/hematological risks; and, most importantly, had a sedentary lifestyle (without regular exercise; exercise frequency ≤ once weekly, duration < 20 min). Informed consent was obtained from all subjects after the experimental procedures were explained. These subjects

were randomly divided into the HIIT (n = 18), MICT (n = 18), and control (CTL, n = 18) groups. All subjects arrived at the testing center at 9:00 AM to eliminate any possible circadian effect.

Training protocols

Both the HIIT and MICT groups performed exercise regimens on a stationary bicycle ergometer (Corival 400, Lode) 5 times a week for 6 weeks. For comparison, the CTL group did not undergo any exercise, but their physical activity and daily diet were carefully monitored and recorded. HIIT subjects warmed up for 3 min at 30% VO_{2max} before five cycles, and each cycle included 3 min at 80% VO_{2max} with a 3-min active recovery period at 40% VO_{2max}. Finally, the session was terminated with a 3-min cool-down at 30% VO_{2max}. The MICT group underwent the same warm-up and cool-down phases as the HIIT group, but the training periods were 30 min at 60% VO_{2max}. Both training protocols were isovolumetric with the same duration (i.e., HIIT exercise volume: {6 min [40% VO_{2max} + 80% VO_{2max}] × 5 cycles} = MICT exercise volume: 30 min [60% VO_{2max}]). To achieve the desired exercise intensity, each subject used a heart rate (HR) monitor (Tango, SunTech Medical). During the exercise, the work rate of the bicycle ergometer was continuously adjusted to match the exercise intensity with the target HR. The percentage of HR reserve (%HRR) is widely considered to be equivalent to the percentage of VO2 reverse for exercise prescription purposes. Accordingly, the target HR of HIIT and MICT were calculated using the following equations:

Peak HR = 220 − age (1)

%HHR = % (peak HR − resting HR) + resting HR (2)

Target HR of HIIT = 3 − minute intervals at 40% HHR and 80% HRR (3)

Target HR of MICT = sustained 60% HRR (4)

The groups were asked to record their daily activities and nutritional intake using the short form of the International Physical Activity Questionnaire and a written diet record, respectively. Subjects were asked to refrain from regular extra exercise until the end of the study. Moreover, all subjects completed the experiments with a participant compliance rate of 100%.

Cardiopulmonary exercise test

To assess aerobic capacity, a cardiopulmonary exercise test (CPET) on a cycle ergometer (Corival 400, Lode B.V., Netherlands) was performed 2 days before and after the intervention, which is sufficient to recover CO following HE [37]. All subjects underwent exercise using a face mask to measure min ventilation (VE), oxygen consumption (VO_2), and carbon dioxide production (VCO_2) breath by breath using a computer-based system (MasterScreen CPX, CareFusion, USA). After a 5-min baseline resting period, a 2-min warm-up period (60 rpm, unloaded pedaling) was initiated, followed by incremental work (30 W elevation for each 3 min) until exhaustion (i.e., progressive exercise to VO_2). The criteria used to define VO_2 were as follows: (i) the level of VO_2 increased by <2 mL/kg/min over at least 2 min; (ii) HR exceeded

its predicted maximum; (iii) the respiratory exchange ratio exceeded 1.2; and (iv) the venous lactate concentration was >8 mM. These criteria were consistent with the American College of Sports Medicine guidelines for exercise testing [38]. During CPET, continuous monitoring of 12-lead electrocardiography, blood pressure, and pulse oxygen saturation was performed. In addition, the ventilation threshold was determined when VE/VO_2 increased without a corresponding increase in the VE-to-VCO_2 ratio, end-tidal PO_2 increased without a decrease in end-tidal PCO_2, or a deviation from linearity for VE.

Conventional echocardiography

A standard echocardiographic examination according to the American Society of Echocardiography guidelines was performed at each stage [39]. Each subject underwent echocardiography 4 days before and after the intervention in an air-conditioned normobaric hypoxia chamber (Colorado Mountain Room, USA) [40]. The hypoxia chamber was maintained at a temperature of 22°C ± 0.5°C with a relative humidity of 60% ± 5%; a CO_2 scrubber eliminated CO_2 in the air (< 3500 ppm), and the O_2 concentration was set at 12%, which corresponded to an altitude of 4460 m. All subjects were positioned at a 30° semiupright position oriented in a left lateral 60° semisupine position and secured to the echocardiography table (Angio with Echo Cardiac Stress Table, Lode B.V., Netherlands). The parameters were measured using the Siemens ACUSON SC2000™ ultrasound system (Siemens Healthineers, Germany) with the 4V1C probe (4.5 MHz). Images of subjects with regular breathing patterns and no breath holding were captured at end expiration. The RV outflow tract (RVOT) was obtained from a modified apical four-chamber view, and the flow immediately proximal to the pulmonary artery valve during systole was detected to calculate both maximal velocity and pulsed-wave blood VTI. Doppler imaging was used to measure peak tricuspid annular velocities through the cardiac cycle in early diastole (E') and diastolic transmitral blood flow velocities for peak early (E) fillings. Tricuspid annular plane systolic excursion was measured by placing an M-mode cursor through the tricuspid annulus and measuring peak systolic motion. The RA pressure (RAP) was estimated from the inferior vena cava (IVC) size during inspiration and during forced inhalation at rest. The IVC diameter was measured just proximal to the entrance of the hepatic veins. Pulmonary vascular resistance (PVR) was calculated using the formula PVR = ([TR velocity/RVOT VTI] × 10 + 0.16), which has shown a good correlation with invasively derived PVR [41]. All data were recorded over three cycles, and the averages were calculated. RV basal cavity diameter (RVD1), mid-cavity diameter (RVD2), RV longitudinal diameter (RVD3), and RV area at end-diastole and end-systole were evaluated in the modified apical four-chamber view, as shown in Supplementary Fig. S3 [42]. All measurements were independently recorded from three independent image frames, enabling reliable quantification.

Speckle-tracking echocardiography of hypoxic exercise (HE)

STE was immediately performed after the conventional data were collected completely under hypoxic conditions (12% FiO_2) as previously described [31]. Resting images were acquired after the subject was placed in the aforementioned position for 10 min. The exercise images were conducted using

semirecumbent cycling with a 50-W resistance for 3 min and acquired at the third minute of cycling to ensure that subjects had reached a steady-state HR (i.e., HR changes <10 bpm within 10 s and <110–120 bpm) [43]. Three consecutive cardiac cycles were evaluated for each acquisition. The 2D-STE analysis was performed offline by the same echocardiographer, who was blinded to the group allocation and image sequence, using semiautomatic strain software (ACUSON SC2000™ system, Siemens Healthineers, Germany).

A modified apical four-chamber view was used to assess STE longitudinal and radial parameters of the right ventricle and right atrium. Briefly, after manual tracing, the end-systolic RV endocardial border, a region of interest, was automatically generated; its width and position were manually readjusted to include the entire myocardial wall when it showed poor-quality tracking by visual assessment. The software automatically divides the right ventricle into a 6-segment model as a more robust analysis recommend by Muraru et al. [32], whereas the right atrium was automatically divided into a 3-segment model. The RV strain and SR were calculated using the average peak segmental values displayed by the software using a 6-segment model. The compliance rate of this study was 100%, and no subject was excluded due to inadequate images.

Volumetric analysis in RA function

RA volumes were assessed offline using semiautomatic strain software (Siemens ACUSON SC2000™ ultrasound system, Siemens Medical Solutions USA Inc., Mountain View, CA) on dedicated 2D-STE sets in the apical four-chamber view. The border-tracing process was similar to the abovementioned STE protocol. RA maximum volume (RA_{max}) was detected at the end of LV systole just before mitral valve opening, and RA minimum volume (RA_{min}) was acquired at the end of LV diastole just after mitral valve closure. Atrial function is most often assessed using 2D volumetric analysis, such as reservoir, conduit, and booster pump functions. The volume immediately before atrial contraction (onset of P wave) is denoted as $RA_{pre\text{-}a}$, which represents the preload before atrial contraction. Figure 4 shows the schematic RA time-volume curve.

(1) **Reservoir volume**: the filling or expansion volume, calculated as $RA_{max} - RA_{min.}$

(2) **Conduit volume**: the passive emptying volume from venous return during early ventricular diastole, calculated as $RA_{max} - RA_{pre\text{-}a}$.

(3) **Booster volume**: the RA stroke volume (SV), calculated as $RA_{pre\text{-}a} - RA_{min.}$

Test-retest reliability

A subgroup (n = 20) was assessed for test-retest variability in RV radial and longitudinal strains. Each participant had two separate echocardiograms using the same set of 2D-STE images under normoxic conditions that were approximately 24 hours apart to reduce the impact of physiological variation. The echocardiographer was blinded to the original images and used a standard echocardiographic protocol

for each acquisition. Offline analyses were randomized by the same echocardiographer and performed using available software (Siemens ACUSON SC2000™ ultrasound system, Siemens Medical Solutions USA Inc., Mountain View, CA) [44].

Statistical analysis

Quantitative data were expressed as the mean ± SEM. Data analysis was performed using IBM SPSS Statistics V22.0. Experimental results were analyzed by repeated-measure ANOVA and Bonferroni post hoc tests to compare aerobic capacity and cardiac mechanics at the beginning of the study and after 6 weeks of intervention. Linear regression analyses were performed using Pearson's method to assess univariate associations between echocardiographic data. Intra-reproducibility was assessed using the intraclass correlation coefficient (ICC), coefficient of variance (CV), and Cronbach alpha value [45]. The threshold for statistical significance was set at $P < 0.05$.

Declarations

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AUTHOR CONTRIBUTION

J.S. Wang and Y.C. Huang were involved in conception and design of research; Y.C. Huang performed experiments; J.S. Wang and Y.C. Huang analyzed data, interpreted results of experiments, prepared the Figures and drafted the paper; J.S. Wang and Y.C. Huang edited and revised the paper; J.S. Wang, Y.C. Huang, C.C. Hsu, and T.C. Fu approved the final version of paper.

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Tables

Due to technical limitations, table 1-4 is only available as a download in the Supplemental Files section.

Figures

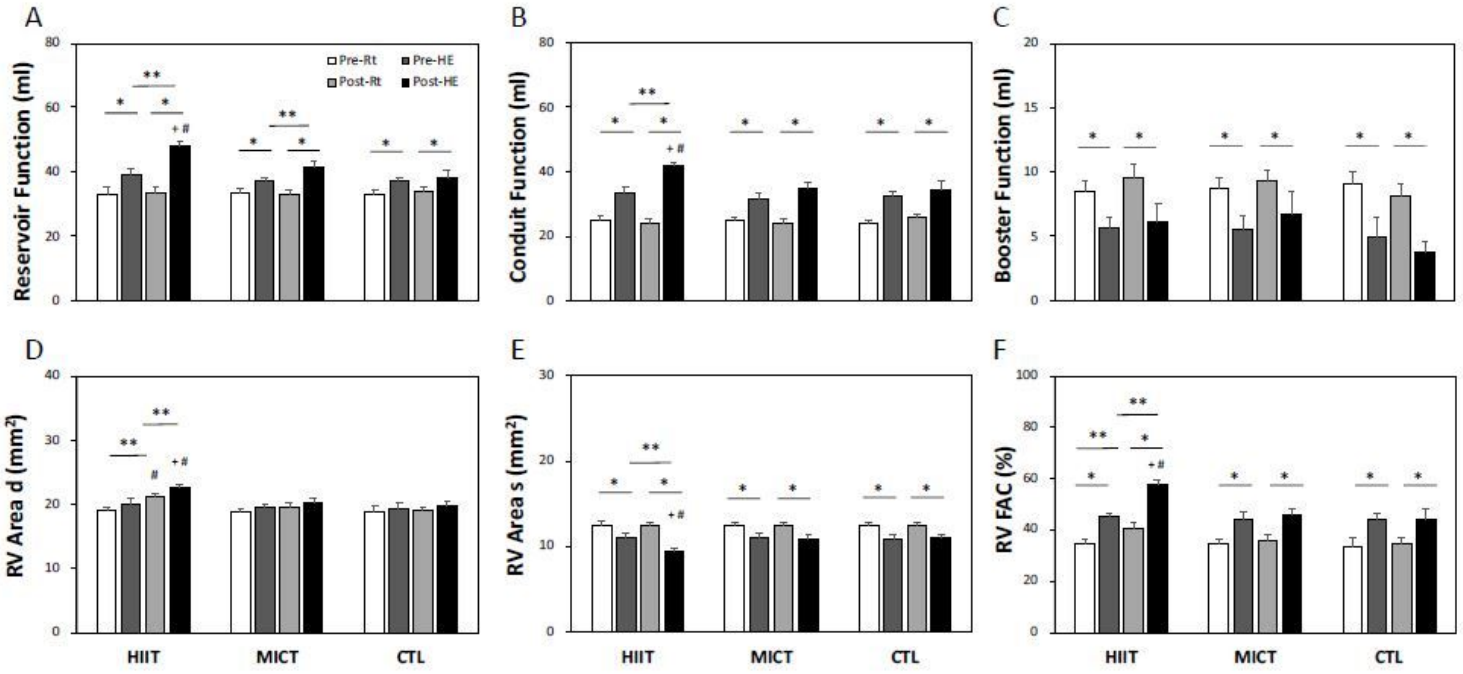
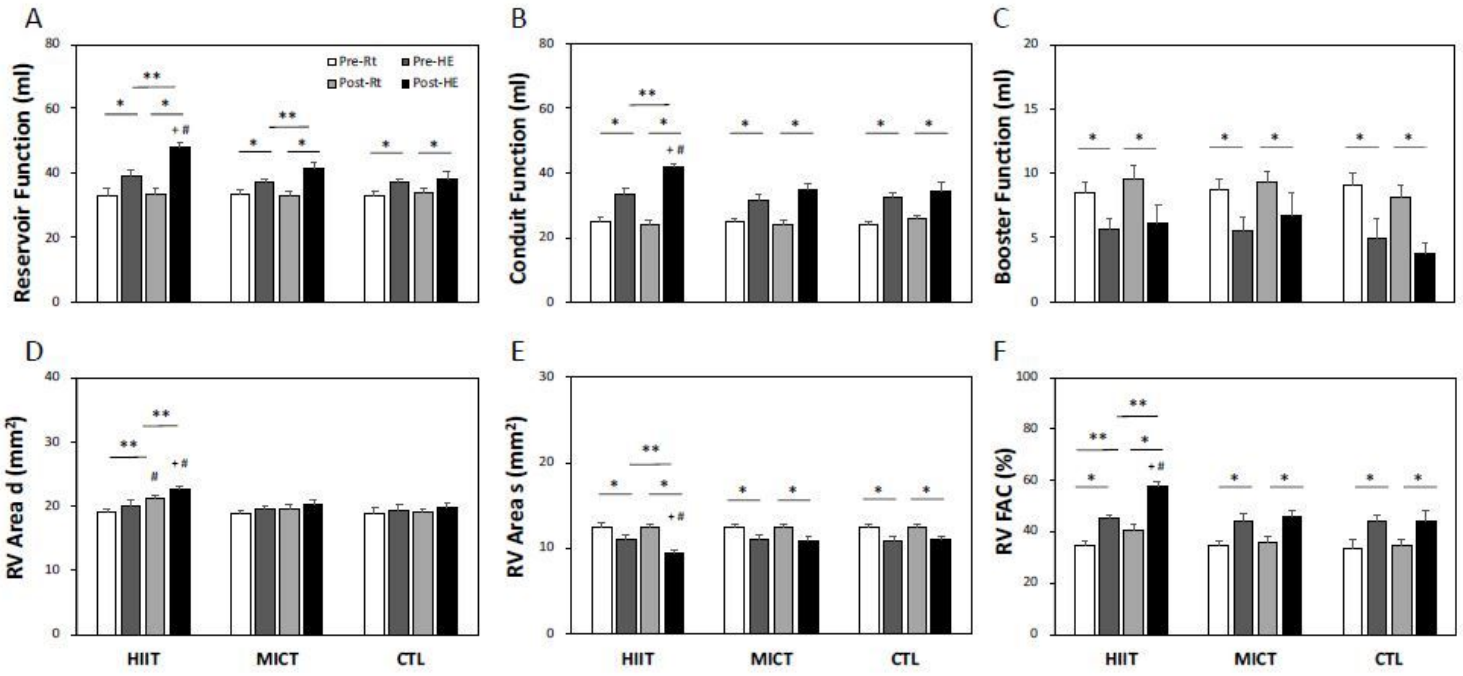


Figure 1

Comparisons of the effects of various exercise regimens on RA volumes and RV area parameters at rest or during HE. (A) Reservoir function; (B) Conduit function; (C) Booster function; (D) RV area in end-diastole; (E) RV area in end-systole; (F) RV fractional area change (FAC). HIIT, high-intensity interval training group; MICT, moderate-intensity continuous training group; CTL, control group; Pre-Rt, resting before the intervention; Pre-HE, during HE before the intervention; Post-Rt, resting after the intervention; Post-HE, during HE after the intervention. Values are the mean±SEM. * P<0.05, Rt vs. HE; ** P<0.05, Pre vs. Post; + P<0.05, HIIT vs. MICT; # P<0.05, HIIT or MICT vs CTL.



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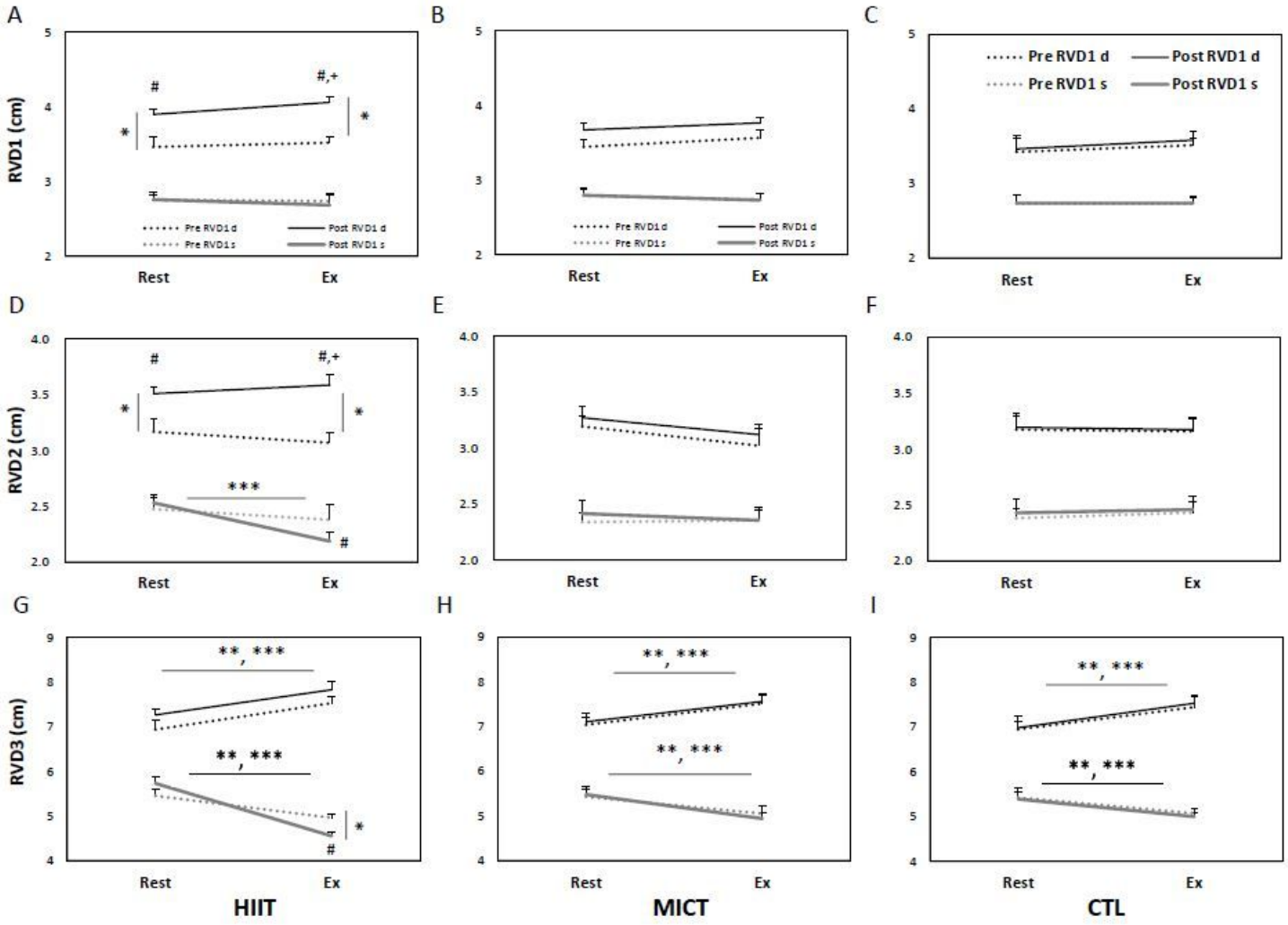
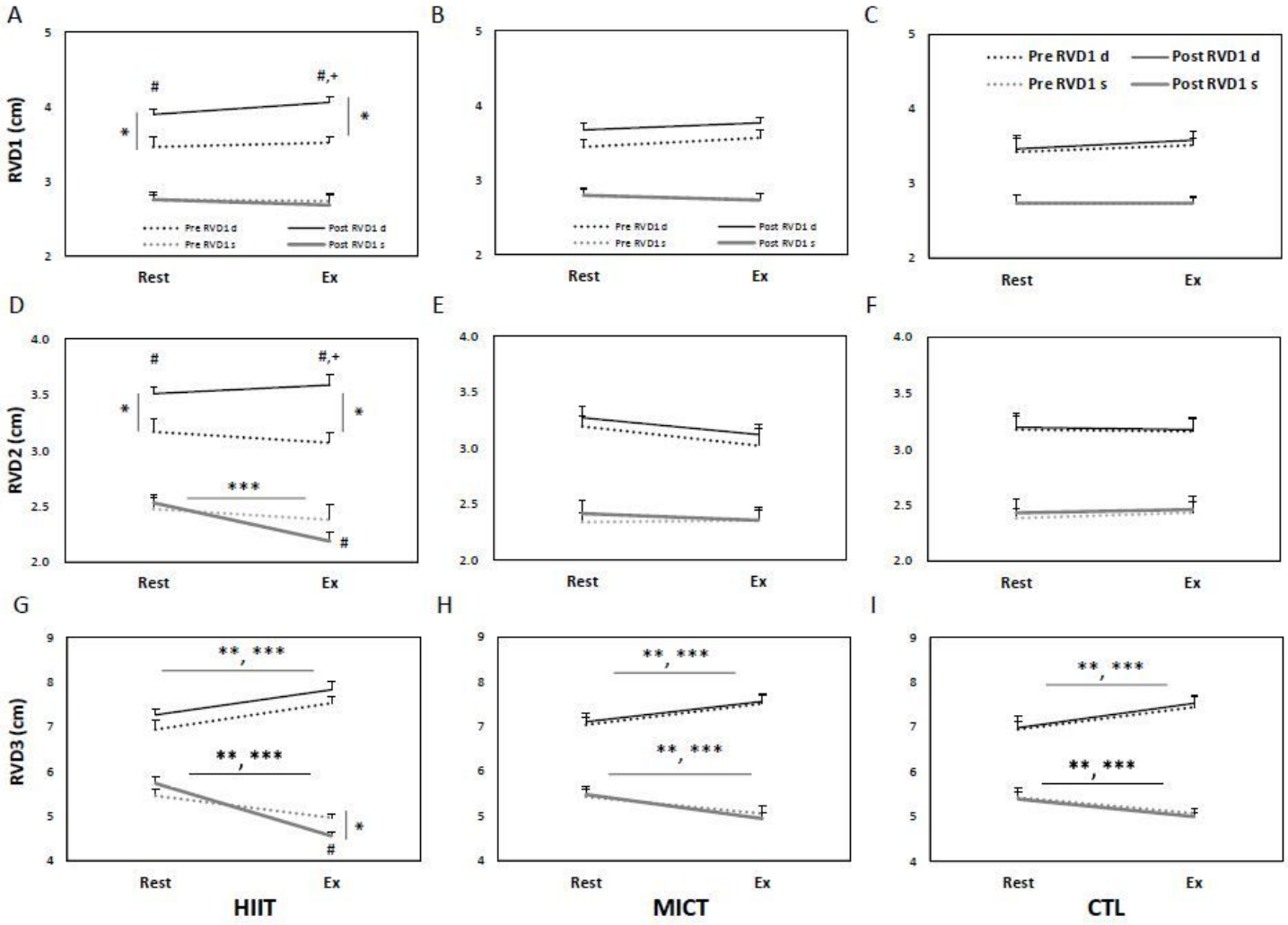


Figure 2

Comparisons of the effects of various exercise regimens on RV dimensions at rest or during HE. (A) RVD1 in HIIT; (B) RVD1 in MICT; (C) RVD1 in CTL; (D) RVD2 in HIIT; (E) RVD2 in MICT; (F) RVD2 in CTL; (G) RVD3 in HIIT; (H) RVD3 in MICT; (I) RVD3 in CTL. HIIT, high-intensity interval training group; MICT, moderate-intensity continuous training group; CTL, control group; Pre RVD d, RVD in end-diastole before training; Post RVD d, RVD in end-diastole after training; Pre RVD s, RVD in end-systole before training; Post RVD s, RVD in end-systole after training. Values are the mean±SEM. * P<0.05, Pre vs. Post; ** P<0.05, Pre-Rt vs. Pre-HE; *** P<0.05, Post-Rt vs. Post-HE; + P<0.05, HIIT vs. MICT; # P<0.05, HIIT or MICT vs CTL.



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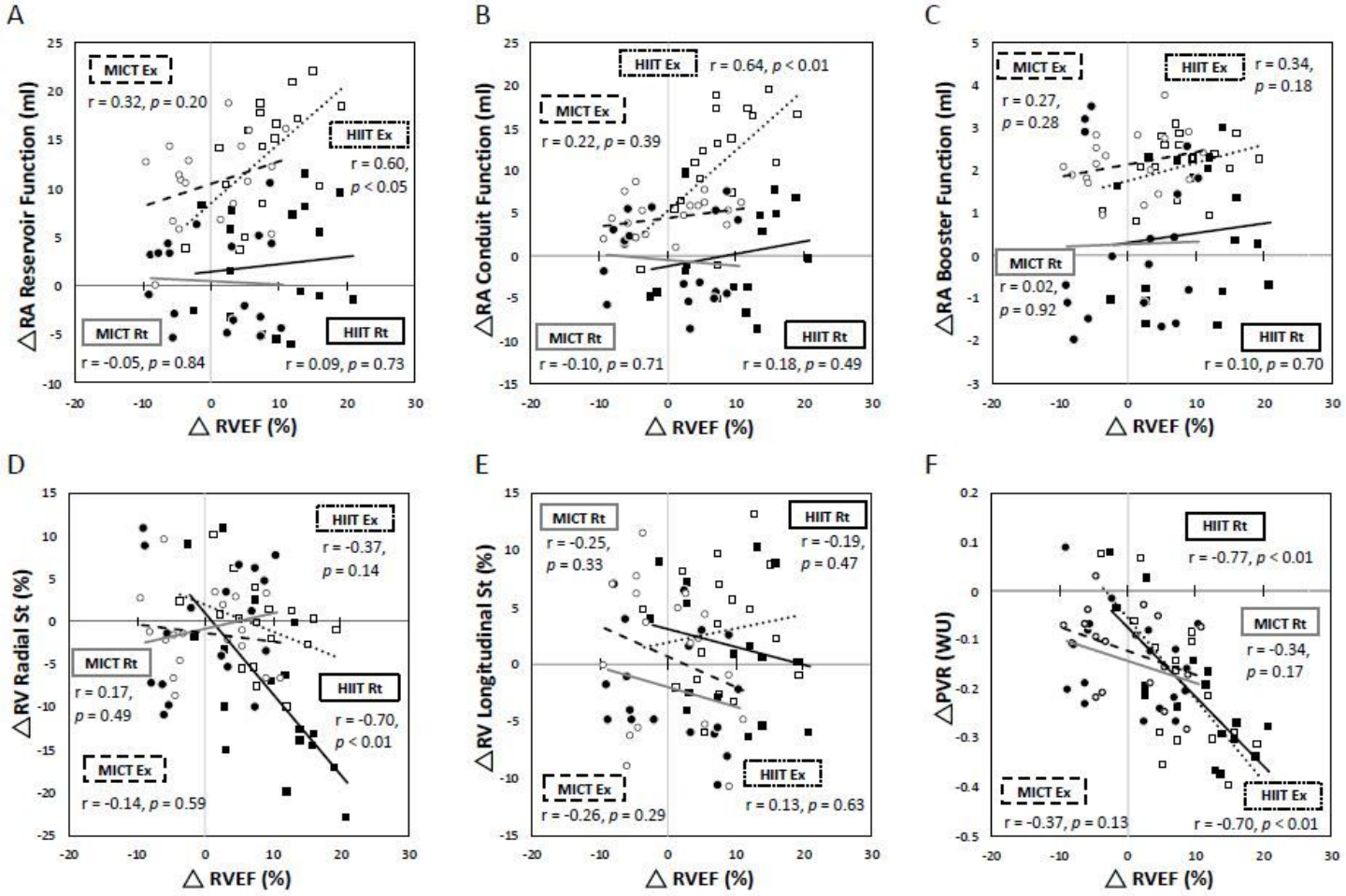
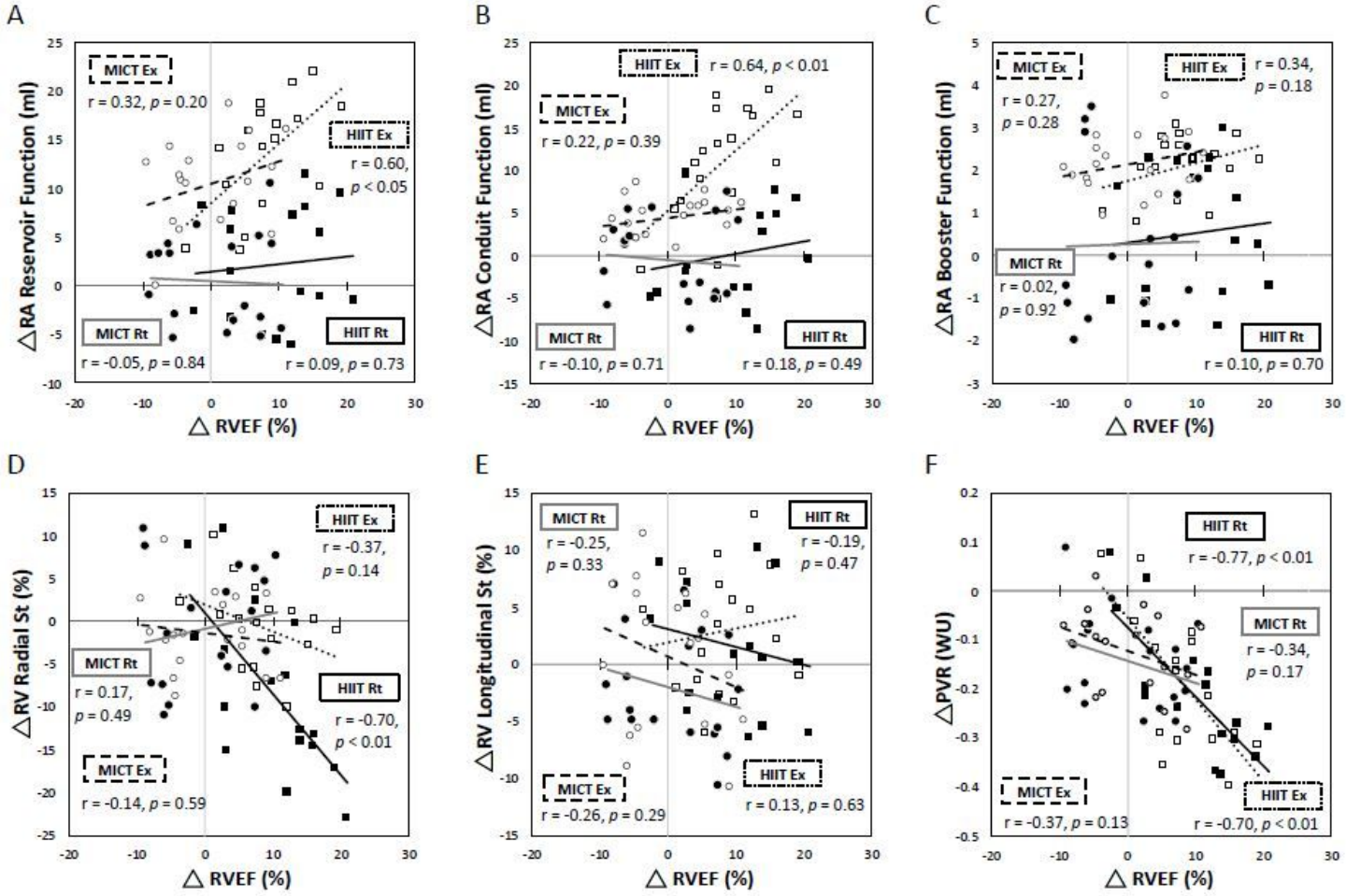


Figure 3

Correlations between changes in RVEF and RA functions, RV mechanics and PVR at rest or during HE following various interventions. RA, right atrium; RV, right ventricle; HIIT, high-intensity interval training group; MICT, moderate-intensity continuous training group; Ex, during HE; Rt, at rest. RVEF, right ventricle ejection fraction; St, strain; PVR, pulmonary vascular resistance. ●(closed circles), MICT Rt; ● (open circles), MICT Ex; ■ (closed squares), HIIT Rt; □(open squares), HIIT Ex; Δ, postintervention minus preintervention. The solid line indicates the trend line of HIIT Rt; the dotted line indicates the trend line of HIIT Ex; the gray line indicates the trend line of MICT Rt; and the dashed line indicates the trend line of MICT Ex.



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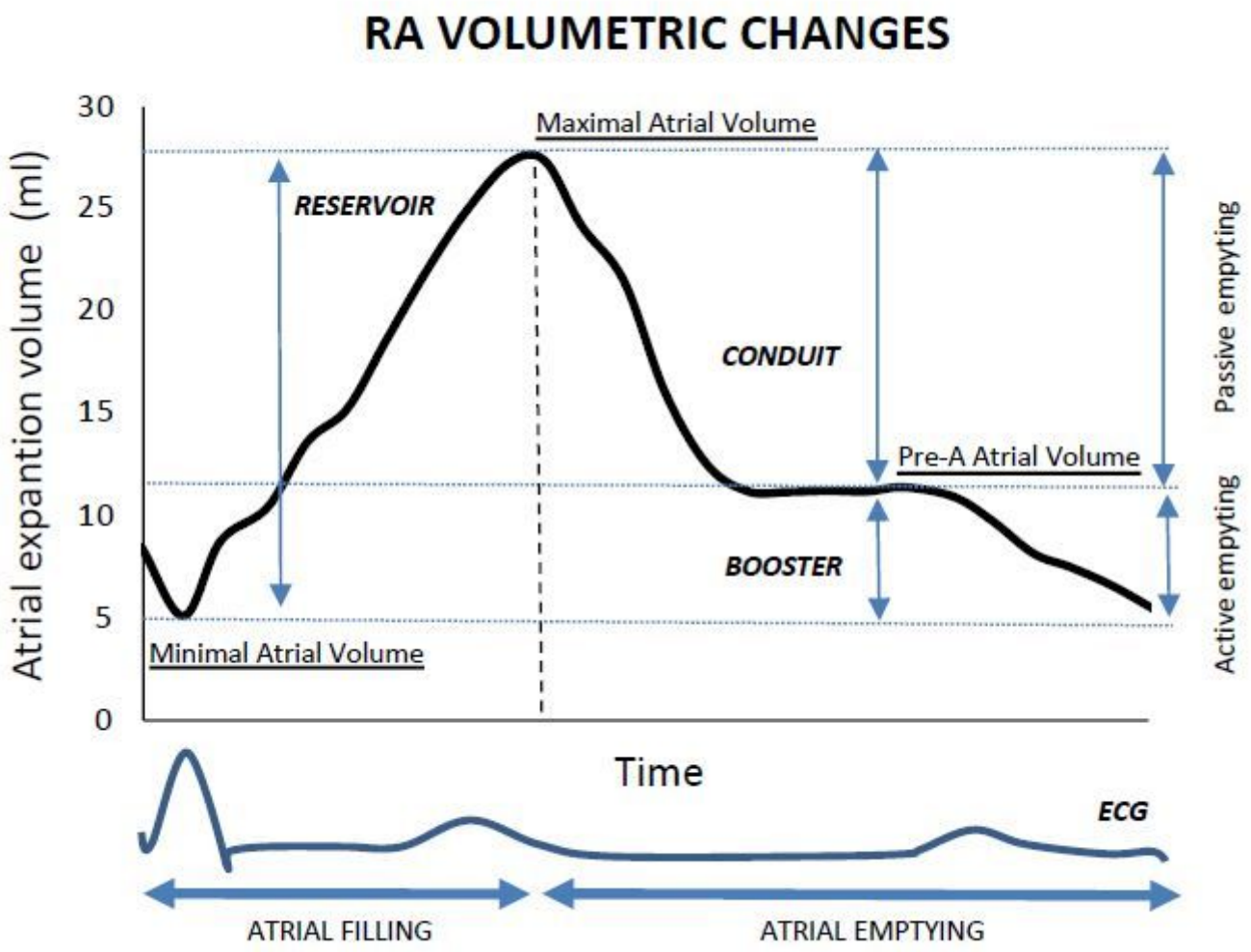
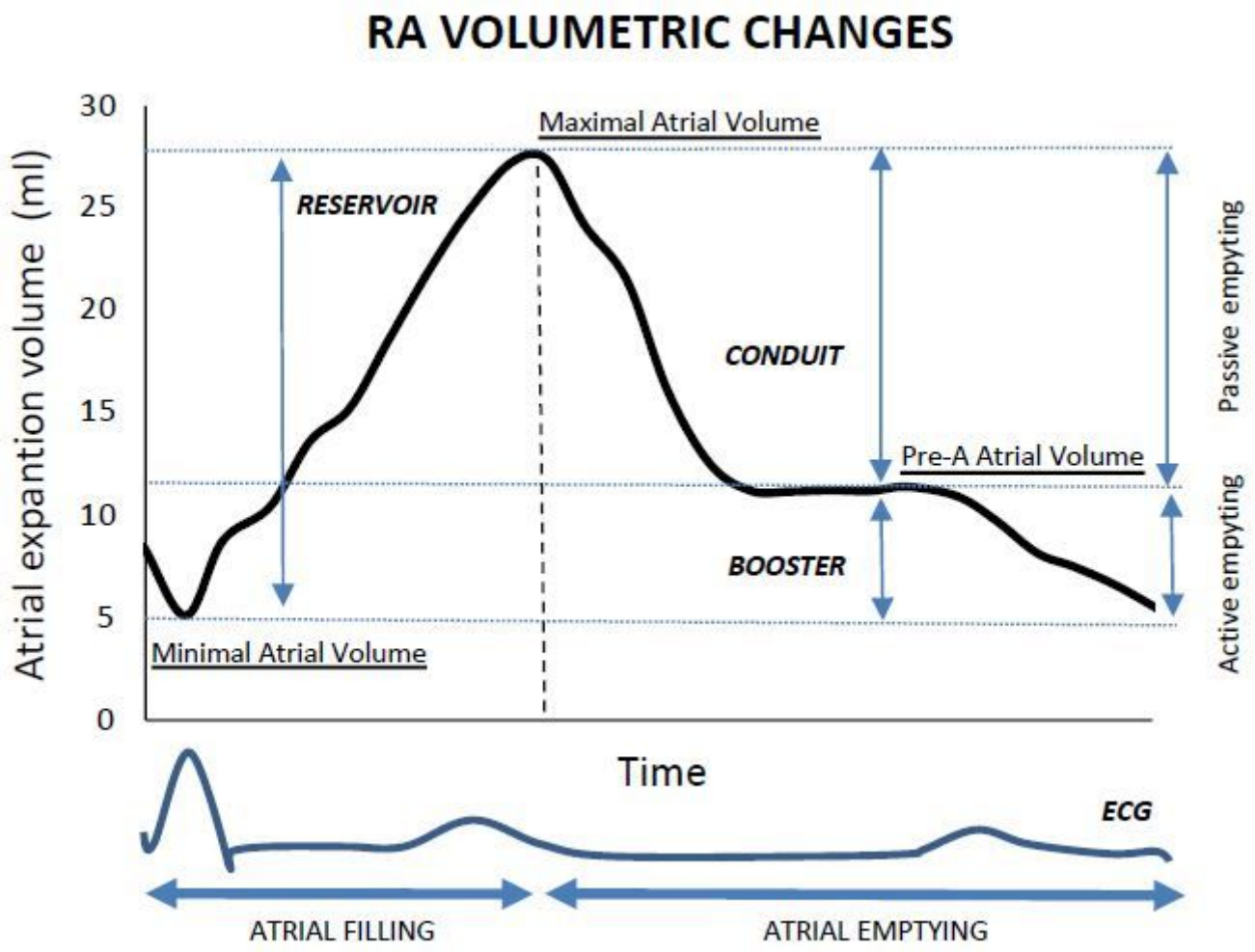


Figure 4

Schematic RA time-volume curve. RA time-volume curve with the assessment of parameters of atrial function. Reservoir, conduit, and booster volumes are calculated from atrial volumes at special time points. Reservoir function=Vmax-Vmin; Conduit function=Vmax-Vpre-A; Booster function=Vpre-A-Vmin; RV Vmax, maximum RV volume; RV Vmin, minimum RV volume; Pre-A: preatrial contraction.



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