

Review Article

High-intensity interval training and hypertension: maximizing the benefits of exercise?

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Abstract: Essential arterial hypertension is the most common risk factor for cardiovascular morbidity and mortality. Regular exercise is a well-established intervention for the prevention and treatment of hypertension. Continuous moderate-intensity exercise training (CMT) that can be sustained for 30 min or more has been traditionally recommended for hypertension prevention and treatment. On the other hand, several studies have shown that high-intensity interval training (HIT), which consists of several bouts of high-intensity exercise (~85% to 95% of HR_{MAX} and/or VO_{2MAX} lasting 1 to 4 min interspersed with intervals of rest or active recovery, is superior to CMT for improving cardiorespiratory fitness, endothelial function and its markers, insulin sensitivity, markers of sympathetic activity and arterial stiffness in hypertensive and normotensive at high familial risk for hypertension subjects. This compelling evidence suggesting larger beneficial effects of HIT for several factors involved in the pathophysiology of hypertension raises the hypothesis that HIT may be more effective for preventing and controlling hypertension.

Keywords: Exercise, hypertension, autonomic nervous system, endothelial function, arterial stiffness

Introduction

Essential arterial hypertension is the most common risk factor for cardiovascular morbidity and mortality, affecting approximately one billion individuals worldwide, and is associated with substantial health care expenditure [1, 2]. The association between blood pressure (BP) and greater incidence of cardiovascular disease (CVD) begins with BP levels as low as 115/75 mmHg, and doubles for each 20/10 mmHg increase in systolic/diastolic BP [3].

Regular exercise is a well-established intervention for the prevention and treatment of several chronic diseases, including hypertension [4, 5]. Higher levels of physical activity and cardiorespiratory fitness have shown to reduce the risk of hypertension in healthy normotensive persons [6, 7]. Moreover, exercise can reduce BP in hypertensive adults [8-11], and has shown to improve several factors involved in the pathophysiology of hypertension [11-15].

Continuous moderate-intensity exercise training (CMT) that can be sustained for 30 min or more

has been traditionally recommended for hypertension prevention and treatment [4, 5]. However, several studies have shown that high-intensity interval training (HIT), which consists of several bouts of high-intensity exercise (~85% to 95% of HR_{MAX} and/or VO_{2MAX}) lasting 1 to 4 min interspersed with intervals of rest or active recovery [11, 14, 15], is superior to CMT for improving cardiorespiratory fitness [13-15], endothelial function and its markers [13, 15], insulin sensitivity [15], markers of sympathetic activity [13, 14], arterial stiffness [11, 13], and blood glucose and lipoproteins [15] in hypertensive patients and normotensive individuals at high familial risk for hypertension. Because these greater HIT-derived benefits for preventing and controlling hypertension occurred with thrice-weekly exercise programs, and lack of time is one of most cited barriers for not exercising [16], prescribe HIT may have important implications for exercise compliance.

The purpose of present manuscript is to discuss the compelling evidence suggesting larger beneficial effects of HIT for several factors involved in the pathophysiology of hypertension, which

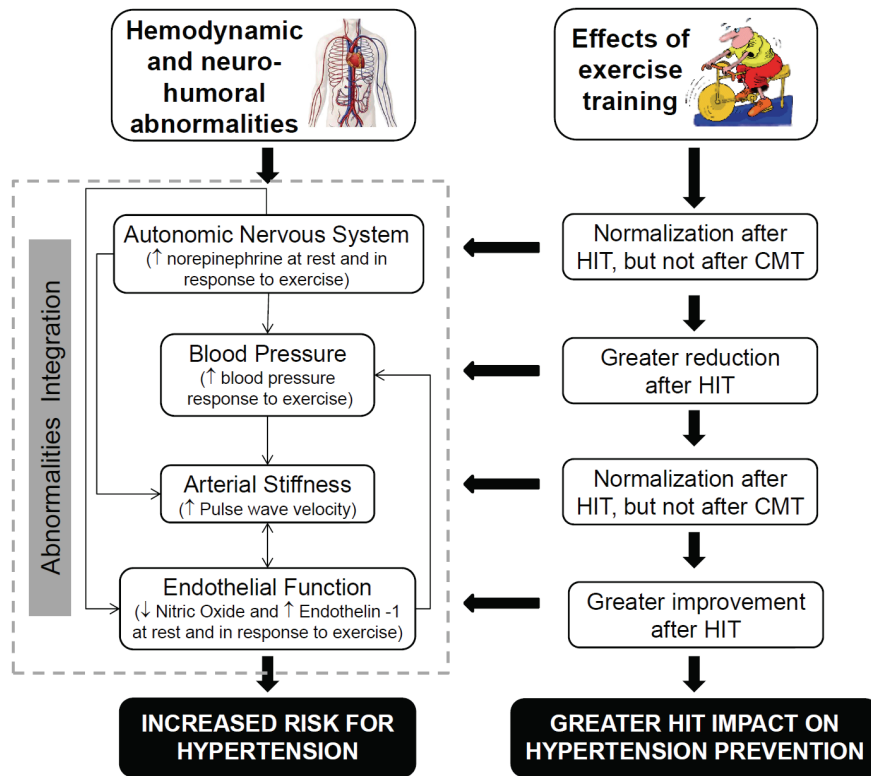


Figure 1. Schematic representation of key abnormalities (and their integration) of young normotensive individuals at high familial risk for hypertension, the effects of exercise training (HIT vs. CMT), and the implications for hypertension prevention. Adapted from [13, 14, 27]. HIT, high-intensity interval training. CMT, continuous moderate-intensity training.

support the hypothesis that HIT may be more effective for preventing and controlling hypertension.

Effects of HIT on cardiorespiratory fitness and implications for hypertension

The association between cardiorespiratory fitness and health is robust and well established. Higher levels of cardiorespiratory fitness are associated with lower incidence of hypertension in both men and women [7, 17-19]. For example, results from a 15-yr follow-up of the CARDIA study showed that each 1-min decrease in maximal treadmill test duration was associated with a 19% risk of developing hypertension, and suggested that 21% of the hypertension cases could be avoided by increasing cardiorespiratory fitness levels [19]. The association between cardiorespiratory fitness and mortality is also consistent. Of all established risk factors, low cardiorespiratory fitness seems to be the strongest predictor of mortality in both healthy and CVD subjects [20, 21]. Moreover, increased cardiorespiratory fitness has been shown to reduce the risk of mortality even in subjects aged 70 years and older [22, 23].

There is a close relationship between exercise intensity performed and cardiorespiratory fitness. In this context, HIT has been shown to be more effective than CMT for improving cardiorespiratory fitness in different populations [13-15, 24-26]. In a pilot study in subjects with metabolic syndrome, which included hypertensive patients, maximal oxygen consumption (VO_{2MAX}) increased by 35% and 16% after HIT and CMT, respectively (group difference, $P < 0.01$) [15]. In a study by our group with young normotensive young women at high familial risk for hypertension (see reference 27 for abnormalities of this population), greater increases in VO_{2MAX} were found in HIT (16%) than CMT group (8%) during a 16-wk follow-up (**Figure 1** shows the hemodynamic and neuro-humoral abnormalities of this population, and the effects of exercise training (HIT vs. CMT) on these abnormalities) [13, 14]. Moreover, HIT was also more effective than CMT for improving several markers of submaximal aerobic capacity, including VO_2 at respiratory compensation point, tolerance time to reach anaerobic threshold and tolerance time to reach respiratory compensation point (**Table 1**) [14]. In sum, these studies underscore the superiority of HIT to improve

Table 1. Oxygen consumption and exercise tolerance during a graded exercise test before and after 16 weeks of HIT, CMT or control intervention in young normotensive women at high familial risk for hypertension.

Variable	HIT (N = 11)		CMT (N = 11)		CON (N = 12)	
	Before	After	Before	After	Before	After
VO _{2AT} (mL.kg ⁻¹ .min ⁻¹)	17.3 ± 2.9	19.9 ± 2.9 ^a	17.4 ± 4.0	19.1 ± 3.7 ^a	18.2 ± 3.7	18.2 ± 3.7
VO _{2RCP} (mL.kg ⁻¹ .min ⁻¹)	24.4 ± 4.4	29.8 ± 5.0 ^a	25.1 ± 4.4	27.3 ± 5.2 ^a	25.1 ± 4.0	25.1 ± 4.0
VO _{2MAX} (mL.kg ⁻¹ .min ⁻¹)	29.3 ± 3.6	33.9 ± 4.6 ^a	29.9 ± 4.0	32.3 ± 5.6 ^a	29.8 ± 3.5	29.8 ± 3.7
RER	1.13 ± 0.07	1.12 ± 0.07	1.12 ± 0.08	1.12 ± 0.05	1.12 ± 0.08	1.12 ± 0.08
TT _{AT} (min)	4.5 ± 1.2	6.7 ± 0.8 ^a	3.8 ± 1.1	5.3 ± 1.3 ^{a,b}	4.3 ± 1.2	4.1 ± 1.0 ^b
TT _{RCP} (min)	8.5 ± 1.2	12.5 ± 0.9 ^a	7.7 ± 1.8	10.1 ± 1.9 ^{a,b}	8.4 ± 1.3	8.3 ± 1.0 ^{b,c}
TT _{MAX} (min)	11.3 ± 1.3	15.5 ± 1.6 ^a	10.4 ± 1.8	13.3 ± 1.7 ^{a,b}	11.0 ± 1.9	11.1 ± 1.3 ^{b,c}

HIT, high-intensity interval training group; CMT, continuous moderate-intensity training group; CON, nonexercise control group; TT, tolerance time; VO₂, oxygen uptake; AT, anaerobic threshold; RCP, respiratory compensation point; MAX, maximal effort. ^a Different from before follow-up at same group (p<0.01). ^b Different from HIT at same period (p<0.05). ^c Different from CME at same period (p<0.05). (Adapted from [14] Ciolac EG, et al. Heart rate response to exercise and cardiorespiratory fitness of young women at high familial risk for hypertension: effects of interval vs continuous training. *Eur J Cardio Prev Rehabil* 2011; 18: 824-830. ©2011 The European Society of Cardiology. Used with permission).

cardiorespiratory fitness, which may have an important implication for hypertension incidence and mortality risk.

Effects of HIT on blood pressure

In contrast to cardiorespiratory fitness, the acute (postexercise hypotension) and chronic effects of exercise on resting and ambulatory BP appears not be influenced by exercise intensity. Previous studies by our group analyzing the acute and chronic effects of high-intensity interval and steady-state exercise in long-term treated hypertensive patients showed that both exercise programs were equally effective for reducing ambulatory BP [8, 11]. In young normotensive women at high familial risk for hypertension, we found no significant difference between a 16-wk HIT or CMT exercise program on exercise-induced reduction of ambulatory BP [13], although no significant reductions were found after high-intensity or steady-state exercise sessions [28]. In a study with metabolic syndrome subjects, resting BP was reduced after a 16-wk HIT or CMT exercise program with no significant difference between programs [15].

On the other hand, the intensity of exercise program has affected BP response to graded exercise test. We found that HIT was more effective than CMT to reduce systolic and diastolic BP response to a graded exercise test in young normotensive women at high familial risk for hypertension after 16 weeks of training (**Figure 2**)

[13]. This greater reduction may have important implications for hypertension prognosis, as supported by the association between exaggerated BP response to exercise and incidence of future hypertension [29], and the greater BP response to exercise commonly found among this high risk population [27].

HIT and markers of autonomic nervous system activity

Although the precise mechanism is not completely understood, increased activation of the sympathetic nervous system has a key role in the pathogenesis of hypertension [27]. According to our knowledge, there is no study analyzing the effects of HIT on sympathetic activity (or its markers) in hypertensive patients. However, the effects of HIT on markers of sympathetic activity in normotensive at high familial risk for hypertension have been investigated by our group. When investigating the plasma norepinephrine response to a graded exercise test in young normotensive women at high familial risk for hypertension before and after a 16-wk of HIT, CMT or control intervention, we found that HIT reduced resting (after 60 of resting), exercise (immediately after last stage of test) and recovery (10 min after end of test) norepinephrine levels, but CMT reduced only resting and exercise norepinephrine levels [13]. Moreover, greater norepinephrine reductions were found in the HIT group, which resulted in post-intervention norepinephrine levels lower than that observed in the control group (and similar

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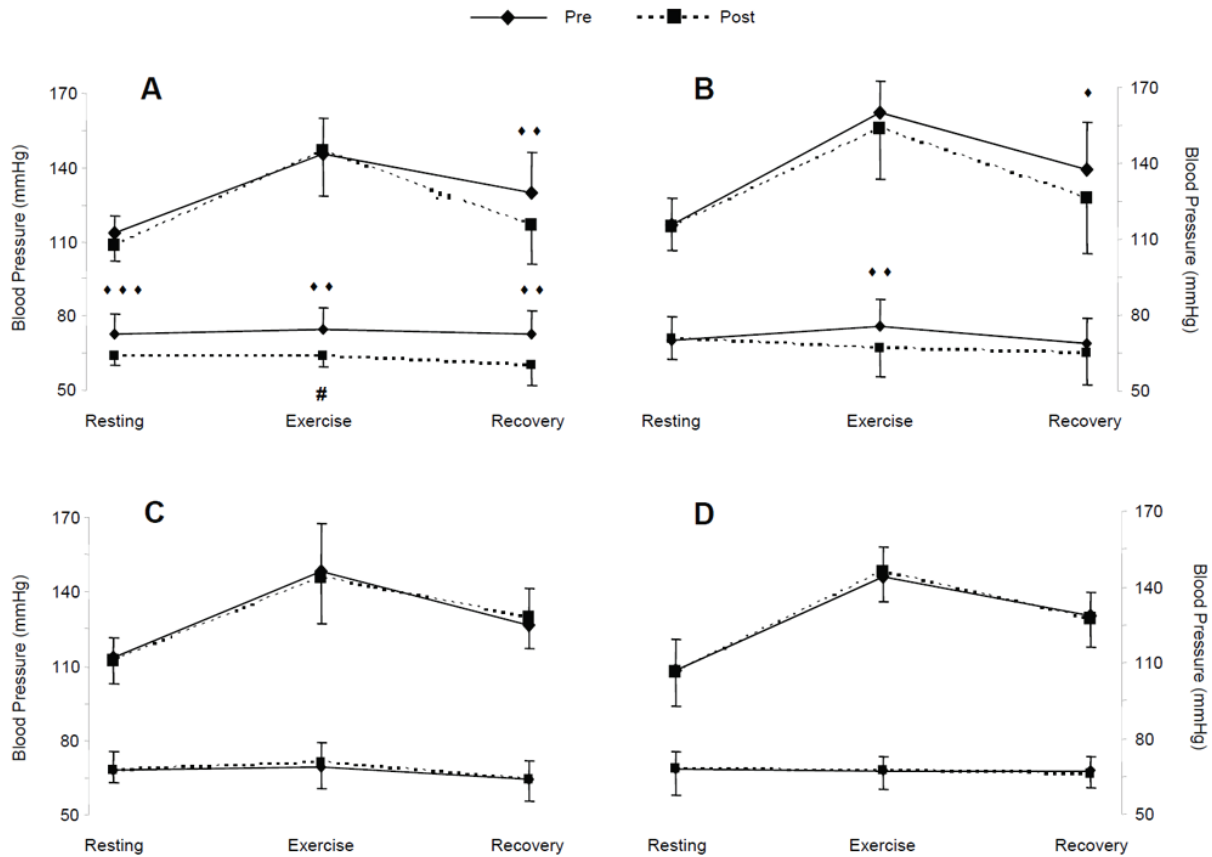


Figure 2. Blood pressure response to a graded exercise testing before and after 16 weeks of HIT, CMT or control intervention in young normotensive women at high familial risk for hypertension. (A) HIT, high-intensity interval training group. (B) CMT, continuous moderate-intensity training group. (C) ConFH+, nonexercise control group at familial risk for hypertension. (D) ConFH-, nonexercise control group without familial risk for hypertension. Data are presented as mean \pm standard deviation. # Different from ConFH+ at the same period ($P<0.05$). Different from after follow-up in the same group (* $P<0.05$; ** $P<0.01$; *** $P<0.001$). (Reprinted from [13] (Ciolac EG, et al. Effects of high-intensity aerobic interval training vs. moderate exercise on hemodynamic, metabolic and neuro-humoral abnormalities of young normotensive women at high familial risk for hypertension. *Hypert Res.* 2010; 33: 836-843). ©2010 The Japanese Society of Hypertension. Used with permission).

to that observed in women without familial risk for hypertension). On the other hand, no post-intervention significant differences were observed between CMT and control group (Figure 3) [13].

The evaluation of the heart rate response (HR) to exercise is also an easy and inexpensive tool that provides a wealth of information for the interaction of the autonomic nervous system and cardiovascular system at various phases of rest, exercise and recovery [30]. According to this, we also analyzed the HR response to exercise in normotensive women at high familial risk for hypertension, before and after a 16-wk HIT, CMT and control intervention, and found that

HIT, but not CMT, was effective for improving recovery HR during follow-up (Figure 4) [14]. Since the recovery HR is mainly related to an increase in vagal tone which occurs immediately after exercise cessation [31], this improvement in recovery HR observed only after HIT suggests a greater exercise-induced improvement in parasympathetic reaction of the women following HIT than CMT. Moreover, because impaired recovery HR response to exercise has been associated with several pathophysiological abnormalities of hypertension [32-34], and is an independent risk factor for coronary heart disease, cardiovascular disease and cardiovascular mortality [32-35], the greater HIT-induced improvement in recovery heart rate response to exercise

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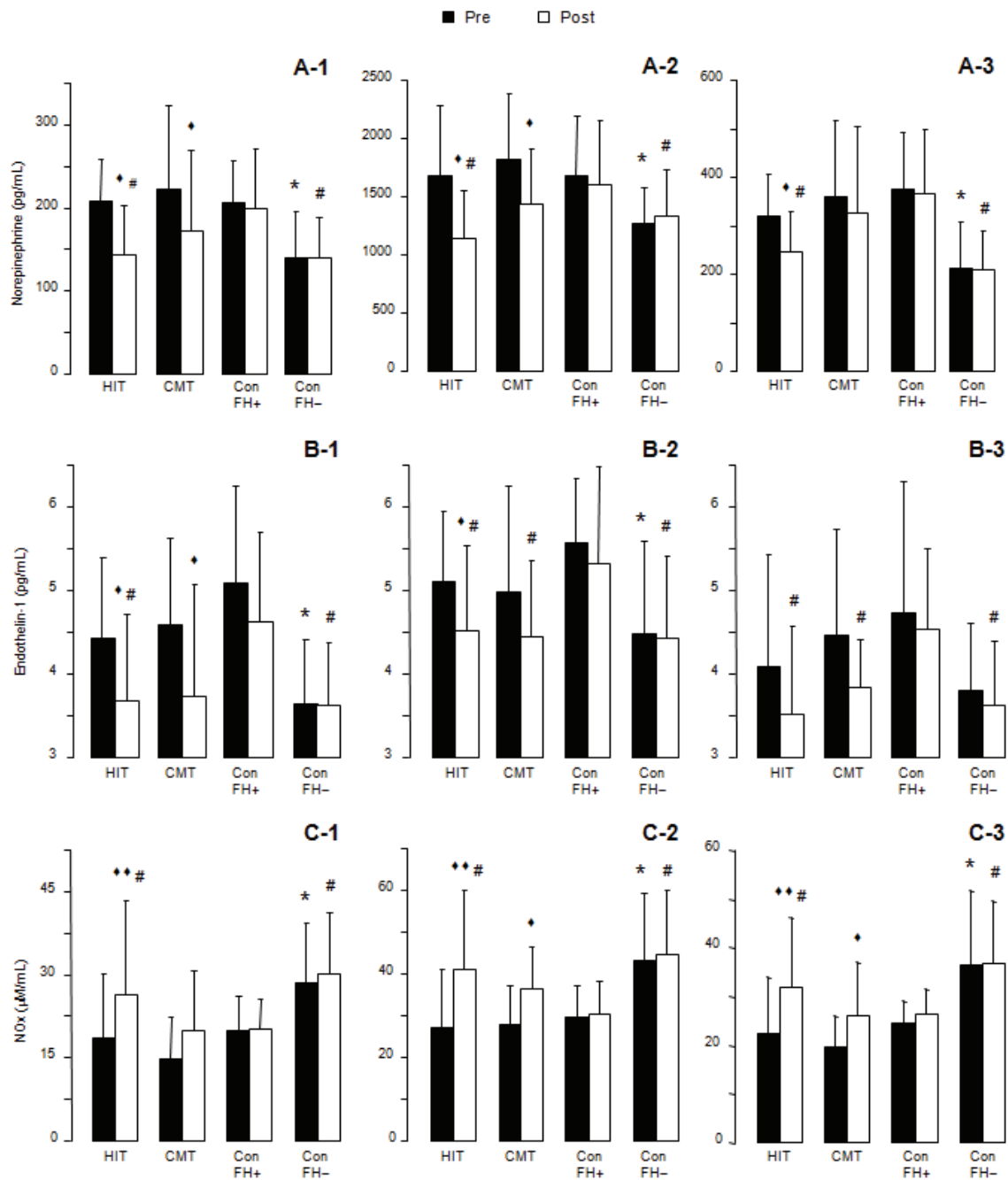


Figure 3. Norepinephrine (A), endothelin-1 (B) and NOx (C) response to a graded exercise testing before and after 16 weeks of HIT, CMT or control intervention in young normotensive women at high familial risk for hypertension. 1, resting phase (blood sample collected after 60 min of supine resting). 2, exercise phase (blood sample collected immediately after last stage of exercise). 3, recovery phase (blood sample collected 10 min after last stage of exercise). Data are presented as mean±standard deviation. HIT, high-intensity interval training group. CMT, continuous moderate-intensity training group. ConFH+, nonexercise control group at familial risk for hypertension. ConFH-, nonexercise control group without familial risk for hypertension. * Different from HIT, CMT and ConFH+ before follow-up ($P < 0.05$). # Different from ConFH+ after follow-up ($P < 0.05$). ** Different from before follow-up in the same group ($P < 0.05$); *** $P < 0.01$). (Reprinted from reference [13] (Ciolac EG, et al. Effects of high-intensity aerobic interval training vs. moderate exercise on hemodynamic, metabolic and neuro-humoral abnormalities of young normotensive women at high familial risk for hypertension. *Hypert Res* 2010; 33: 836-843). ©2010 The Japanese Society of Hypertension. Used with permission).

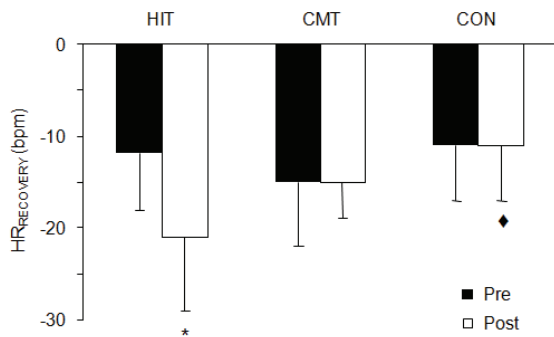


Figure 4. Recovery heart rate to a graded exercise testing (first minute decrease) before and after 16 weeks of HIT, CMT or control intervention in young normotensive women at high familial risk for hypertension. Data are presented as mean±standard deviation. HIT, high-intensity interval training group; CMT, continuous moderate-intensity training group; CON, nonexercise control group; bpm, beats per minute. * Different from before follow-up in the same group (P < 0.01). † Different from HIT after follow-up (P < 0.05). (Adapted from reference [14] (Ciolac EG, et al. Heart rate response to exercise and cardiorespiratory fitness of young women at high familial risk for hypertension: effects of interval vs continuous training. *Eur J Cardiovasc Prev Rehabil* 2011; 18: 824-830). ©2011 The European Society of Cardiology. Used with permission).

may have important clinical implications.

Effects of HIT on endothelial function

Exercise intensity also appears to affect exercise-induced improvements of endothelial function in hypertension. For example, HIT was more effective than CMT for improving endothelial function (9% vs 5% in HIT and CMT, respectively – group difference, P<0.001) in metabolic syndrome subjects (most of the subjects were hypertensive at baseline) [15]. In this same study, nitric oxide (NO) availability was improved after HIT (36%) but not CMT, and several factors that influence nitric oxide bioavailability (blood glucose, insulin sensitivity and oxidized low-density lipoprotein) were normalized after HIT only [15].

We confirm this greater benefit of HIT for endothelial function with our already cited study with normotensive women at high familial risk for hypertension [13]. After the experimental protocol, the HIT improved resting, exercise and recovery levels of plasma nitrite/nitrate (NOx) and endothelin-1 during a graded exercise test, but CMT improved only exercise and recovery NOx,

and resting endothelin-1 levels. With these greater improvements, HIT but not CMT group showed higher NOx and lower endothelin-1 levels than the control group after follow-up (**Figure 3**). The reason for the superiority of HIT for improving endothelial function is not fully understood, but it seems reasonable to suggest that the low- and high-intensity training exercise programs affect shear stress in the arterial wall differently during exercise training and that this may yield differences in molecular responses [13, 15].

Arterial stiffness, hypertension and effects of HIT

The aging process leads to a progressive increase in arterial stiffness, especially in large (central) arteries, which is accelerated by hypertension [36]. Moreover, young healthy subjects with familial risk for hypertension have showed increased arterial stiffness before any increase in BP [13, 27, 37]. This greater increase has important clinical implication, because central arterial stiffness has shown to be an independent predictor of cardiovascular and all-cause mortality in hypertensive patients [38]. Although regular aerobic exercise appears to attenuate age-associated arterial stiffness and to reduce established arterial stiffness in normotensive subjects [39], CMT interventions have failed to show any benefit in hypertensive patients [40, 41]. In the other hand, a study by our group showed a reduction in arterial stiffness of hypertensive subjects after 16 weeks of HIT, but not CMT [11]. Similar results were found in our study with normotensive women at familial risk for hypertension, where a significant arterial stiffness reduction was found after 16 weeks of HIT, but not CMT [13]. Moreover, this higher HIT-induced reduction normalized arterial stiffness level in this high-risk population (**Figure 5**) [13].

Since that several mechanisms involved in age-related arterial stiffness are accelerated in the presence of hypertension [42], the above mentioned studies suggest that exercise training programs of higher intensity (that is, HIT) may be more effective in reducing arterial stiffness in populations that already have some alterations in this variable.

Conclusion and perspectives

A number of studies within the last few years have consistently showed greater health-related

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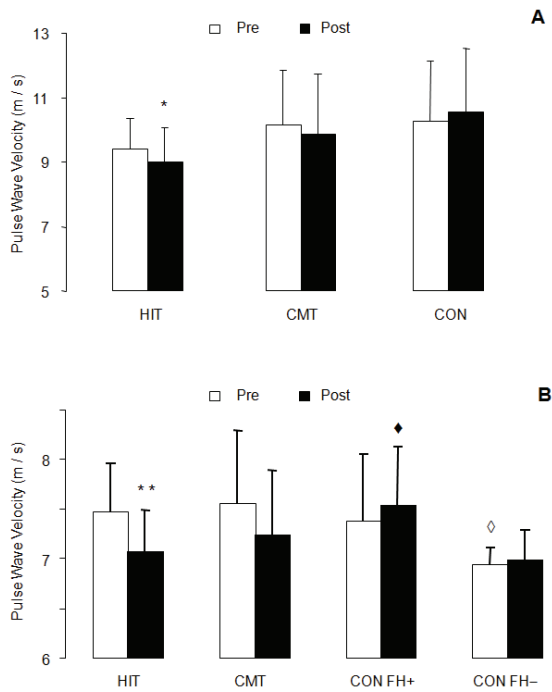


Figure 5. Arterial stiffness (pulse wave velocity) before and after 16 weeks of HIT, CMT or control intervention in (A) long-term treated hypertensive patients and (B) young normotensive women at high familial risk for hypertension. Data are presented as mean±standard deviation. HIT, high-intensity interval training group; CMT, continuous moderate-intensity training group; CON, nonexercise control group; FH+, with familial risk for hypertension; FH-, without familial risk for hypertension; m/s, meters per second. ^à Different from HIT, CMT and CON FH+ before follow-up ($P < 0.001$). [˜] Different from HIT and CON FH- after follow-up ($P < 0.05$). Different from before follow-up in the same group (* $P < 0.05$; ** $P < 0.01$). (Adapted from reference [13] (Ciolac EG, et al. Effects of high-intensity aerobic interval training vs. moderate exercise on hemodynamic, metabolic and neurohumoral abnormalities of young normotensive women at high familial risk for hypertension. *Hypert Res* 2010; 33: 836-843) and [11] (Guimarães GV, et al. Effects of continuous versus interval exercise training on the blood pressure and arterial stiffness in treated hypertensive subjects: a randomized controlled study. *Hypert Res* 2010; 33: 627-632) ©2010 The Japanese Society of Hypertension. Used with permission).

benefits of HIT when compared to traditional CMT. Although large multicenter prospective studies are needed to advance our conclusions, studies by our group and others indicate that exercise intensity may have an important role in preventing and controlling hypertension, as

shown by the greater benefits of HIT than CMT for reversing key alterations present in the physiopathology of this disease in both hypertensive patients and normotensive subjects at high familial for hypertension.

On the hand, the optimum dosage of HIT still needs to be established. In this context, large trials focused in investigating different combinations of exercise intensity and duration, number of exercise intervals, relative intensity and duration of recovery period between exercise intervals, as well as frequency of training are welcome. Since a large percentage of population fails to meet the minimum exercise guidelines, and lack of time is one of most cited barriers for not exercising,[16] determination of the best relation between exercise quantity (frequency and duration) and health benefits may have important implications for exercise compliance.

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