

# Exercise Training in Heart Failure: High-intensity Interval Training versus Moderate-intensity Continuous Training

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## Abstract

Prevalence of heart failure (HF) increases over time and is associated with high mortality. Shortness of breath, exercise intolerance, and low quality of life related to health are the common problems in HF patients despite optimum pharmacological therapy. Exercise training counteracts the progression of devastating compensatory mechanisms of HF, leading to improvement in functional capacity and quality of life. Resistance training improves peak oxygen uptake, quality of life, and walking performance in HF patients. Adherence is central to training for the best result. Any exercise training program whether continuous or interval training is sufficient to improve the prognosis, quality of life, and anatomic function.

**Keywords:** Exercise, heart failure, oxygen uptake, rehabilitation, training

## INTRODUCTION

Prevalence of heart failure (HF) increases over time and is associated with high mortality (5-year survival rate of 35%–55%).<sup>[1–4]</sup> Shortness of breath, exercise intolerance, and low quality of life related to health are the common problems in HF patients despite optimum pharmacological therapy.<sup>[5]</sup>

Various studies indicated that physical fitness is a prognostic factor for HF patients, in which low physical fitness is associated with high mortality rate.<sup>[6,7]</sup> Previous studies indicated that physical training increases physical fitness, cardiovascular function, and quality of life.<sup>[8–12]</sup> Peak aerobic capacity can be directly measured by peak oxygen uptake ( $VO_2$  peak) and is the best predictor of cardiovascular and all-cause mortality in cardiovascular patients.<sup>[13,14]</sup>

Physical training is recommended for HF patients.<sup>[15]</sup> However, there are differences regarding which level of intensity and exercise formats leads to best results.

## Exercise training

### Mechanism

Exercise training reverses autonomic dysfunction in patients with HF, which shifts from predominantly sympathetic to vagal

activity and reduces circulating renin-angiotensin-aldosterone system neurohormones,<sup>[16]</sup> resulting in improved cardiac function, reduced vasoconstriction with better peripheral and skeletal blood delivery, and improved exercise tolerance. It also produces antioxidative effects (through reduction of vascular expression of NADPH oxidase and AT1) which decrease reactive oxygen species production, resulting in improved acetylcholine-mediated coronary vasodilatation and reduced Ang-II-induced vasoconstriction.<sup>[16]</sup>

Regular exercise training can have an anti-inflammatory effect marked by increased plasma levels of the anti-inflammatory cytokine interleukin 10 and can modulate the innate immune system, influencing macrophage and lymphocyte function.<sup>[16]</sup> Exercise affects skeletal muscle's oxygen use and oxidative capacity, which are improved by increased activity of oxidative enzymes and mitochondrial content, leading to improvement in

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peak  $\text{VO}_2$  and lactate threshold and delayed onset of anaerobic metabolism.

Exercise training improves heart function by restoring cardiomyocyte contractility and calcium sensitivity.<sup>[16]</sup> It may minimize the stunning effects and maximize the preconditioning effects of brief ischemic episodes. All these training-induced changes can effectively counteract the progression of deleterious compensatory mechanisms of HF, leading to improvement in functional capacity and quality of life.<sup>[16]</sup>

## Principles of exercise regiment(s)

### Continuous training regiment(s)

Continuous training (CT) is typically performed at moderate-to-high exercise intensities in steady-state conditions of aerobic energetic yield, which allows the patient to perform prolonged training sessions (up to 45–60-min duration).<sup>[15]</sup> It is safe, efficient, and well tolerated by patients, and hence it is recommended by the Heart Failure Association guidelines.

### High-intensity training

In interval training (INT) protocol, an alternate short bout (10–30 s) of moderate-to-high intensity (50%–100% peak exercise capacity) exercise, with a longer recovery (80–60 s) phase, is performed at low or no workload. Recent trials demonstrated INT, especially high-intensity INT (HIIT), to be more effective.<sup>[15]</sup>

### High intensity or continuous training?

Some evidences supported that INT is more effective to improve left ventricular ejection fraction (LVEF) and left ventricular end-diastolic diameter.<sup>[17]</sup> A recent meta-analysis showed that an increase in exercise capacity, represented by the peak  $\text{VO}_2$ , was similar between training modalities and the influence of a certain training modality on ventilation over carbon dioxide ( $\text{VE}/\text{VCO}_2$ ) slope was not found to be significantly different from other training modalities.  $\text{VO}_2$  efficiency slope seemed to improve significantly with INT compared to CT (only one study). Quality of life seems to improve significantly with combined INT and strength training.<sup>[17]</sup> Another meta-analysis showed that in clinically stable HF with reduced ejection fraction patients, INT is more effective than CT for improving peak  $\text{VO}_2$ , but not the LVEF at rest.<sup>[18]</sup> Adherence to exercise training is very important and this is often problematic in HF due to time constraints and lack of energy.<sup>[19,20]</sup> A HIIT training with lower training frequency and high-intensity intervals of moderate duration might address these two major factors of noncompliance, hence improving adherence. A low-frequency high-intensity training (HIT) with high-intensity intervals of moderate duration is feasible and successful in improving fitness. These might be a component of optimal exercise protocol for HF patients to achieve long-term benefits and adherence in the future.<sup>[20]</sup>

The risk of cardiovascular events concerning HIT has been demonstrated to be low in patients with coronary artery disease; however, its safety has not been confirmed in those with HF with reduced EF (HFrEF) in a large-scale

investigation.<sup>[21]</sup> Most patients with HFrEF have relatively impaired exercise hemodynamic in the initial sessions of exercise training.<sup>[21]</sup> There was a trial evaluating modified HIT (CT in the first 12 sessions followed by 24 HIT sessions) compared to optimal medical treatment only, in which supervised continuous aerobic training at ventilator anaerobic threshold for 50 min/day, 3 days/week for 4 weeks, and then 3-min intervals at 40% and 80%  $\text{VO}_2$  reserve for 50 min/day, 3 days/week for 8 weeks, demonstrated an improved peak cardiac-pumping capacity with reduced cardiac afterload which simultaneously increases ventilation efficiency during exercise in patients with HFrEF, giving time for adaption in initial sessions before proceeding to HIIT.<sup>[21]</sup> Any exercise training program seems sufficient to improve the prognosis, quality of life, and anatomic function.<sup>[17]</sup>

Despite concerns regarding patient adherence, several studies have shown irrefutable advantages of HIT in patients with cardiac failure. It is interesting that HIT protocols, the total exercise volume, and time commitment have been significantly lower compared to moderate-intensity training, and yet its use still shows various positive physiological benefits that are at least comparable with moderate-intensity protocols. It is also important to note that HIT has been shown to be safe, tolerable, and enjoyable for patients with cardiovascular disease, eliminating any major concerns of an increase in adverse effect risk.<sup>[22]</sup>

However, several trials have failed to show any comparable benefit of HIT compared to continuous moderate-intensity training [Tables 1 and 2]; however, the authors of these trials stated that the lack of comparable evidence resulted from the small sample.<sup>[20,23]</sup>

In one randomized trial of 27 patients with stable, postinfarction HF who received optimal medical therapy, aerobic INT at high intensity (at 95% of peak heart rate) reversed left ventricular remodeling and improved left ventricular relaxation; these benefits were not observed with moderate CT (at 70% of peak heart rate). At this trial, reversal of left ventricular remodeling and improved left ventricular relaxation were observed. In addition, HIT was associated with a greater increase in peak exercise levels.<sup>[24]</sup>

A Cochrane database review revealed that patients who undergo HIT showed an increase in 6-min walk distance mean of 41 m; this increase in functional capacity means that patients may be able to participate in their routine daily activities more easily and comfortably.<sup>[25]</sup>

A meta-analysis including seven randomized trials comparing HIT to moderate-intensity CT in clinically stable patients with HF with reduced ejection fraction revealed greater improvements in exercise tolerance with HIT.<sup>[18]</sup>

Two studies by Benda *et al.* and Ellingsen *et al.* failed to show statistically significant differences between CT and HIT in terms of physical fitness improvement [Table 3].<sup>[26]</sup> Exercise in patients with HF is indeed associated with beneficial cardiac remodeling; however, after 12 h of

**Table 1: Maximal incremental cycling test**

Parameter	CT (n=10)		HIT (n=10)		P		
	Post	Pre	Post	Time	Time	Group	Time*group
VO <sub>2</sub> peak (mL/min)	1881±214	1887±27	1662±562	1792±559	0.06	0.44	0.08
VO <sub>2</sub> peak (mL/min/kg)	21.2±3.6	21.3±3.7	19.1±4.1	20.4±4.3	0.10	0.14	0.09 <sup>#</sup>
VO <sub>2</sub> peak (percentage predictor VO <sub>2</sub> peak)	86±8	87±10	79±17	85±16	0.044	0.48	0.08
Maximal workload (watt)	145±22	152±26	126±38	142±45	<0.001	0.24	0.07
Maximal heart rate (/min)	129±19	132±24	126±16	125±15	0.78	0.30	0.51
VE/VCO <sub>2</sub> slope	32.2±3.3	32.7±5.8	28.7±5.8	29.4±7.7	0.52	0.18	0.91
VO <sub>2</sub> at AT (mL)	1030±287	1248±388	1033±319	1090±225	0.041	0.54	0.22
Maximal O <sub>2</sub> /HR (mL)	16.2±2.2	16.7±2.8	14.0±4.0	15.4±3.8	0.006	0.25	0.13

Data are presented as mean±SD. P values refer to a two-way repeated measures ANOVA between the two training groups. One participant in the CT group did not reach VO<sub>2</sub> peak, and therefore only VE/VCO<sub>2</sub> slope and VO<sub>2</sub> at AT could be determined. <sup>#</sup>For statistical reasons, data were analyzed with three separate tests to determine time, group, and time\*group P values. SD: Standard deviation, CT: Continuous training, HIT: High-intensity training, VE/VCO<sub>2</sub>: Ventilation over carbon dioxide, VO<sub>2</sub> peak: Peak oxygen uptake

**Table 2: Echocardiographic left ventricular volumes, systolic function, and strain and diastolic function**

	CT (n=10)		HIT (n=10)		P		
	Pre	Post	Pre	Post	Time	Group	Time*group
<b>Systolic function</b>							
LVEDV (ml)	154±24	159±28	194±39	204±44	0.26	0.002	0.64 <sup>#</sup>
LVESV (ml)	98±14	102±19	134±32	132±40	0.87	0.037	0.63
Stroke volume (ml)	56±13	57±13	61±14	72±16	0.06	0.16	0.12
LVEF (%)	36±4	36±5	32±7	36±9	0.09	0.57	0.07
Cardiac output (L/min)	3.5±0.6	3.4±0.7	3.5±0.8	4.3±1.0	0.20	0.21	0.07
Cardiac index (L/min/m <sup>2</sup> )	1.7±0.3	1.6±0.3	1.7±0.4	2.1±0.5	0.22	0.14	0.08
Longitudinal strain (%)	-9±3	-9±3	-9±3	-8±3	0.60	0.47	0.38 <sup>#</sup>
Circumferential strain (%)	-10±2	-10±3	-9±3	-8±3	0.22	0.43	0.19
Radial strain (%)	23±7	22±6	23±8	20±8	0.13	0.71	0.48
Area strain (%)	-17±4	-15±6	-17±5	-14±5	0.044	0.73	0.97
IVCT-L (ms)	52±7	50±10	49±12	58±7	0.18	0.56	0.029
IVCT-S (ms)	57±14	59±11	53±9	56±11	0.35	0.46	0.87
<b>Diastolic function</b>							
IVRT-L (ms)	145±32	149±27	142±27	159±27	0.13	0.75	0.38
IVRT-S (ms)	160±36	148±22	164±41	170±37	0.60	0.45	0.22 <sup>#</sup>
E/A	1.15±0.71	1.17±0.89	1.53±1.42	1.60±1.53	0.49	0.36	0.59 <sup>#</sup>
S/D	1.38±0.74	1.17±0.34	1.00±0.40	1.26±0.59	0.85	0.48	0.14
E/E'-L	6.8±1.9	6.7±1.9	10.3±4.4	9.8±6.3	0.71	0.07	0.74
E/E'-S	10.1±4.1	11.1±5.2	12.6±9.8	11.8±11.2	0.93	0.67	0.42

Data are presented as mean±SD. P values refer to two-way repeated measures ANOVA between the two training groups. <sup>#</sup>For statistical reasons, data were analyzed with three separate tests to determine time, group, and time\*group P values. Four-dimensional data were available for seven patients in the CT group and eight patients in the HIT group. IVCT-L, IVRT-C, IVRT-S, and E/E'-L were available for nine patients in the HIT group. IVCT-S and E/E'-S were available for eight patients in the HIT group. IVCT-L and S/D ratio were available for nine patients in the CT group. IVRT-L and E/A ratio was available for eight patients in the CT group. LVEDV: Left ventricular end-diastolic volume, LVESV: Left ventricular end-systolic volume, IVCT-L/S: Isovolumetric contraction time, lateral/septal, IVRT-L/S: Isovolumetric relaxation time, lateral/septal, E/A ratio: Peak mitral flow velocity during early filling/peak mitral flow velocity during atrial contraction, S/D: Systolic flow velocity pulmonary vein/diastolic flow velocity pulmonary vein, E/E'-L/S: Peak mitral flow velocity during early filling/peak mitral annulus velocity during early filling, lateral/septal, SD: Standard deviation, CT: Continuous training, HIT: High-intensity training

training regiment(s) by Benda *et al.*, no improvements in cardiac structure and function at rest were found. Although increase in maximal oxygen pulse suggests an increase in stroke volume during exercise, it is to be noted that previous studies that reported significant structural and functional changes were generally using training periods that exceed 6 months. These studies also failed to show a superior effect of HIT to improve vascular function, which contrasts the

other studies. Improvement was indeed found in the subscale for physical functioning after exercise training, but not for the total quality of life. The lack of improvement in quality of life may relate to the relatively “good” quality of life at baseline on patients at these trials, which was well above that of other studies, and consequently provides a little space for further improvement. Quality of life in these studies was assessed using the SF-36 questionnaire. However, this

**Table 3: Main echocardiography and cardiopulmonary testing measures at baseline, 12 weeks, and 52 weeks with unadjusted changes**

	RRE (n=73)			MCT (n=65)			HIIT (n=77)		
	Baseline	12 weeks	52 weeks	Baseline	12 weeks	52 weeks	Baseline	12 weeks	52 weeks
LVEDD (mm)	68 (67-69)	69 (65-71)	66 (63-67)	69 (66-72)	67 (65-70)	64 (61-70)	68 (65-70)	63 (62-68)	63 (62-66)
LVEF (%)	30 (28-32)	28 (27-30)	28 (27-32)	29 (26-32)	27 (25-31)	33 (26-37)	29 (26-31)	31 (29-31)	28 (26-32)
VO <sub>2</sub> peak (mL kg <sup>-1</sup> min <sup>-1</sup> )	18.4 (16.8-19.6)	17.4 (15.7-19.8)	18.2 (15.8-20.0)	16.2 (15.3-18.7)	17.0 (15.7-19.6)	16.4 (15.0-18.6)	16.8 (15.8-17.8)	18.2 (16.3-20.0)	17.1 (15.5-18.6)
NT-proBNP (ng/L)	895 (635-1110)	821 (594-1079)	626 (419-1116)	976 (725-1348)	821 (580-1169)	698 (544-1021)	1052 (837-1472)	909 (722-1484)	813 (585-1615)
Change		Baseline-12 weeks	Baseline-52 weeks		Baseline-12 weeks	Baseline-52 weeks		Baseline-12 weeks	Baseline-52 weeks
LVEDD (mm)		0.0 (0.0-2.0)	-2.0 (-4.0-0.0)		-1.0 (-2.0-1.0)	-3.0 (-7.0-1.4)		-2.0 (-3.6-1.0)	-3.0 (-5.0-1.0)
LVEF (%)		-0.6 (-2.4-1.4)	1.1 (-0.8-3.0)		0.7 (-1.8-2.6)	0.7 (-1.5-4.4)		1.7 (0.0-4.5)	-0.2 (-3.1-2.8)
VO <sub>2</sub> peak (mL kg <sup>-1</sup> min <sup>-1</sup> )		-0.1 (-0.9-0.4)	-0.4 (-1.3-0.4)		1.1 (0.5-1.7)	1.2 (-0.2-1.4)		0.9 (0.0-1.4)	0.1 (-0.4-1.0)
NT-proBNP (ng/L)		9 (-43-112)	-25 (-108-76)		2 (-91-97)	-101 (-130-30)		19 (-76-129)	112 (-24-236)

Values are median with 95% CI of the median. There were no differences between the groups at baseline (Kruskal-Wallis test,  $P=0.68, 0.83, 0.21, \text{ and } 0.30$ ). HIIT: High-intensity interval training, LVEDD: Left ventricular end-diastolic diameter, LVEF: Left ventricular ejection fraction, MCT: Moderate continuous training, NT-proBNP: N-terminal prohormone of brain natriuretic peptide, RRE: Recommended regular exercise, VO<sub>2</sub> peak: Peak oxygen uptake, CI: Confidence interval

caveat indicates that patients with lower quality of life prior to exercise training may demonstrate a larger benefit from the intervention.<sup>[20,26]</sup>

## CONCLUSION

Significant differences between CT and HIT in terms of physical fitness are not demonstrable. Preference between the former two remains unresolved in patients with HF. A more conservative approach is needed to prescribe moderate-intensity CT regiment(s) and switch to HIIT should the patient is unable to comply with the CT regiment(s).

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## Conflicts of interest

There are no conflicts of interest.

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