ORIGINAL RESEARCH ARTICLE

Feasibility of high-intensity interval training in patients with left ventricular assist devices: a pilot study

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Abstract

Aims   Patients with left ventricular assist device (LVAD) suffer from persistent exercise limitation despite improvement of their heart failure syndrome. Exercise training (ET) programmes to improve aerobic capacity have shown modest efficacy. High-intensity interval training (HIIT), as an alternative to moderate continuous training, has not been systematically tested in this population. We examine the feasibility of a short, personalized HIIT programme in patients with LVAD and describe its effects on aerobic capacity and left ventricular remodelling.

Methods and results   Patients on durable LVAD support were prospectively enrolled in a 15-session, 5 week HIIT programme. Turndown echocardiogram, Kansas City Cardiomyopathy Questionnaire, and cardiopulmonary exercise test were performed before and after HIIT. Training workloads for each subject were based on pretraining peak cardiopulmonary exercise test work rate (W). Percentage of prescribed training workload completed and adverse events were recorded for each subject. Fifteen subjects were enrolled [10 men, age = 51 (29–71) years, HeartMate II = 12, HeartMate 3 = 3, and time on LVAD = 18 (3–64) months]. Twelve completed post-training testing. HIIT was well tolerated, and 90% (inter-quartile range: 78, 99%) of the prescribed workload (W) was completed with no major adverse events. Improvements were seen in $a\dot{V}O_2$ at ventilatory threshold [7.1 (6.5, 9.1) to 8.5 (7.7, 9.3) mL/kg/min, $P = 0.04$], work rate at ventilatory threshold [44 (14, 54) to 55 (21, 66) W, $P = 0.05$], and left ventricular end-diastolic volume [168 (144, 216) to 159 (124, 212) mL, $n = 7$, $P = 0.02$]. HIIT had no effect on maximal oxygen consumption ($\dot{V}O_{2peak}$) or Kansas City Cardiomyopathy Questionnaire score.

Conclusions   Cardiopulmonary exercise test-guided HIIT is feasible and can improve submaximal aerobic capacity in stable patients with chronic LVAD support. Further studies are needed on its effects on the myocardium and its potential role in cardiac rehabilitation programmes.

Introduction

Left ventricular assist devices (LVADs) are an established therapy for advanced heart failure (HF) with proven mortality benefit.[1] With 2 year survival now exceeding 80%,[2] the focus within the field has shifted towards optimization of quality of life for LVAD recipients.[3] Accordingly, it is notable that significant impairments in functional capacity with detrimental impacts on health status persist after implantation.[4,5]

Available evidence consistently demonstrates the safety and benefits of therapeutic exercise training (ET) in this population,[6–8] but its implementation in clinical practice remains limited.[9] This has been partially attributed to insufficient knowledge in the field.[10] Currently available studies have employed a large variety of training modalities or have mostly enrolled patients shortly after LVAD implantation, when improvements in functional capacity are already expected because of amelioration of the HF syndrome.[11–13]

The most consistently tested ET modality in LVAD patients is moderate continuous training (MCT), which leads to modest improvements in peak oxygen uptake ($\dot{V}O_{2peak}$) and quality of life scores compared with usual care or home-based exercise.[7,14] More research is needed on the efficacy of alternative ET modalities, especially for patients on long-term support. Ideally, a training modality with significant benefits and limited time commitment could be incorporated into outpatient cardiac rehabilitation programmes.

High-intensity interval training (HIIT) is a type of training that uses very short intervals of very intense cardiovascular exercise followed by recovery periods of lower exercise intensity or complete rest. This allows for the achievement of overall high training workloads with low total exercise volume.[15]

High-intensity interval training is highly efficient at improving aerobic capacity compared with MCT in healthy individuals and in patients with HF.[16,17] However, adherence to the training schedule can limit its widespread use in HF patients, as demonstrated by larger studies.[18] This training modality has not been systematically applied to the LVAD population, with only rare reports available in the literature.[19,20]

The effects of HIIT on skeletal muscle metabolism are well described and can be seen after training programmes as short as 2 weeks.[16,21] HIIT was also shown to induce reverse left ventricular (LV) remodelling in one study of patients with ischaemic cardiomyopathy.[17] Hence, this modality could improve aerobic capacity even at fixed LVAD speeds, when the rise in cardiac output is normally insufficient to sustain maximal effort levels,[22] by improving the function of the intrinsic LV[23] and peripheral muscle oxidative capacity.[24]

In this pilot study, we hypothesized that a short, personalized HIIT programme could be completed without major adverse events by stable LVAD patients. We also examined the effects of HIIT on aerobic exercise capacity and LV function.

Methods

Study design

Patients with ongoing LVAD support at Montefiore Medical Center between 2017 and 2018 were screened for participation (Figure 1). To be considered, patients had to be in stable clinical condition, at least 3 months after LVAD implantation, and be of age 18 years or older. Exclusion criteria were recent frequent hospital readmissions (>1 over previous 3 months), inability to complete a cardiopulmonary exercise test (CPX), concomitant participation in cardiac rehabilitation, and inability to provide written informed consent. The study protocol was approved by the Einstein Institutional Review Board of the Albert Einstein College of Medicine.

After written informed consent, patients completed a Kansas City Cardiomyopathy Questionnaire (KCCQ), turndown echocardiogram (first 10 patients), and cycle ergometer-based CPX. A 15-session, supervised HIIT programme was then prescribed to be completed over 5 weeks (three sessions per week). All baseline testing was repeated in the same order after completion of training.

Subject testing

Turndown echocardiograms were planned for the first 10 subjects enrolled as an exploratory analysis of the LV remodelling effects of HIIT. Studies were performed only if the international normalized ratio was >2. Speed was progressively reduced to 6000 r.p.m. in HeartMate II (HM2) and 4000 r.p.m. in subjects with HeartMate 3 (HM3).[25] Images were obtained by a trained sonographer while on full LVAD support and 15 min after reaching lower speed target. Studies were interpreted by an experienced echocardiographer blinded to the testing sequence.

A KCCQ 23-item form was completed by each subject independently before and after training.

A symptom-limited CPX was performed using an upright cycle ergometer (Corival CPET, Lode B.V. Medical Technology, Groningen, the Netherlands) and an MGC metabolic cart (Ultima™ CardiO₂®, St Paul, MN). A 15 W/min ramp protocol was applied. Continuous pulse oximetry and electrocardiogram monitoring were performed. Subjects were asked to fast for at least 4 h prior to testing, and all medications were continued before each test. Predicted $\dot{V}O_{2peak}$ was calculated using the Wasserman/Hansen equation. Rate of perceived exertion (RPE) was recorded using the Borg scale (6–20 points) at each stage and at peak exercise. LVAD settings were not adjusted during testing. Device speed, power, and flow were recorded at baseline and at peak exercise.

To exclude a learning effect of repeated testing, the first 12 subjects enrolled completed two baseline CPX within 5 days. An interim analysis showed no learning effect on measures of gas exchange despite increased measures of effort on the second test (Supporting Information, Table S1). Repeated baseline testing was discontinued for subsequent subjects. For subjects with two baseline tests, the second test was used for comparison with post-training values.

Gas exchange data were analysed independently by two experienced cardiologists who were blinded to the order of testing. Parameters were reported as 30 s averages. Peak oxygen consumption ($\dot{V}O_{2peak}$) was identified as the highest instantaneous value before exhaustion. Ventilatory threshold (VT) was determined using the V-slope method. Ratio of minute ventilation to carbon dioxide was calculated at peak exercise. Peak power output (PPO) was the highest workload (W) achieved prior to exercise discontinuation.

Figure 1 Patient flow during the study. Patients considered for the study had to be in stable clinical condition, at least 3 months after left ventricular assist device implantation and be of age 18 years or older.
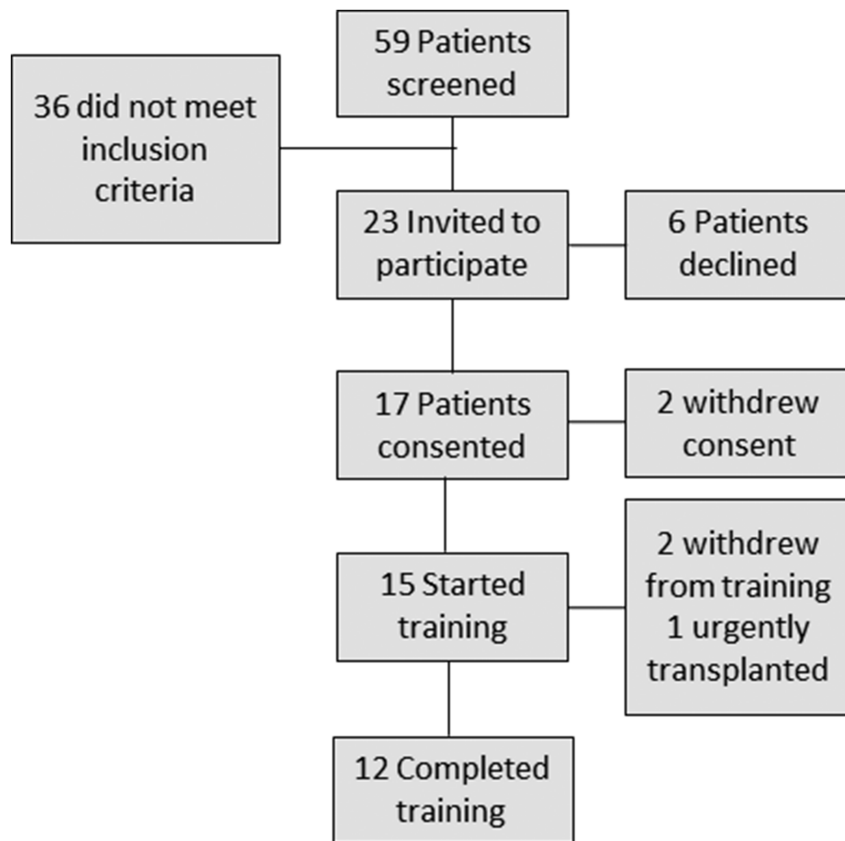
Exercise training

Each subject was prescribed with a 15-session HIIT programme to be completed over 5 weeks. This duration of training was chosen as a feasible protocol for ambulatory patients who continued to carry out normal daily activities. Prior studies have shown significant improvements in aerobic capacity and skeletal muscle adaptations after HIIT protocols as short as six sessions.[21]

All sessions were supervised by a physician and could be interrupted upon subject's request or at the physician's discretion. Training was completed using the same cycle ergometer utilized during CPX testing. Each training session lasted 30 min: 3 min warm-up and six 30 s high-intensity intervals, each followed by a 4 min active recovery period. Similar protocols have proven to be efficacious in healthy individuals.[26]

Workloads prescribed for each subject were individualized based on the peak work rate or PPO achieved during baseline CPX. For the first three sessions ('induction phase'), prescribed workloads were 40% PPO warm-up, 80% PPO intervals, and 30% PPO recovery periods. Workloads were increased on the fourth training session to 50% PPO warm-up, 100% PPO high-intensity intervals, and 40% PPO recovery

periods. Reduction to the 'induction phase' workloads was allowed during any subsequent session where prescribed workloads were not tolerated. Watts were adjusted manually during each session on the cycle ergometer by the supervising staff. RPE and heart rate (HR) were recorded at each high-intensity interval and 2 min into every other recovery period. LVAD settings were not adjusted during training. All medications were continued at previously prescribed doses throughout the training period.

Major adverse events during training were defined as sustained ventricular tachycardia or supraventricular tachycardia with haemodynamic collapse, sustained reductions in LVAD speed due to 'suck-down' effect, driveline exit-site infection, syncope, and cardiac arrest. Subjects who opted to stop the training programme before its completion were invited to perform post-training testing after their last training session.

Measures of interest

The primary measure of interest was the percentage of total prescribed workload (W) completed by each subject during

the training programme. Exploratory measures of interest were as follows: (i) change in oxygen consumption at peak exercise ($\dot{V}O_{2peak}$) and at VT ($\dot{V}O_2$ at VT); (ii) left ventricular volumes at target low speed during turndown echocardiogram; (iii) KCCQ overall summary score and physical limitation subscale score; and (iv) workloads performed during CPX.

Statistical analysis

Nominal data are presented as percentages of total and continuous data as means (±standard deviations), medians and ranges (min–max), or inter-quartile ranges (IQRs) (25th, 75th percentile) as appropriate. Wilcoxon signed-rank test was used to compare within subject values before and after training. Alpha level was set at <0.05 for all analyses. All analyses were performed using JMP 14 software, SAS Institute Inc., Cary, NC.

Results

Study cohort

Fifty-nine patients were screened for participation (*Figure 1*). Twenty-three met inclusion criteria. Six declined to participate because of inability to commit to the training schedule. Two withdrew consent before baseline testing because of scheduling conflicts and were removed from data analyses.

Fifteen subjects underwent baseline testing (*Table 1*). Twelve completed post-training testing. Two others withdrew early because of training intolerance, and one was urgently listed for transplant because of LVAD malfunction (short-to-shield phenomenon).

Enrolled subjects were aged 51 (29–71) years; 66% were male; 93% were of non-White race; 80% had non-ischaemic cardiomyopathy; and 80% had HM2. Median time of LVAD support prior to training was 18 months (range 3–64 months). Prevalence of beta-blocker therapy was 93%, 33% for angiotensin-converting enzyme inhibitor/angiotensin receptor blocker, and 40% for loop diuretics. Medications were not changed during the study protocol. One-third of the subjects had a history of atrial fibrillation.

Feasibility of high-intensity interval training in left ventricular assist device patients

No major adverse events occurred during training including any driveline exit-site infection. No sessions were discontinued by the supervising physician. One subject had a minor adverse event: recurrent asymptomatic supraventricular tachycardia that occurred after the planned increase in workloads during the fourth training session. This patient

Table 1 Baseline characteristics

Age (years)	51 (29–71)
BMI (kg/m²)	30 (24–48)
Sex (male, %)	10 (66%)
Race	
Black (%)	9 (60%)
Hispanic (%)	5 (33%)
Aetiology of CMP	
Non-ischaemic (%)	12 (80%)
Ischaemic (%)	3 (20%)
Time with LVAD (months)	18 (3–64)
LVAD type	
HM2 (%)	12 (80%)
HM3 (%)	3 (20%)
VAD strategy	
BTT (%)	12 (80%)
DT (%)	3 (20%)
ICD (%)	13 (87%)
Atrial fibrillation (%)	5 (33%)
Beta-blockers (%)	14 (93%)
Mineralocorticoid receptor antagonist (%)	0
ACE-I/ARB (%)	5 (33%)
Loop diuretics (%)	6 (40%)
Sodium (mEq/L)	141 ± 4
Creatinine (mEq/L)	1.2 ± 0.4
Haemoglobin (g/dL)	11.5 ± 2.3
Lactate dehydrogenase (U/L)	300 ± 75
Age-predicted maximal heart rate (b.p.m.)	168 (157, 185)
Predicted $\dot{V}O_{2peak}$ (mL/kg/min)	26 (22, 28)
Baseline $\dot{V}O_{2peak}$ (mL/kg/min)	11.9 (9.5, 14.8)
Peak heart rate during HIIT (b.p.m.)	118 (99, 136)
Recovery heart rate during HIIT (b.p.m.)	110 (94, 127)
Total workload completed per session (W)	1047 (745, 1438)
Percentage of total prescribed workload completed (total W in training period)	90 (78, 99)
Training duration (days)	35 (33, 40)
Time from end of training to testing (days)	2 (1, 8)

ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BTT, bridge to transplant; CMP, cardiomyopathy; DT, destination therapy; HM2, HeartMate II; HM3, HeartMate 3; ICD, implantable cardioverter device; LVAD, left ventricular assist device; VAD, ventricular assist device.
Values are counts (%), means ± standard deviation, median (range), or median (inter-quartile range: 25th, 75th percentile).

completed the training programme using the protocolized lower workloads intended for the first three sessions in all 15 sessions.

In the analysis of percentage of prescribed workload completed, all enrolled subjects who began the training programme were included to reflect overall tolerance to HIIT (*n* = 15). Median workload completed per session was 1047 W (745, 1438 W), which represented 90% (IQR: 78, 99%) of the total prescribed workload (*Table 1*). The median number of sessions completed was 13 (range: 6–15). Eight subjects (53%) completed all 15 sessions, three (20%) completed 13 sessions, one completed 12 sessions, one completed 11 sessions, one completed 10 sessions, and one completed 6 sessions. Subjects who withdrew before completion were invited to return for final testing.

Resting HR before the first training session was 80 (IQR: 74, 88) b.p.m. Median age-predicted maximal HR was

168 (IQR: 157, 185) b.p.m. Training HR was 118 (IQR: 99, 136) b.p.m. during high-intensity intervals and 110 (IQR: 94, 127) b.p.m. during recovery periods (*Figure 2*). RPE during high-intensity intervals was 13 (IQR: 11, 15). A consistent increment was noted on Training Session 4 with the protocolized increase in workloads, with no change in subsequent training sessions (*Figure 3*, $P = 0.7$, for comparison of median RPE across training sessions).

No difference was noted in LVAD flow increase from rest to peak exercise before and after training in subjects with either LVAD type.

Physiological response to high-intensity interval training

High-intensity interval training led to a significant improvement in $\dot{V}O_2$ at VT [7.1 (6.5, 9.1) to 8.5 (7.7, 9.3) mL/kg/min, $P = 0.04$] with small improvements in submaximal work rates [44 (14, 54) to 55 (21, 66) W, $P = 0.05$]. There was no improvement in $\dot{V}O_{2peak}$ [11.9 (9.5, 14.8) to 12 (10.0, 15.0) mL/kg/min, $P = 0.6$] (*Table 2* and *Figure 4*). Improvements in oxygen uptake were larger in subjects with the lowest baseline aerobic capacity. Subject's baseline submaximal and maximal oxygen uptake was strongly correlated with improvements in $\dot{V}O_2$ at VT ($R^2 = 0.54$, $P = 0.006$) and modestly correlated with improvements in $\dot{V}O_{2peak}$ ($R^2 = 0.32$, $P = 0.05$), respectively (Supporting Information, *Figure S2*).

Left ventricular remodelling after high-intensity interval training

Of the initial 10 subjects with turndown echocardiograms, pre-imaging and post-imaging were available in only seven: two were deferred because of subtherapeutic international normalized ratio at the time of planned post-training imaging, and one had suboptimal windows. These seven subjects were all supported with HM2 = 7; 57% ($n = 4$) were male; median age was 53 (IQR: 30, 64) years; and duration of LVAD support was 29 (IQR: 26, 31) months. All were on a beta-blocker, while only one was on angiotensin-converting enzyme inhibitor. HIIT resulted in a significant reduction in LV end-diastolic volume [168 (144, 216) to 159 (124, 212) mL, $P = 0.02$] but no improvements in LV end-systolic volume [118 (94, 152) to 99 (90, 147) mL, $P = 0.08$] or ejection fraction [30 (23, 31) to 28 (27, 30), $P = 0.3$] (*Table 3* and Supporting Information, *Figure S1*). Importantly, all seven subjects showed some reduction in LV end-diastolic volume. Other parameters such as mitral regurgitation severity (mild 62% vs. 67%, $P = 0.9$) and right ventricular systolic pressure (31, IQR: 21, 40 mmHg vs. 26, IQR: 18, 45 mmHg, $P = 0.7$) remained unchanged.

Quality of life

Kansas City Cardiomyopathy Questionnaire overall summary and physical limitation subscale scores did not show significant improvements after this 5 week HIIT programme. Other

Figure 2 Heart rate (HR) during training. HR was measured for every subject at rest and during each high-intensity interval (peak) and 2 min into every other recovery period (recovery). APMHR, age-predicted maximal HR (220 − age). Columns and error bars are medians and inter-quartile range.
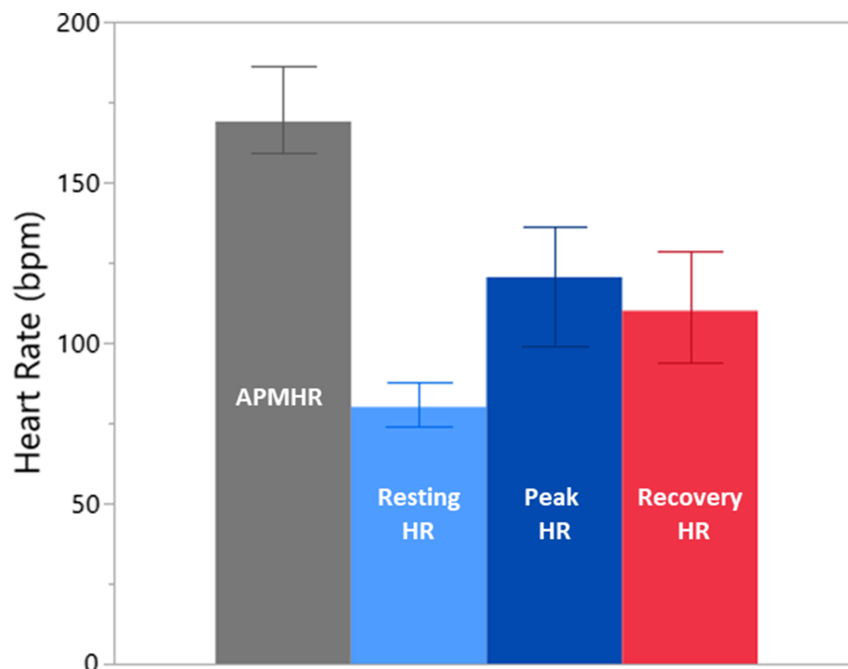
Figure 3 Rate of perceived exertion during high-intensity intervals over time. Lines represent progression of median score on Borg scale (6–20 points) for each subject during each high-intensity interval across all training sessions.
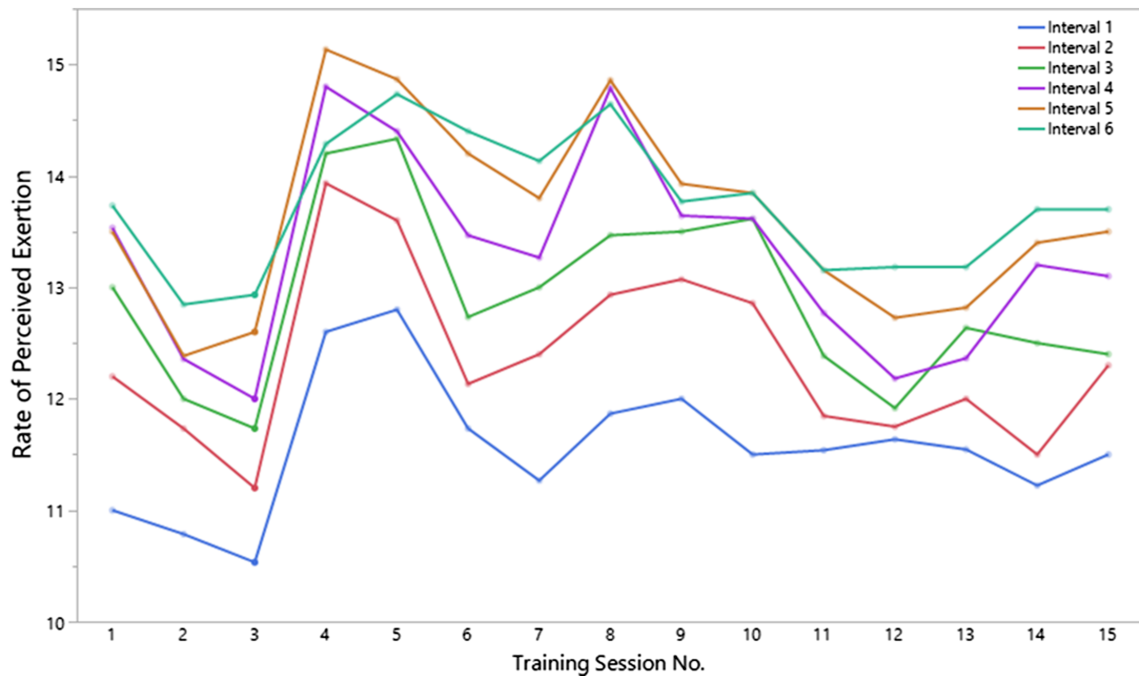

Table 2 Cardiopulmonary exercise parameters (N = 12)

	Baseline	Post-HIIT	*P*-value
$\dot{V}O_{2peak}$ (mL/kg/min)	11.9 (9.5, 14.8)	12 (10, 15)	0.6
$\dot{V}O_2$ at VT (mL/kg/min)	7.1 (6.5, 9.1)	8.5 (7.7, 9.3)	0.04*
Heart rate at VT (b.p.m.)	100 (86, 109)	96 (86, 109)	0.9
Peak heart rate (b.p.m.)	120 (103, 145)	109 (97, 141)	0.3
Respiratory exchange ratio (RER)	1.3 (1.2, 1.4)	1.3 (1.16, 1.3)	0.16
Ventilatory efficiency (VE/VCO₂)	40 (35, 44)	42 (37, 43)	0.88
FEV1 (L)	2.3 (2.1, 2.4)	2.4 (2.1, 2.6)	0.7
Work rate at VT (W)	44 (14, 54)	55 (21, 66)	0.054
Peak work rate (W)	99 (25, 141)	100 (67, 124)	0.18
Exercise time (s)	540 (439, 595)	528 (391, 633)	0.33
Peak rate of perceived exertion (RPE)	16 (14, 17)	15 (14, 17)	0.7
HM2 pump speed (r.p.m.)	9110 ± 363	9111 ± 363	0.8
HM3 pump speed (r.p.m.)	5300 ± 216	5350 ± 70	0.7
HM2 flow increment rest to peak (L/min)	1.0 (1.0, 1.5)	1.2 (0.7, 1.8)	0.8
HM3 flow increment rest to peak (L/min)	0.7 (0.1, 0.9)	0.5 (0.2, 0.7)	0.5
KCCQ overall summary score	72 (60, 79)	64 (53, 84)	0.5
KCCQ physical limitation subscale score	75 (62, 88)	75 (62, 92)	0.51

HIIT, high-intensity interval training; HM2, HeartMate II; HM3, HeartMate 3; KCCQ, Kansas City Cardiomyopathy Questionnaire; RER, respiratory exchange ratio; VCO₂, volume of exhaled carbon dioxide; VE, ventilation; VT, ventilatory threshold.
Values are means ± standard deviation or medians (inter-quartile range: 25th, 75th percentile).
*Difference of baseline vs. post-HIIT, $P < 0.05$.

subscales in the questionnaire did not change significantly after training (*Table 2*).

Discussion

The main finding of this study is that a personalized, CPX-guided HIIT protocol is feasible in stable LVAD patients on prolonged support. After 204 supervised sessions, there were no major adverse events.

Although only 25% of subjects initially screened for inclusion were enrolled in this study, 80% of those enrolled completed at least 80% of the training sessions. This suggests that HIIT can be tolerated by a subset of LVAD patients. Although, the applicability of HIIT in this population may be limited, it cannot be estimated accurately from this study given that our exclusion criteria

Figure 4 Change in oxygen consumption after high-intensity interval training. Maximal ($\dot{V}O_{2peak}$) and submaximal [$\dot{V}O_2$ at ventilatory threshold (VT)] oxygen consumption during cardiopulmonary exercise test before and after 5 weeks of high-intensity interval training (HIIT). Columns and bars represent medians and inter-quartile range.
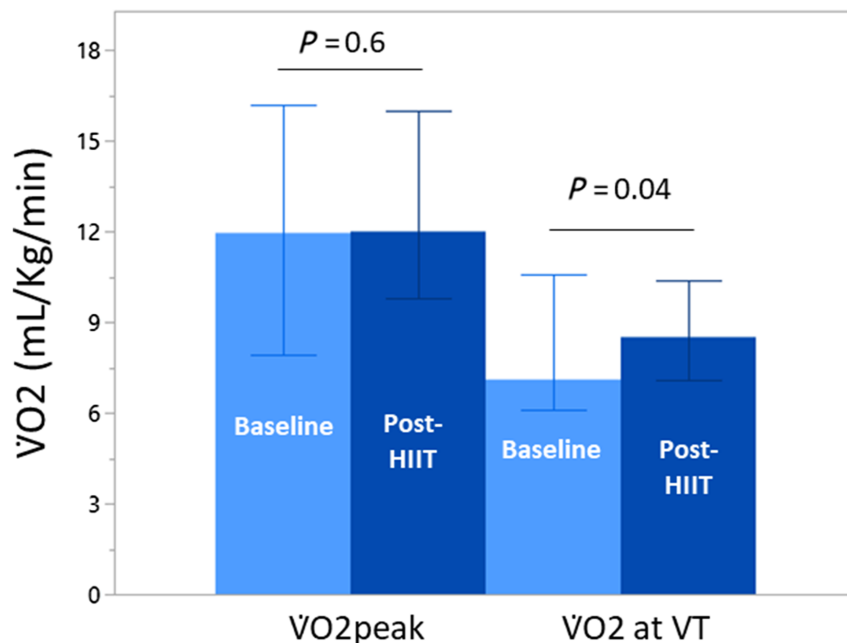

Table 3 Turndown echocardiogram ($N = 8$)

	Baseline	Post-HIIT	*P*-value
Left ventricular end-diastolic diameter (cm)	6.5 (5.7, 6.9)	6.5 (5.7, 7.2)	0.9
Left ventricular end-diastolic volume (mL)	168 (144, 216)	159 (124, 212)	0.02*
Left ventricular end-systolic volume (mL)	118 (94, 152)	99 (90, 147)	0.08
Left ventricular ejection fraction (%)	30 (23, 31)	28 (27, 30)	0.3

HIIT, high-intensity interval training.
Values are medians (inter-quartile range: 25th, 75th percentile).
*Difference of baseline vs. post-HIIT, $P < 0.05$.

were largely arbitrary because of the lack of pre-existing data in this field.

Our HIIT protocol used each subject's baseline peak work rate (W) during CPX to guide training intensity. The customary use of training HR for this purpose would have been inadequate given the high prevalence of chronotropic incompetence and impaired HR recovery in this patient group[27,28] (*Figure 2*).

We increased workloads after the first three sessions, and RPE increased accordingly in all subjects on Training Session 4. In subsequent sessions, RPE did not vary significantly but showed a downward trajectory reflecting adaptation to training (*Figure 3*, $P = 0.7$).

After only fifteen 30 min sessions, HIIT led to a significant improvement in submaximal exercise capacity ($\dot{V}O_2$ at VT). Despite the absence of a control group, prior data would suggest that these improvements can be attributed to the effects

of HIIT, given the prolonged time on LVAD support and clinical stability of this cohort. Improvements in functional capacity are unlikely at this stage without a directed intervention.[8]

The greatest improvements in submaximal capacity were seen in the most deconditioned subjects. Those with the lowest baseline $\dot{V}O_{2peak}$ values [<12 mL/kg/min ($N = 6$)] saw the greatest (15%) improvement in $\dot{V}O_2$ at VT ($P = 0.006$) (Supporting Information, *Figure S2*).

Intriguingly, we also observed LV reverse remodelling at a time when remodelling due to unloading is expected to plateau.[29] The observed magnitude of decrease in diastolic LV volumes was small, 5% over a 5 week period, but provides important insights into the effects of HIIT.

Prior to this study, HIIT had rarely been reported in the LVAD population. In one case report, a severely deconditioned patient, unable to tolerate MCT, improved after a short heart rate-guided HIIT programme.[20] In another

study, 12 patients completed an unspecified HIIT protocol as part of a multimodal cardiac rehabilitation programme with improvement in cerebral blood flow during CPX.[30]

Our findings open a pathway for the systematic application of this training modality in LVAD patients. Future studies should directly compare HIIT with MCT in patients with the lowest aerobic capacity and investigate its effects on peripheral and central determinants of oxygen consumption. We suggest that baseline CPX peak work rate, and not HR, should serve to guide training intensity, and protocolized adaptations in workloads should be contemplated to preserve high RPEs throughout the training programme.

One important question that remains is why $\dot{V}O_{2peak}$ values did not follow the improvements seen in $\dot{V}O_2$ at VT. Without interventions to increase CO, such as increasing the LVAD speed during exercise[31] or providing rate response pacing in patients with chronotropic incompetence,[28] LVADs provide sufficient flow to support submaximal efforts but not peak exercise.[22] Hence, HIIT may have increased $\dot{V}O_2$ at VT through improvements in peripheral determinants of oxygen consumption, such as mitochondrial oxidative capacity[21] and capillary density of skeletal muscle.[32]

Other reasons for the lack of improvement in $\dot{V}O_{2peak}$ may include the small size and heterogeneity of our sample ($n = 12$ HM2 and $n = 3$ HM3) or the short duration of our training protocol (5 weeks).

However, improvements in $\dot{V}O_{2peak}$ may not be a paramount goal in this patient population. $\dot{V}O_{2peak}$ has a weak correlation with 6 min walk test distance in patients with LVAD compared with unsupported HF patients.[33] Therefore, improvements in submaximal exercise capacity, reflected by $\dot{V}O_2$ at VT, may be more relevant for improvements in health status.[4]

Another important question is why we saw no consistent improvements in KCCQ scores. This may be explained by insensitivity of this questionnaire to detect short-term changes in clinically stable LVAD.[3] On the other hand, our intervention was limited to physical training, and multimodal interventions affecting different subscales of the questionnaire may be needed to drive perceptible improvements in the overall score.[7]

Study limitations

The main limitation of our study is the lack of a control group to compare the effect of HIIT with standard of care; however, improvements in exercise capacity without ET are concentrated during the first 3 to 6 months after LVAD implantation, and most patients in our cohort had passed this period.

A second limitation is the lack of progressive increments in training workloads after the fourth training session. Although the stability of RPE scores confirms a consistent effort intensity throughout training, some patients were training at

suboptimal effort levels (RPE < 13), and a further increase in workloads was not contemplated in our protocol.

A third limitation is the short duration of our training protocol. This duration was chosen based on prior studies where HIIT showed significant benefits after even shorter training periods[21] and because patients in our study were asked to coordinate the training session schedule with their usual activities and other medical care. This would have complicated compliance with a longer duration protocol. However, patients on long-term support may require longer periods of ET to see greater improvements.[8]

And lastly, White patients were largely under-represented in our sample, which could limit the generalizability of our results.

Conclusions

In conclusion, a personalized, CPX-guided HIIT protocol is feasible in stable patients on LVAD support. More studies are needed to evaluate its effects on central and peripheral determinants of aerobic capacity.

Conflict of interest

U.P.J. serves as a consultant for Abbott Inc. but receives no honoraria. No other relevant conflicts of interest are reported.

Funding

None.

Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1. Left Ventricular End-Diastolic Volume (LVEDV) before and after HIIT ($n = 7$)– LVEDV was measured during device turndown before and after training. HIIT resulted in a significant reduction in LVEDV: 168 (144, 216) mL to 159 (124, 212) mL.
Figure S2. Association between improvement in oxygen consumption and baseline level of fitness. Subject's baseline submaximal and maximal oxygen uptake was strongly correlated with improvements in $\dot{V}O_2$ at VT ($R2 = 0.54$, $P = 0.006$) and modestly correlated with improvements in $\dot{V}O_{2peak}$ ($R2 = 0.32$, $P = 0.05$) respectively
Table S1. Reproducibility of CPX parameters.

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