ORIGINAL REPORT

EFFECTS OF EXERCISE TRAINING ON PHYSICAL ACTIVITY IN HEART FAILURE PATIENTS TREATED WITH CARDIAC RESYNCHRONIZATION THERAPY DEVICES OR IMPLANTABLE CARDIOVERTER DEFIBRILLATORS

Hidetoshi YANAGI, PhD^{1,2}, Harumi KONISHI, RN³, Saori YAMADA, RN³, Kazufumi KITAGAKI, MSc¹, Michio NAKANISHI, MD^{1,4}, Taku HARADA, MD, PhD² and Masahiro KOHZUKI, MD, PhD²

From the ¹Department of Cardiovascular Rehabilitation, National Cerebral and Cardiovascular Center, Osaka, ²Department of Internal Medicine and Rehabilitation Science, Disability Science, Tohoku University Graduate School of Medicine, Sendai, ³Department of Nursing, National Cerebral and Cardiovascular Center and ⁴Department of Cardiovascular Medicine, National Cerebral and Cardiovascular Center, Osaka, Japan

Objective: This study elucidated the effects of exercise training on physical activity, 6-min walk distance, and all-cause hospitalization rates in patients with chronic heart failure, and evaluated factors contributing to changes in physical activity.

Design: Prospective cohort observational study. Patients and methods: Patients (n=62) who completed an exercise training programme after implantable cardioverter-defibrillator or cardiac resynchronization therapy treatment between May 2017 and May 2018 were included. Patients exercised for 20–50 min 3–5 times weekly for 3 months and were assigned to the active (\geq 10 min/day) or non-active

(<10 min/day) group based on changes in walking times between baseline and 3 months, as assessed by the International Physical Activity Questionnaire. Results: The 6-min walk distance improved in both groups with exercise training. Physical activity level did not increase in some patients, despite improvements in exercise tolerance. Depression improved significantly in the active group, but no correlation was found with physical activity. Factors contributing to physical activity changes were not identified. The all-cause hospitalization rate was lower in the active group during follow-up (mean 10.5 months). Conclusion: Exercise training effectively increased 6-min walk distance regardless of physical activity. Non-active patients experienced increased all-cause hospitalizations. Increasing physical activity improves patient outcomes.

Key words: exercise; defibrillator; heart failure.

Accepted Aug 6, 2020; Epub ahead of print Aug 24, 2020

J Rehabil Med 2020; 52: jrm00111

Correspondence address: Masahiro Kohzuki, 1-1 Seiryo-cho, Aoba-ku, Sendai 980-8574, Japan. E-mail: kohzuki@med.tohoku.ac.jp

Patients with heart failure (HF) experience ventricular tachycardia or ventricular fibrillation with a recurrence rate of 10–20% (1). Implantable cardioverter-defibrillator (ICD) and cardiac resynchronization therapy (CRT) defibrillator (CRT-D) are highly effective for decreasing mortality from ventricular tachycardia or ventricular fibrillation (2, 3). CRT is a highly effective treatment for drug-refractory systolic heart failure (HF)

LAY ABSTRACT

Patients who completed an exercise training programme after implantable cardioverter-defibrillator or cardiac resynchronization therapy treatment in our institution between May 2017 and May 2018 were included. The aim of this study was to determine the effects of exercise training on walking time, 6-min walk distance, and hospitalization rate. Patients exercised for 20–50 min 3–5 times weekly for 3 months. Training helped patients with implantable cardioverter-defibrillator or cardiac resynchronization therapy improve the 6-min walk distance, regardless of changes in physical activity. However, the non-active group had higher rates of all-cause hospitalization. Increasing physical activity improves patient outcomes.

patients with a wide QRS complex (3, 4). Treatment with CRT results in left ventricular (LV) reverse remodelling, based on the findings of a decrease in LV size and/or increase in LV ejection fraction (LVEF), which reduces morbidity and mortality (3). However, studies have shown that clinically significant anxiety disorders and depressive symptoms are prevalent among patients with ICD and CRT defibrillator (CRT-D) (5, 6).

Decreased physical activity (PA) is common, regardless of shock exposure, among patients with ICD and CRT-D (7–9). After ICD or CRT treatment, exercise training (ET) has been reported to improve exercise capacity without adverse events (4, 10–12). In addition, reports suggest that this improves the patients' prognosis. Increased PA in patients with ICD or CRT-D is associated with decreased HF hospitalization and mortality rates (13, 14). However, the effects of ET on PA in patients with ICD and CRT-D are unclear. Therefore, this study aimed to elucidate the effects of ET on PA and 6-min walk distance (6MWD) or all-cause hospitalization, and to clarify factors contributing to the change in PA in chronic HF patients with ICD or CRT.

METHODS

Ethical considerations

This study was conducted in accordance with ethical standards on human experimentation and with the Declaration of Helsinki 1975, revised 1983. In particular, the study protocol was approved by the ethics committee of the National Cerebral and Cardiovascular Center (approval number M26-015), where the study was performed. All patients provided written informed consent.

Study design and participants

This prospective observational cohort study included patients who completed a 3-months ET programme after ICD, CRTpacemaker (CRT-P) or CRT-D treatment at our institution between May 2017 and May 2018. Patients were eligible for the ET programme if they met any of 3 criteria (LVEF $\leq 40\%$, percent predicted peak oxygen uptake $\leq 80\%$, and B-type natriuretic peptide level \geq 80 pg/ml) and had been referred to the programme at their physicians' discretion. Between May 2017 and May 2018, 65 patients met the inclusion criteria. Two patients died, and 1 did not complete the questionnaire; thus, 62 participants were included in the analysis. Treatment for HF was tailored to all patients based on current guidelines, which were consistent throughout the study period (15). HF patients treated with an ICD or CRT were evaluated in prospective observational studies at baseline (at the beginning of the ET programme), 3 months (at the end of the 3-months ET programme), and 6 months (3 months after the end of ET programme).

After 3 months of ET, participants were categorized into 2 groups according to the walking time assessed by the International Physical Activity Questionnaire (IPAQ). Based on the change in walking time between baseline and 3 months, patients who walked ≥ 10 min/day were allocated to the "active group" (n=33) and those <10 min/day were allocated to the "non-active group" (n=29, Fig. 1), based on a study that reported a 10-min increase in PA reduced HF hospitalization risk by 4% (13). After identifying the 2 groups, baseline data were analysed retrospectively.

Exercise programme

A description of the exercise protocol has been published previously (4). The 3-months ET programme began with supervised in-hospital sessions consisting of walking, bicycle ergometer, and low-intensity resistance training for 20-40 min sessions 3-5 times per week, followed by home ET combined with once- or twice-weekly supervised in-hospital ET sessions. The duration increased to 30-60 min, and the intensity of the endurance exercise was determined individually at a heart rate corresponding to 40-60% of the heart rate reserve (maximum heart rate minus resting heart rate), anaerobic threshold level obtained on baseline cardiopulmonary exercise testing, or at level 12-13 ("a little hard") of the 6-20 scale perceived rating of exercise (original Borg scale). All patients were encouraged to continue home ET with an individualized exercise prescription, based on the cardiopulmonary exercise testing or 6-min walk test results at baseline and 3 months. Individualized exercise prescriptions were tailored throughout the study period based on current guidelines (16).

Physical activity

PA was assessed using the IPAQ score and step count. IPAQ has high reliability and validity when monitoring PA across diverse populations (17) and has, therefore, become the most widely used questionnaire to assess PA. In addition, the reliability and validity of the Japanese version have been verified (18). This study used the IPAQ short form, and activities of different intensities were reported for each domain. Domains were divided into vigorous PA, moderate PA, and walking. Weekly duration estimates for vigorous and moderate PA were calculated by multiplying the time spent performing the activity in a typical day by the number of days in the past week spent performing that activity. Weekly durations were then multiplied by metabolic equivalent (MET) values for the different activities to calculate MET-minutes per week for each intensity level. To determine sedentary time, patients were instructed to think about the time they spent sitting or lying at work, at home, while doing course work, and during leisure time. Time spent sleeping was excluded from sedentary time. Then they were asked to estimate the total number of h and min per day they spend sitting or lying time. Walking time was calculated as time (min) × frequency (times/week)/7. Participants were interviewed immediately after completing IPAQ to prevent recall bias.

A description of the step count protocol has been published previously (19). Briefly, all patients wore a triaxial accelerometer (AM500N; Acos Co. Ltd, Nagano, Japan) 24 h a day for 8 days, except while bathing and sleeping (19). Continuous data from the final 7 days of the 8-day collection period were used to assess daily patient PA (19). Step counts were recorded after age, sex, height, and weight were entered for each patient. In addition, the active MET was set to 2.8, according to a previous study on the activity amount targeting the device (18, 20). The active step count was steps at 2.8 METs, and the active activity time was the activity time at 2.8 METs. IPAQ and step counts were assessed at baseline. Furthermore, IPAQ findings and step counts were assessed at the 3rd (from 8 days before the end of the 3-months period to the end of the 3-months period) and 6th months (from 8 days before the end of the 6-months period to the end of the 6-months period) follow-up examinations.



Fig. 1. Study design flowchart.

JRM

Physical performance

This study followed a previously published protocol for measuring isometric knee extensor muscle strength (IKEMS) (4). In summary, IKEMS was measured using the μ -Tas MF-1 assembly (Anima Co. Ltd, Tokyo, Japan) (21) at baseline and after 3 months of ET. A 6-min walk test was also performed at baseline and after 3 months of ET. Participants were asked to walk continuously for 6 min with maximum effort, and the distance was recorded.

Depression and quality of life

Symptoms of depression were measured using the Patient Health Questionnaire-9 (PHQ-9), with items mirroring the diagnostic criteria for major depressive disorders (22). Patients were asked to rate items on the questionnaire on a scale from 0 (not at all) to 3 (nearly every day) according to their symptoms during the past 2 weeks (22, 23). Scores in the PHQ-9 range from 0 to 27, and a cut-off score >10 was used to detect patients with clinically relevant levels of depression (23, 24).

Quality of life (QOL) was assessed using the Japanese version of the Medical Outcomes Study 36-Item Short-form Health Survey (SF-36) questionnaire (25–27). The SF-36 consists of a physical component summary (PCS), mental component summary (MCS), and role component summary (RCS) score. The final score (range 0–100) was calculated according to recommendations from the SF-36 guidelines, with higher scores representing a better QOL (25–27). The patient PHQ-9 and SF-36 data were evaluated at baseline and at 3 and 6 months.

Statistical analyses

Data are expressed as mean and standard deviation (SD) unless otherwise stated. Categorical variables were compared using Fisher's exact test. Comparisons between groups were analysed using the unpaired Student's *t*-test or Wilcoxon rank-sum test, depending on normality of distribution. Comparisons

within groups were analysed using the paired *t*-test or Wilcoxon signed-rank test. Based on a study by Abraham et al. (28), that used increases in the 6MWD to determine sample size, a sample size of 20 was required to detect an increase of 53 m in the 6MWD in patients with HF after CRT, with a standard deviation of ± 66 m, power of 0.80, and α value set at p < 0.05 (2-tailed). Analysis of covariance (ANCOVA) was used to examine changes during the 3-months ET programme with the corresponding baseline measurement used as a covariate. Spearman's rank correlation coefficients were used to evaluate the relationships between change in walking time and other variables of interest. Differences of all-cause hospitalizations, HF hospitalization, and ICD therapy (excluding CRT-P) in the active and non-active group were compared using Kaplan-Meier survival curves and compared using the log-rank test. All statistical analyses were performed using JMP Pro version 14.2.0 (SAS Institute, Cary, NC, USA). For all tests, p < 0.05 was considered statistically significant.

RESULTS

Attendance at the supervised in-hospital ET sessions during the 3-months ET programme

was similar in the 2 groups (active group: mean 16 (SD10), non-active group: mean 16 (SD 9), p=0.887). Fourteen participants (42%) in the active group completed <12 sessions of the supervised in-hospital sessions. Among the remaining participants, 2 (6%) completed all 36 sessions; 6 (18%) completed 24–36 sessions. In the non-active groups, 10 of the 29 (34%) completed <12 sessions of the supervised in-hospital sessions. In the remaining participants, 2 (7%) completed all 36 sessions; 2 (7%) completed 24–36 sessions.

During the 3-months ET programme, there were no exercise-related adverse events, such as ventricular tachycardia, ventricular fibrillation, the occurrence of anti-tachycardia pacing or shock, lead dislocation, deterioration of the surgical wound site, or device malfunction.

Patient characteristics

There were no significant differences in patient characteristics between the active and non-active groups (Table I). In both, active and non-active groups, the number of patients receiving CRT was 19.

Changes during the 3-months exercise training programme

There was a significant improvement in 6MWD in both groups (p < 0.01). However, the PHQ-9 score significantly improved only in the active group (p < 0.01). The active group also showed significant improve-

Table I. Patient characteristics

	Active	Non-active	
Variable	(<i>n</i> = 33)	(<i>n</i> =29)	<i>p</i> -value
Age, years, mean (SD)	63 (14)	61 (16)	0.640
Male sex, n (%)	23 (70)	20 (69)	0.950
Body mass index, kg/m ² , mean (SD)	21.4 (3.5)	21.1 (4.0)	0.763
Old myocardial infarction, n (%)	8 (24)	14 (48)	0.065
Peripheral artery disease, n (%)	7 (21)	1 (3)	0.057
Orthopaedic disease, n (%)	11 (33)	10 (34)	0.924
Cerebrovascular disease, n (%)	6 (18)	1 (3)	0.067
CRT-D, n (%)	15 (45)	18 (62)	0.336
Left ventricular ejection fraction, %, mean (SD)	26 (13)	28 (15)	0.615
Left ventricular end-diastolic diameter, mm, mean (SD)	64 (13)	61 (13)	0.378
Left ventricular end-systolic diameter, mm, mean (SD)	56 (17)	53 (14)	0.447
BNP level, pg/ml, mean (SD)	307 (229)	362 (333)	0.447
eGFR, ml/min/1.73 m ² , mean (SD)	51 (21)	54 (26)	0.569
Frailty, n (%)	5 (15)	6 (21)	0.843
Prefrail, n (%)	19 (58)	16 (55)	
Robust, n (%)	9 (27)	7 (24)	
Medication, n (%)			
Diuretic	27 (82)	24 (83)	0.923
Angiotensin-converting enzyme inhibitor	17 (52)	15 (52)	0.987
β-blocker	32 (97)	26 (90)	0.332
Inotropic drug	6 (18)	7 (24)	0.565
Angiotensin-receptor blocker	7 (21)	4 (14)	0.446
Anti-arrhythmic drugs	15 (45)	18 (62)	0.213

CRT-D: cardiac resynchronization therapy – defibrillator; BNP: B-type natriuretic peptide; eGFR: estimated glomerular filtration rate; SD: standard deviation.

p. 4 of 7 H. Yanagi et al.

Table II. Changes in variables during the 3-months exercise training programme

	Active group/Non- active group n	Active group		Non-active group	
Variable		Baseline Mean (SD)	3 months Mean (SD)	Baseline Mean (SD)	3 months Mean (SD)
6MWD, m	33/24	450 (128)	512 (116)*	453 (91)	493 (112)*
IKEMS, kgf	33/24	30 (12)	34 (11)*	29 (15)	31 (13)
IKEMS/BW, kgf/kg	33/24	51 (14)	55 (13)*	50 (16)	54 (14)
IPAQ					
Sedentary time, min/day	33/29	855 (224)	547 (282)*	679 (281)	681 (234)
Walking, MET-minutes/week	33/29	296 (414)	1,567 (2,134)*	1,013 (1,815)	379 (443)*
Moderate PA, MET-minutes/week	33/29	140 (463)	640 (1,315)*	168 (375)	288 (884)
Vigorous PA, MET-minutes/week	33/29	167 (641)	255 (626)	375 (1,224)	251 (546)
Walking time, min/day	33/29	15 (21)	80 (109)*	52 (93)	19 (23)*
Pedometer			· · ·		
Step count, steps/day	17/14	3,926 (2,652)	5,604 (3,361)*	4,102 (2,768)	3,336 (3,265)
Activity time, min/day	17/14	48 (28)	68 (31)*	53 (26)	45 (37)
Active step count, step/day	17/14	3,135 (2413)	4,516 (3,081)*	3,271 (2,615)	2,518 (2,943)
Active activity time, min/day	17/14	36 (25)	51 (28)*	41 (26)	33 (32)
PHQ-9	33/29	4.7 (3.9)	3.0 (3.4)*	3.5 (3.6)	4.8 (4.2)
MOS 36-Item Short-Form Health Survey			()		
PCS	32/28	33 (15)	38 (12)*	36 (11)	35 (14)
MCS	32/28	53 (9)	55 (10)	53 (11)	52 (11)
RCS	32/28	40 (16)	45 (13)*	37 (19)	44 (14)*

*p<0.05 vs baseline

6MWD: 6-min walk distance; ET: exercise training; IKEMS: isometric knee extensor muscle strength; IPAQ: International Physical Activity Questionnaire; BW: body weight; PA: physical activity; MET: metabolic equivalents; MOS: Medical Outcomes Study; PHQ: Patient Health Questionnaire; PCS: physical component summary; MCS: mental component summary; RCS: role component summary; SD: standard deviation.

ment in IKEMS, sedentary time, walking according to the IPAQ, walking time, step count, PCS, and RCS (p < 0.01) (Table II).

In the non-active group, walking according to the IPAQ and walking time decreased significantly (Table II). However, RCS improved significantly.

Significant differences were found between the groups. The sedentary time, walking, walking time according to the IPAQ, active step count, PHQ-9, and PCS were better in the active group than in the non-active group (Table III).

Follow-up and adverse events

The mean PHO-9 of the active group was significantly worsened between 3 and 6 months (3.0 (SD3.4) to 4.0 (SD 3.8), p=0.037). There was a significant increase in walking according to the IPAQ in the non-active group from 3 to 6 months (mean 379 MET-minutes/week (SD 443) to 768 MET-minutes/week (SD 765), p<0.001). Other factors did not change significantly. There were no significant differences in HF hospitalization or ICD therapy (4 active (4 from anti-tachycardia pacing) vs 6 non-active (3 from anti-tachycardia pacing)) between the active and non-active groups. However, during a mean follow-up of 10.5 months, the number of allcause hospitalizations was higher in the non-active group than that in the active group, with 13 (11 from cardiac causes) and 6 (4 from cardiac causes) all-cause hospitalizations, respectively (p=0.037) (Fig. 2A–C). No significant differences in all-cause hospitalizations were shown among patients in the ICD and CRT groups in the active and non-active groups.

Univariate analysis of change in walking time by exercise training between baseline and 3 months with clinical characteristics

Change in walking time was significantly related to walking (r=-0.28; p=0.031) and walking time (r=-0.28; p=0.029) according to the IPAQ at baseline (Table IV). However, the correlation coefficient was low. Other factors were not significantly related (Table IV).

Table III. Adjusted mean difference in outcomes after exercise training

	Estimate	Standard error	<i>p</i> -value
6MWD, m	10.76	6.82	0.121
IKEMS, kgf	1.00	0.77	0.204
IKEMS, kgf/kg	0.44	1.19	0.711
Sedentary time, min/day	-83.00	34.98	0.021
Walking, MET-minutes/week	702.66	205.42	0.001
Moderate PA, MET-minutes/week	176.76	145.63	0.230
Vigorous PA, MET-minutes/week	23.80	71.48	0.740
Walking time, min/day	35.85	10.48	0.001
Step count, step/day	587.35	309.31	0.063
Activity time, min/day	5.84	3.93	0.142
Active step count, step/day	554.21	252.68	0.032
Active activity time, min/day	5.46	3.09	0.083
PHQ-9	-1.20	0.41	< 0.001
PCS	2.75	1.34	0.045
MCS	1.39	1.09	0.208
RCS	-0.11	1.49	0.944

Estimated value in the active group compared with the non-active group. 6MWD: 6-min walk distance; ET: exercise training; IKEMS: isometric knee extensor muscle strength; IPAQ: International Physical Activity Questionnaire; BW: body weight; PA: physical activity; MET: metabolic equivalents; MOS: Medical Outcomes Study; PHQ: Patient Health Questionnaire; PCS: physical component summary; MCS: mental component summary; RCS: role component summary.





Fig. 2. Kaplan-Meier curves for all-cause hospitalizations, heart failure (HF) hospitalization, and implantable cardioverter-defibrillator (ICD) therapy in the active and non-active groups. The rate of all-cause hospitalization is significantly higher in the non-active group (2A). Heart failure hospitalization (2B) and defibrillation therapy events (2C) do not show any significant difference.

Table IV. Univariate analysis of change in walking time by exercise training (ET) between baseline and 3 months with clinical characteristics

	n	r	<i>p</i> -value
Age	62	0.07	0.582
Body mass index	62	0.12	0.356
LVEF	62	-0.09	0.469
LV end-diastolic diameter	62	0.16	0.211
LV end-systolic diameter	62	0.14	0.271
BNP	62	-0.11	0.389
eGFR	62	-0.08	0.514
Number of ET sessions	62	0.03	0.829
6MWD	62	0.03	0.792
IKEMS, kgf	62	0.07	0.598
Sedentary time	62	0.23	0.076
Walking	62	-0.28	0.031
Moderate PA	62	-0.17	0.186
Vigorous PA	62	-0.10	0.422
Walking time	62	-0.28	0.029
Step count	33	0.07	0.583
Activity time	33	0.03	0.806
Active step count	33	0.07	0.588
Active activity time	33	0.03	0.844
PHQ-9	62	0.02	0.876
PCS	60	-0.07	0.585
MCS	60	0.03	0.805
RCS	60	0.13	0.334

LV: left ventricular; LVEF: left ventricular ejection fraction; BNP: B-type natriuretic peptide; eGFR: estimated glomerular filtration rate; ET: exercise training; 6MWD: 6-min walk distance; ET: exercise training; IKEMS: isometric knee extensor muscle strength; IPAQ: International Physical Activity Questionnaire; BW: body weight; PA: physical activity; MET: metabolic equivalents; MOS: Medical Outcomes Study; PHQ: Patient Health Questionnaire; PCS: physical component summary; RCS: nental component summary; RCS: role component summary.

DISCUSSION

Results from patients who were treated with CRT or ICD and completed ET showed that the PA level did not increase in some patients, despite improvements in exercise tolerance associated with ET. To our knowledge, this is the first study to report changes in the PA of patients receiving CRT who completed ET.

Gad et al. reported that 3 months after CRT treatment without ET, patient step counts were significantly reduced (29). Furthermore, it has been reported that the PA of HF patients after ICD and CRT treatment without ET increased, but the measuring device used in the studies was a single-axis accelerometer (13, 14). Therefore, it is difficult to compare the results of the studies with those of the present study, because a tri-axial accelerometer and a different measurement algorithm were used. Nonetheless, a 10-min increase in PA among ICD or CRT-D patients resulted in decreased HF hospitalization and mortality rates (13, 14). However, it remains unclear whether exercise tolerance or daily step count is a prognostic indicator in HF patients after ICD and CRT treatment. To date, exercise tolerance has often been used as a prognostic indicator. In this study, patients treated with CRT or ICD who completed ET showed a significant increase in

Journal of Rehabilitation Medicine

p. 6 of 7 H. Yanagi et al.

6MWD. Therefore, it has been shown that completing this ET may contribute to improving their prognosis. Furthermore, the active group also showed significant improvement in IKEMS, sedentary time, walking according to the IPAQ, walking time, step count, PCS, and RCS (p<0.01). A recent study reported that daily step counts objectively measured by an accelerometer may be a prognostic indicator of mortality rather than peak oxygen uptake in Japanese outpatients with HF who did not receive ICD or CRT treatment (19). Therefore, these results reveal why the all-cause hospitalization rate was lower in the active group.

In this study, the non-active group had higher rates of all-cause hospitalization than the active group. No patients in either group experienced exercise-related adverse events, including ICD therapy and HF hospitalization, similar to the findings of previous reports (4, 10). Steinhaus et al. reported that 16% of patients with ICD or CRT-D implants who participated in ET had ICD therapy during follow-up (12). In this study, 17.5% of all patients at 12.2 months had adverse events unrelated to ET, including ICD therapy. However, despite the improvement in exercise tolerance, the non-active group had significantly more all-cause hospitalizations. Izawa et al. reported that a reliable indicator of mortality among patients with HF was daily step count, with a cut-off of 4,889 steps/day (19). The step count was lower than the cut-off value in the non-active group. Furthermore, the American Heart Association recently released a Science Advisory that highlighted the deleterious association between sedentary behaviour and cardiovascular disease morbidity and mortality (30). In this study, sedentary time did not significantly improve in the non-active group; hence this group was considered to have a poorer prognosis, with a higher risk of all-cause hospitalization. However, it remains unclear whether hospitalization decreases due to longer increments of PA or if patients with lower levels of PA are more susceptible to re-admission.

Among patients with ICD and CRT-D, clinically significant anxiety disorders and depressive symptoms are prevalent (5, 6). Moreover, with no relation to shock exposure, low PA has been described (7, 8). Using PHQ-9 in this study, the active group showed significant improvement from baseline to 3 months, whereas the non-active group tended to deteriorate. Therefore, we surmised that changes in PA and depression were related. However, no correlation was found between PA and depression, possibly because the baseline score was higher than that in a previous report (31).

Borland et al. reported that group-based exercise did not improve the PA level in patients with chronic heart failure and comorbidity (32). Our results show that the PA level did not increase in some patients, despite improvement in exercise tolerance associated with ET. This study had some limitations. First, this study lacked a control (non-exercise) group from a single institute. Secondly, it included a small number of patients from a single centre. Moreover, an accelerometer could not be obtained in all patients. However, a study assessing PA in patients undergoing CRT had a similar sample size (29). This study had a small sample size, and therefore shock and anti-tachycardia pacing treatments in ICD therapy were not delineated. Thirdly, the participation rate of supervised ET was low in the active and non-active groups; however, there was no difference between the 2 groups. Therefore, the impact on PA was small. Finally, it was difficult to calculate the sample size between groups, and the study may thus have been underpowered.

In conclusion, patients who underwent ET after CRT or ICD treatment showed a significant increase in 6MWD regardless of the change in PA. Nevertheless, the non-active group had higher rates of all-cause hospitalization than the active group. Future studies should focus on constructing exercise programmes to decrease hospitalization risk for patients, especially for those who do not show increased PA.

ACKNOWLEDGEMENTS

The authors acknowledge the support of Mieko Akachi, Yukihiro Shimada, Noriyuki Fukui, and Taiki Sato in preparing this manuscript.

Funding. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

The authors have no conflicts of interest to declare.

REFERENCES

- Mitchell LB. Clinical trials of antiarrhythmic drugs in patients with sustained ventricular tachyarrhythmias. Curr Opin Cardiol 1997; 12: 33–40.
- Connolly SJ, Hallstrom AP, Cappato R, Schron EB, Kuck KH, Zipes DP, et al. Meta-analysis of the implantable cardioverter defibrillator secondary prevention trials. AVID, CASH and CIDS studies. Antiarrhythmics vs Implantable Defibrillator study. Cardiac Arrest Study Hamburg. Canadian Implantable Defibrillator Study. Eur Heart J 2000; 21: 2071–2078.
- McAlister FA, Ezekowitz J, Hooton N, Vandermeer B, Spooner C, Dryden DM, et al. Cardiac resynchronization therapy for patients with left ventricular systolic dysfunction: a systematic review. JAMA 2007; 297: 2502–2514.
- 4. Yanagi H, Nakanishi M, Konishi H, Yamada S, Fukui N, Ki-

JRIV

tagaki K, et al. Effect of Exercise Training in Heart Failure Patients Without Echocardiographic Response to Cardiac Resynchronization Therapy. Circ Rep 2019; 1: 55–60.

- 5. Sears SF Jr, Conti JB. Quality of life and psychological functioning of icd patients. Heart 2002; 87: 488–493.
- Mastenbroek MH, Pedersen SS, Meine M, Versteeg H. Distinct trajectories of disease-specific health status in heart failure patients undergoing cardiac resynchronization therapy. Qual Life Res 2016; 25: 1451–1460.
- Burgess ES, Quigley JF, Moran G, Sutton FJ, Goodman M. Predictors of psychosocial adjustment in patients with implantable cardioverter defibrillators. Pacing Clin Electrophysiol 1997; 20: 1790–1795.
- Lemon J, Edelman S, Kirkness A. Avoidance behaviors in patients with implantable cardioverter defibrillators. Heart Lung 2004; 33: 176–182.
- Isaksen K, Munk PS, Giske R, Larsen AI. Effects of aerobic interval training on measures of anxiety, depression and quality of life in patients with ischaemic heart failure and an implantable cardioverter defibrillator: A prospective non-randomized trial. J Rehabil Med 2016; 48: 300–306.
- Patwala AY, Woods PR, Sharp L, Goldspink DF, Tan LB, Wright DJ. Maximizing patient benefit from cardiac resynchronization therapy with the addition of structured exercise training: a randomized controlled study. J Am Coll Cardiol 2009; 53: 2332–2339.
- Pandey A, Parashar A, Moore C, Ngo C, Salahuddin U, Bhargava M, et al. Safety and Efficacy of Exercise Training in Patients With an Implantable Cardioverter-Defibrillator: a Meta-Analysis. JACC Clin Electrophysiol 2017; 3: 117–126.
- Steinhaus DA, Lubitz SA, Noseworthy PA, Kramer DB. Exercise Interventions in Patients With Implantable Cardioverter-Defibrillators and Cardiac Resynchronization Therapy: A SYSTEMATIC REVIEW AND META-ANALYSIS. J Cardiopulm Rehabil Prev 2019; 39: 308–317.
- Conraads VM, Spruit MA, Braunschweig F, Cowie MR, Tavazzi L, Borggrefe M, et al. Physical activity measured with implanted devices predicts patient outcome in chronic heart failure. Circ Heart Fail 2014; 7: 279–287.
- Kramer DB, Jones PW, Rogers T, Mitchell SL, Reynolds MR. Patterns of physical activity and survival following cardiac resynchronization therapy implantation: the ALTITUDE activity study. Europace 2017; 19: 1841–1847.
- 15. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur Heart J 2016; 37: 2129–2200.
- JCS Joint Working Group. Guidelines for rehabilitation in patients with cardiovascular disease (JCS 2012). Circ J 2014; 78: 2022–2093.
- Craig CL, Marshall AL, Sjöström M, Bauman AE, Booth ML, Ainsworth BE, et al. International physical activity questionnaire: 12-country reliability and validity. Med Sci Sports Exerc 2003; 35: 1381–1395.
- Murase N, Katsumura T, Ueda C, Inoue S. Validity and reliability of Japanese version of International physical activity questionnaire. J Health Welfare Stat 2002; 49: 1–9 (in Japanese).
- 19. Izawa KP, Watanabe S, Oka K, Hiraki K, Morio Y, Kasahara

Y, et al. Usefulness of step counts to predict mortality in Japanese patients with heart failure. Am J Cardiol 2013; 111: 1767-1771.

- 20. Kawabata M, Fantoni C, Regoli F, Raffa S, Pastori F, Fratini S, et al. Activity monitoring in heart failure patients with cardiac resynchronization therapy. Circ J 2007; 71: 1885–1892.
- Kamiya K, Masuda T, Tanaka S, Hamazaki N, Matsue Y, Mezzani A, et al. Quadriceps Strength as a Predictor of Mortality in Coronary Artery Disease. Am J Med 2015; 128: 1212–1219.
- 22. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med 2001; 16: 606–613.
- Mastenbroek MH, Van't Sant J, Versteeg H, Cramer MJ, Doevendans PA, Pedersen SS, et al. Relationship between reverse remodeling and cardiopulmonary exercise capacity in heart failure patients undergoing cardiac resynchronization therapy. J Card Fail 2016; 22: 385–394.
- Manea L, Gilbody S, McMillan D. Optimal cut-off score for diagnosing depression with the Patient Health Questionnaire (PHQ-9): a meta-analysis. CMAJ 2012; 184: E191–E196.
- 25. Fukuhara S, Suzukamo Y. Manual of SF-36v2 Japanese version: Institute for Health Outcome and Process Evaluation Research. Kyoto: iHope International; 2004.
- Suzukamo Y, Fukuhara S, Green J, Kosinski M, Gandek B, Ware JE. Validation testing of a three-component model of Short Form-36 scores. J Clin Epidemiol 2011; 64: 301–308.
- Mediano MFF, Mendes FSNS, Pinto VLM, Silva PSD, Hasslocher-Moreno AM, Sousa AS. Reassessment of quality of life domains in patients with compensated Chagas heart failure after participating in a cardiac rehabilitation program. Rev Soc Bras Med Trop 2017; 50: 404–407.
- Abraham WT, Fisher WG, Smith AL, Delurgio DB, Leon AR, Loh E, et al. Cardiac resynchronization in chronic heart failure. N Engl J Med 2002; 346: 1845–1853.
- Gad SA, Martin S, Kimber S, Williams R, Gulamhusein S, Lockwood E, et al. Impact of Cardiac Resynchronization Therapy on Daily Physical Activity in Heart Failure Patients. J Cardiopulm Rehabil Prev 2018; 38: E1–E4.
- Young DR, Hivert MF, Alhassan S, Camhi SM, Ferguson JF, Katzmarzyk PT, et al. Sedentary Behavior and Cardiovascular Morbidity and Mortality: A Science Advisory From the American Heart Association. Circulation 2016; 134: e262–e279.
- Ford J, Sears S, Ramza B, Reynolds DW, Nguyen P, Fedewa M, et al. The Registry Evaluating Functional Outcomes of Resynchronization Management (REFORM): quality of life and psychological functioning in patients receiving cardiac resynchronization therapy. J Cardiovasc Electrophysiol 2014; 25: 43–51.
- 32. Borland M, Rosenkvist A, Cider A. A group-based exercise program did not improve physical activity in patients with chronic heart failure and comorbidity: a randomized controlled trial. J Rehabil Med 2014; 46: 461–467.
- 33. Smolis-Bąk E, Dąbrowski R, Piotrowicz E, Chwyczko T, Dobraszkiewicz-Wasilewska B, Kowalik I, et al. Hospitalbased and telemonitoring guided home-based training programs: effects on exercise tolerance and quality of life in patients with heart failure (NYHA class III) and cardiac resynchronization therapy. A randomized, prospective observation. Int J Cardiol 2015; 199: 442–447.