European Journal of Cardiovascular Nursing

EUROPEAN SOCIETY OF CARDIOLOGY®

Original Article - Journal Club

European Journal of Cardiovascular Nursing
2015, Vol. 14(1) 34–44

DOI: 10.1177/1474515114521920
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Comprehensive cardiac rehabilitation improves outcome for patients with implantable cardioverter defibrillator. Findings from the COPE-ICD randomised clinical trial

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Abstract

Aims: The aim of this randomised clinical trial was to assess a comprehensive cardiac rehabilitation intervention including exercise training and psycho-education vs 'treatment as usual' in patients treated with an implantable cardioverter defibrillator (ICD).

Methods: In this study 196 patients with first time ICD implantation (mean age 57.2 (standard deviation (SD)=13.2); 79% men) were randomised (1:1) to comprehensive cardiac rehabilitation vs 'treatment as usual'. Altogether 144 participants completed the 12 month follow-up. The intervention consisted of twelve weeks of exercise training and one year of psycho-educational follow-up focusing on modifiable factors associated with poor outcomes. Two primary outcomes, general health score (Short Form-36 (SF-36)) and peak oxygen uptake (VO_2), were used. Post-hoc analyses included SF-36 and ICD therapy history.

Results: Comprehensive cardiac rehabilitation significantly increased VO_2 uptake after exercise training to 23.0 (95% confidence interval (CI) 20.9–22.7) vs 20.8 (95% CI 18.9–22.7) ml/min/kg in the control group (p=0.004 (multiplicity p=0.015)). Comprehensive cardiac rehabilitation significantly increased general health; at three months (mean 62.8 (95% CI 58.1–67.5) vs 64.4 (95% CI: 59.6–69.2)) points; at six months (mean 66.7 (95% CI 61.5–72.0) vs 61.9 (95% CI 56.1–67.7) points); and 12 months (mean 63.5 (95% CI 57.7–69.3) vs 62.1 (95% CI 56.2–68.0)) points (p <0.05). Explorative analyses showed a significant difference between groups in favour of the intervention group. No significant difference was seen in ICD therapy history.

Conclusion: Comprehensive cardiac rehabilitation combining exercise training and a psycho-educational intervention improves VO_2-uptake and general health. Furthermore, mental health seems improved. No significant difference was found in the number of ICD shocks or anti-tachycardia pacing therapy.

Keywords

Arrhythmia, implantable cardioverter defibrillators, comprehensive cardiac rehabilitation, exercise training, psycho-educational intervention

Date received: 17 October 2013; revised: 9 January 2014; accepted: 10 January 2014

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Introduction

Treatment with implantable cardioverter defibrillators (ICDs) has reduced mortality over the past 20 years. This has resulted in new, more extensive guidelines for their implantation.[1] Although the ICD is highly effective in preventing arrhythmic death, patients receiving the ICD may still experience psychological difficulties such as fear of shock and avoidance of physical activity[2,3] and they should receive special attention as their needs differ from ordinary ischaemic rehabilitation.[4] It has been suggested that negative emotions among ICD patients could be the cause rather than the result of arrhythmia and that the psychological stress can increase the risk of shock[5] and mortality.[6] A few small psycho-educational intervention studies have demonstrated improvements in anxiety, depression, quality of life,[7,8] physical outcomes,[9] as well as fewer unplanned hospital admissions and calls to health care providers.[8,9] Now more patients with heart failure receive ICD and the beneficial effect of exercise training on patients with heart failure has been established.[10,11] Even though many ICD patients today have heart failure and receive ICD for primary prevention, their conditions are complicated by their high risk of sudden cardiac death and their mental struggle to live with an implanted device.[4] Furthermore the ICD population is made inhomogeneous by the portion receiving the ICD for secondary prevention, many not having heart failure but arrhythmic disease. The burden does not seem to differ between primary and secondary prevention indication.[12] Exercise training in ICD patients has demonstrated improvements in psychological and physical outcomes [13–17] with improvements of 16–27% in metabolic equivalents (METS) or peak oxygen uptake (VO_2).[13,14,18] In addition, not participating in outpatient rehabilitation has been reported to be associated with ICD shock therapy, after adjusting for physical limitations.[15] As psycho-education and exercise rehabilitation has developed almost separately over the past decade there is now a crucial need to bring together the different approaches to aftercare to get a holistic approach to complex patient issues. Combining a psycho-educational intervention with exercise training (comprehensive cardiac rehabilitation) seems beneficial; however, previous trials are small and underpowered.[13,19] It remains unclear whether ICD specific comprehensive cardiac rehabilitation is beneficial to clinical practice. It is critical to improve patient outcomes by reducing the side effects of ICD treatment and limiting the negative consequences of the high risk of sudden cardiac death to physical and mental health.

The purpose of the COPE-ICD trial (Copenhagen Outpatient ProgrammE-ICD)was to develop and test an ICD specific comprehensive cardiac rehabilitation intervention including exercise training and psycho-educational components.[20] The main hypothesis was that the COPE-ICD programme would improve physical capacity and perceived health and secondarily reduce ICD shocks. Other post-hoc analyses were preplanned and reported separately.[21,22]

Methods

Study design, population and intervention

The design and methods of the COPE-ICD trial have been described in detail elsewhere.[20] The setting was a large university hospital with a volume of approximately 300 annual first time ICD implantations.

Included were patients who received a first time ICD implant, agreed to participate in the entire programme and were randomised prior to hospital discharge. Excluded were patients less than 18 years of age, diagnosed with a psychiatric disease or a somatic disease where the disease per se or its recovery might have influenced the outcome, were assessed to not understand the study instructions or were not given permission by their treating physician to participate in the exercise programme. Patients already enrolled in clinical trials that prohibited additional participation in trials were also excluded.

The ICD specific comprehensive cardiac rehabilitation intervention included exercise-training and psycho-education in addition to usual care and patients were randomised in a 1:1 ratio to intervention or usual care.

The exercise programme began after three months and lasted for 12 weeks with sessions twice a week. A test of aerobic functioning, patients' experiences and usual exercise activities were elements in planning the individual programmes. Patients performed resistance training and aerobic training to gain muscle strength, endurance and to gain afterload reduction due to decrease in systemic vascular resistance. The patients exercised aerobically, at 50–80% of their estimated maximum heart rate, calculated by Karvonen's formula.[23] Resistance training was done at 60–80% of one-repetition maximum. The training pulse was allowed to rise to a maximum 10–15 beats below the ICD activation threshold.[23] The training sessions were either organised as in-hospital supervised group training, in a local hospital rehabilitation setting or at home according to patient preferences. Two physiotherapists with 2–3 years of experience in outpatient exercise training supervised the exercise-training program. Group training at the hospital consisted of the following; 10 min warm up, 8 min biking, 8 min walking/jogging/running, 8 min individual aerobic endurance training e.g. step, stairway or running and resistance training of the major muscle groups. The session ended with a 10 min cool down and relaxation period.

The psycho-educational program began immediately after hospital discharge. The patients consulted a nurse in person or by phone once a month for the first six months, and every two months thereafter, for the following six months. We developed the programme based on a

humanistic approach, focusing on psychosocial support and education. The programme was directed towards the parameters that ICDs reportedly affect. The content was made up of information and education focused on managing life with an ICD, including emotional reactions using a holistic view on the person and establishment of a joint approach to disease management and coping. This component was inspired by Parse's 'human becoming practice' methodologies,[24] interpreted as follows: (a) discuss and give meaning to the past, present and future, (b) explore and discuss events and possibilities and (c) move along with envisioned possibilities. According to this theory there are three ways of changing health: (a) creative imaging, which means to see, to hear and to feel what a situation might be like if it was lived in a different way; (b) affirming personal patterns and value priorities and (c) shedding light on paradoxes, that is looking at the incongruence in a situation and changing the view held of something. The nurse was truly present in the process through discussions, silent immersion and reflection. The topics discussed were: events and experiences leading up to the ICD implantation; present thoughts and questions; implications for everyday life; avoidance-behaviour; exercise training; impact on family; information (including technical) and recommendations; shock and phantom shock, body image; driving and sexuality. The psychoeducational component of the intervention was performed by two nurses, each with 10 years of clinical experience in the care of patients with ICDs. The nurses were able to facilitate contact with, or seek advice from, a physician or an ICD technician.

To ensure adherence to project guidelines, the principal investigator (SKB) was present at all nine consultations with the first two patients that each nurse cared for. Both physiotherapists were present during exercise training to secure uniformity during the first three months.

The 'usual care' programme included medical follow-up as well as standard treatment according to disease specific guidelines. Device parameters were controlled the day after implantation and after two months. Thereafter every six months in-hospital or as remote follow up. All were invited to participate in a two-hour group session at the treating heart centre, which included information about the ICD and exchange of experiences among patients. Usual care patients were not prohibited to engage in exercise training elsewhere. Systematic rehabilitation is not offered for these patients nationally, however local initiatives may occur.

Outcome measures

The assessment of functional capacity reflects the ability to perform activities of daily living that require sustained aerobic metabolism. The primary outcome VO_2 was chosen for the obvious beneficial physical health reasons but also as a mediator for daring to live a more active lifestyle. Exercise capacity was measured by bicycle ergometer just before and after the exercise programme[25] at three and six months. We did not test at baseline due to the risk of leads complications. Instead the Six-Minute Walk Test (6MWT) was performed at baseline in order to be able to see any baseline differences.

The cardiopulmonary testing protocol consisted of a four-minute rest period followed by a 12.5 watt increase every minute until exhaustion or until reaching 5 beats/min heart rate below the ICD activation threshold. Blood pressure and electrocardiogram were continuously monitored. VO_2 was estimated from maximal watt achieved. For the 6MWT, participants walked up and down a 50 m long level hallway, for 6 min. The test was performed according to the guidelines for the 6MWT.[26]

The general health score was the co-primary outcome measure, a measure of self-rated health using the Short Form-36 (SF-36) questionnaire. The SF-36 is a measure of self-rated health. It uses 36 items to measure eight scores: physical function, role-physical, bodily pain, general health, vitality, social functioning, role-emotional and mental health. Scores are calculated for each component and aggregated into two summary scores, a mental component score and a physical component score. Scores range from 0–100; higher scores indicate better perceived health.[27] The SF-36 was administered at baseline, 3, 6 and 12 months. In this study, the Cronbach's alpha was acceptable at 0.80–0.89. Experience to date from nearly 400 randomised controlled clinical trials demonstrate that the SF-36 is very useful for descriptive purposes such as documenting differences between groups or over time.[28] The instrument was chosen for its ability to detect change in self-rated health within many domains in which all (but pain) potentially could be influenced by the COPE-ICD intervention.

ICD therapy was assessed after one year. Both anti-tachycardia pacing (ATP) and ICD shock therapies recorded after exactly 12 months follow-up were assessed. Time to first shock therapy was recorded. All therapies were initially evaluated by a trained technician and subsequently by an electro-physiologist with special competences in device therapy. Only appropriate therapy was included. In the assessment of appropriate vs inappropriate therapy, standard clinical criteria were used including A-V relationship (if available), morphology, regularity of V-signals and onset of tachycardia.

Sample size

Based on current knowledge,[29] we estimated a minimal relevant difference in VO_2 of 15% (standard deviation (SD)=30%). With an alpha=5% and a beta=20%, the required sample size was 128 participants. Based on health

status measures from the general Danish population,[30] the mean general health score in patients with heart disease was estimated to be 60 (SD=22). The minimal relevant difference of rehabilitation was expected to be a score of 10 absolute points. With an alpha=5% and a beta=20%, the required sample size was 154 participants. Taking a drop-out of 20% into account[31] this would require 196 participants.

Blinding

Because of the nature of rehabilitation, the interventions were open to the staff and the patients. A blinded investigator assessor performed data collection and management. Blinded outcome analyses were conducted.

Statistical analyses

Data were analysed using SPSS 17.0. (SPSS Inc., Chicago, Illinois, USA) or SAS 9.1 (SAS Institute, Cary, North Carolina, USA). All analyses were intention to treat (all patients were classified into groups based on the initial treatment intent). Data are presented as mean and SD and percentage where appropriate.

Baseline data are presented as similarities across groups by number and percentage. As recommended, no significant test for detecting baseline differences was done.[32,33]

Mixed model with repeated measures[34,35] was used directly or following suitable transformation of data to fulfil the assumptions of the model (normal distributions and variance homogeneity of the distributions defined by the intervention indicator and time of measurement). The transformation $y=x^3$ was used in case of mental health, physical component score, and mental component score and $y=x^2$ in case of vitality. VO_2 (est.) uptake, maximum watt, METS and total exercise time were log transformed. In four instances (physical function, role-physical, bodily pain and role-emotional) a single transformation fitting all subgroups could not be found. In the latter cases, the distributions of the change from the baseline value to the 12 month value were compared between the two intervention groups using Student's *t*-test or a non-parametric test as appropriate.

Three covariance matrix models: unstructured, spatial power law[35] and compound symmetric were tested, in that order, until a model converged. Occasionally a quadratic time component was included in the full model if it was deemed relevant as judged from inspection of the mean value structure. In this case a type 1 test which is appropriate for polynomial models was used instead of the type 3 test.[35]

Outcome measures defined as the number of times a specified event occurred during 12 months were modelled using the Poisson regression (generalised linear model with Poisson distribution and log as link function).

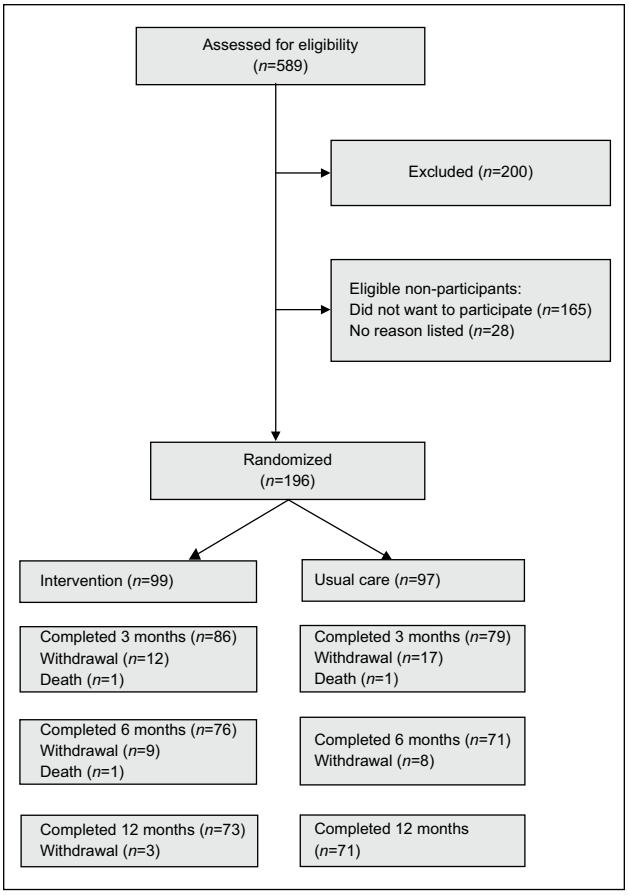

Figure 1. CONSORT flow-chart.

The analyses of the two primary outcome measures were supplemented by analyses with the protocol specified covariates and when more than two measurements were planned the baseline value included. Adjustments of *p*-values were made for multiplicity using Holm's method.[36]

Ethical considerations

Patients gave their written informed consent after receiving oral and written information. All data material was treated in confidentiality and patients were assured anonymity. The trial followed the recommendations of the Declaration of Helsinki II and was approved by the regional Ethics Committee (H-B-2007-014) and the Danish Data Protection Agency (2007-41-0932). The trial is registered at ClinicalTrials.gov (ID: NCT00569478).

Results

During the inclusion period October 2007–November 2009, 589 patients received a first-time ICD implantation at our hospital (Figure 1). A total of 196 patients were included, 99 randomised to the comprehensive cardiac rehabilitation and 97 to usual care.

Table 1. Demographic and physical profile.

	Rehabilitation (n=99)	Usual care (n=97)
Male sex, *n* (%)	79 (80)	76 (78)
Age, years, (±SD)	57.6 (12.9)	56.7 (13.5)
Employed, *n* (%)	41 (42)	50 (52)
Primary prophylactic indication, *n* (%)	63 (64)	67 (69)
VF prior to ICD implantation, *n* (%)	21 (21)	20 (20)
LVEF, mean (±SD) 73% of tot pop ≤35	32.2 (17)	32.7 (18)
NYHA class I, *n* (%)	30 (31)	18 (19)
NYHA class II, *n* (%)	42 (43)	44 (46)
NYHA class III, *n* (%)	24 (25)	32 (33)
NYHA class IV, *n* (%)	2 (2)	1(1)
Body mass index ≥30 (kg/m^2)	24 (24)	19 (20)
Atrial fibrillation	27 (27)	21 (22)
CRT device	14 (14)	9 (9)
History of ischaemic heart disease	45 (46)	57 (59)
Previous myocardial infarction	20 (21)	33 (34)
Previous PCI	28 (29)	29 (30)
Previous CABG	14 (15)	21 (22)
History of heart failure	76 (78)	73 (75)
Diabetes mellitus	12 (12)	10 (10)
Hypertension	18 (18)	23 (24)
Chronic obstructive lung disease	2 (2)	1 (1)
Other chronic diseases	27 (28)	24 (25)

CABG: coronary artery bypass grafting; CRT: cardiac resynchronisation therapy; ICD: implantable cardioverter defibrillator; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association; PCI: percutaneous catheter intervention; SD: standard deviation; VF: ventricular fibrillation.

Non-participants were significantly older than participants in the COPE-ICD trial, mean age 65.2 (SD=12.4), $p \leq 0.0001$. Participants and non-participants were comparable with respect to gender and marital status.

Baseline characteristics

The baseline demographics and clinical characteristics in rehabilitation and usual care groups are well matched and presented in Table 1.

Patient participation in rehabilitation

All patients (100%) in the comprehensive cardiac rehabilitation group participated in the psycho-educational programme. Approximately half (53.2%) of all the consultations were done by phone, with 51.8% of patients choosing to combine telephone and face-to-face consultations during the course of the intervention. The face to face consultations lasted 60 min and the telephone consultations 30 min including charting. In the control group six patients (8.3%) consulted a nurse about living with an ICD. All patients (100%) in the comprehensive cardiac rehabilitation group participated in the exercise training component of the programme: 46% exercised in-hospital, 26% outside the hospital and 28% did both. A total of 65.8% of the patients in the usual care group exercised. 16.8% participated in an exercise programme at a local hospital and 40.8% exercised on their own, 8.2% did both.

Discontinuations

Trial discontinuation did not differ significantly between the intervention groups (28.8% vs 30.3% drop outs; p=0.64). No significant differences between the groups continuing or dropping out were found with regard to SF-36 subscales, sex or age at entry. Given reasons for drop out were co-morbidity, distance and too busy in everyday life.

Outcome

Tables 2 and 3 show the mean value over time of each outcome measure. The comprehensive cardiac rehabilitation significantly influenced both primary outcomes (Figures 2(a) and 2(b)). For VO_2 (est.) the comprehensive cardiac rehabilitation at three months had 21.0 (95% CI: 19.2–22.7) ml/min/kg and at six months 23.0 ml/min/kg (95% CI: 20.9–22.7) vs control 20.9 ml/min/kg (95% CI: 19.1–22.6) at three months and 20.8 ml/min/kg (95% CI: 18.9–22.7) at six months (p=0.003). The scores for general health were 62.8 (95% CI: 58.1–67.5) at three months, 66.7 (95% CI: 61.5–72.0) at six months and 63.5 (95% CI: 57.7–69.3) at 12 months vs control 64.4 (95% CI: 59.6–69.2) at three months, 61.9 (56.1–67.7) at six months and 62.1 (95% CI: 56.2–68.0) at 12 months (p=0.015). In all, three regression parameters were tested in case of general health and two in case of VO_2 (est.). Thus five significance tests were made. Using Holm's correction for multiplicity the adjusted p=0.015 for VO_2 (est.) and p=0.059 for general health.

The mean level of VO_2-uptake increased over time in the intervention group while this was not so in the usual-care group (Table 2). The mean level of general health in the intervention group increased from month 3–6 and then declined again from month 6–12 (Table 3). An analysis with the 12-month values excluded showed a highly significant effect of rehabilitation while this was not the case when the six-month values were excluded and only the 12-month values were retained.

Sensitivity analyses emulating a pessimistic scenario where the level remained constant over time in all patients with missing values were carried out. It appears that if the scenario reflects the truth, the missing values may have caused an upward bias of 43.4% for VO_2 uptake as well as

Table 2. Comparison of exercise and 6 minute walk tests pre- and post cardiac rehabilitation in comprehensive cardiac rehabilitation vs control.

	Rehabilitation (n=99) mean (±SD) 95% CI	Usual care (n=97) mean (±SD) 95% CI	*p*
Exercise test			
VO_2 (est.) (ml/min/kg)			
3 months	20.98 (7.98) 19.2–22.7	20.88 (7.8) 19.1–22.6	0.004
6 months	23.01 (8.91) 20.9–22.7	20.79 (8.1) 18.9–22.7	
Metabolic equivalents (METS)			
3 months	5.9 (2.1) 5.4–6.4	6.3 (4.1) 5.4–7.2	0.006
6 months	6.5 (2.6) 5.9–7.2	5.9 (2.3) 5.4–6.5	
Total exercise time (s)			
3 months	563 (238) 512–615	562 (259) 504–619	0.009
6 months	619 (265) 556–681	562 (272) 498–627	
6 Minute Walk Test (m)			
Baseline	420.2 (112.1) 396.3–444.1	414.7 (118.0) 390.9–438.9	n.s.
3 months	500.2 (94.5) 479.2–521.2	481.0 (106.4) 457.3–504.7	
6 months	519.4 (103.7) 494.5–544.4	483.3 (130.9) 452.6–514.6	

CI: confidence interval; n.s.: not significant; SD: standard deviation.

29.7% for general health and the corresponding *p* values should have been 0.016 and 0.004, respectively. In addition, adjusting for differences in standard errors caused by the emulation of the scenario, the *p* values were 0.062 and 0.022, respectively.

Explorative analyses (Tables 3 and 4) showed that for mental component score, metabolic equivalent and total exercise time a significant linear change was observed in the comprehensive cardiac rehabilitation group as opposed to the usual-care group, where the level remained stable. The number of ICD shocks provided did not differ significantly between the two groups (Table 4). Time to first shock did also not differ significantly between groups (Table 4). Inappropriate shocks were mostly before the intervention began.

Adverse events

No serious cardiac events were detected during exercise intervention or testing. A few incidences of symptomatic atrial fibrillation occurred during exercise and one patient in the rehabilitation group ruptured an Achilles tendon.

Discussion

The, to date, largest comprehensive cardiac rehabilitation trial in patients with an ICD shows a significant improvement in VO_2 (est.) and general health and mental health as a result of the combined intervention.

The comprehensive cardiac rehabilitation intervention was found to significantly improve the primary outcome VO_2 (est.) as well as maximum watt and METS despite the fact many of the control patients were doing unscheduled exercise training. The results confirm previous findings of beneficial effects of exercise training found in many smaller trials.[13,14,18,37] In our randomised controlled trial, 65% of patients in the usual-care group exercised, and 25% did so in an outpatient setting. The significant difference in VO_2 (est.) might be explained by other trials finding that patients following outpatient cardiac rehabilitation tend to exercise more often, four times a week as against non-rehabilitation patients who exercise three times a week, and with a higher intensity, 5.3 vs 3.5 METS in non-rehabilitation patients.[15] The rehabilitation group has larger improvements in the 6MWT than the control group (99.2 m vs 68.6 m), however the difference is not significant. Looking at the 6MWT results it is clear that a large difference occurs in both groups from baseline to three months. This is explained by patients holding back at baseline, since they had ICD implantation the day before. Looking at what happens between three and six months, during exercise training, improvements do occur in the rehabilitation group and not in the control group, which is in compliance with the VO_2 (est.) findings.

The comprehensive cardiac rehabilitation intervention was found to significantly improve general health and post-hoc analyses showed a positive outcome for the mental component scale.

The difference in general health in the present trial may reflect the beneficial effects of systematic rehabilitation and/or the training at a higher intensity. General health showed greatest difference between groups at the sixth month after the trial start. Since the exercise programme started at the third month and stopped again at the sixth month it cannot be excluded that the transient effect on general health was due to the exercise part of the intervention while the rest of the intervention programme was without any appreciable effect on general health. In fact, the pattern

Table 3. Comparison of self-reported health over 12 months in comprehensive cardiac rehabilitation patients and control.

SF-36	Rehabilitation (n=99) mean (±SD) 95% CI	Usual care (n=97) mean (±SD) 95% CI	*p* of effect intervention
General health			
Baseline	58.7 (21.9) 54.0–63.4	59.5 (18.2) 55.4–63.5	0.015
3 months	62.8 (20.9) 58.1–67.5	64.4 (21.8) 59.6–69.2	
6 months	66.7 (22.0) 61.5–72.0	61.9 (24.1) 56.1–67.7	
12 months	63.5 (23.7) 57.7–69.3	62.1 (24.4) 56.2–68.0	
Role-physical			
Baseline	36.6 (42.7) 27.6–45.7	39.1 (42.3) 30.0–48.1	n.s.
3 months	46.9 (38.7) 37.8–55.3	54.1 (42.0) 44.8–63.4	
6 months	59.7 (41.0) 50.0–69.5	56.6 (40.5) 46.8–66.4	
12 months	61.4 (41.9) 51.1–71.7	57.3 (42.7) 47.1–67.4	
Bodily pain			
Baseline	71.2 (27.1) 65.6–76.9	71.2 (27.7) 65.3–77.0	n.s.
3 months	84.4 (22.7) 79.3–89.6	83.4 (21.8) 78.6–88.1	
6 months	84.7 (21.7) 79.6–89.9	86.5 (19.6) 81.8–91.2	
12 months	86.1 (21.8) 80.7–91.4	85.5 (23.7) 79.9–91.1	
Vitality			
Baseline	55.6 (22.9) 50.9–60.4	53.4 (22.8) 48.7–58.4	n.s.
3 months	63.9 (20.6) 59.2–68.5	59.9 (24.3) 54.6–65.2	
6 months	67.8 (20.5) 62.9–72.6	61.6 (23.1) 56.1–67.1	
12 months	67.2 (20.9) 62.1–72.3	60.9 (24.1) 55.2–66.6	
Social functioning			
Baseline	76.8 (25.9) 71.4–82.2	77.7 (24,8) 72.4–83.0	n.s.
3 months	86.7 (18.0) 82.7–90.7	86.7 (21.5) 82.0–91.5	
6 months	90.7 (16.2) 86.3–94.5	88.4 (19.4) 83.8–93.0	
12 months	89.4 (16.7) 85.3–93.5	86.6 (21.5) 81.5–91.7	
Role-emotional			
Baseline	51.0 (43.7) 41.6–60.3	56.3 (39.1) 48.0–64.7	n.s.
3 months	61.5 (40.2) 52.5–70.6	68.7 (36.9) 60.6–76.9	
6 months	71.4 (36.2) 62.8–79.9	68.2 (40.4) 58.3–78.0	
12 months	74.7 (33.1) 66.6–82.9	65.2 (41.2) 55.1–75.2	
Mental health			
Baseline	72.5 (20.6) 68.2–76.8	69.3 (21.3) 64.7–73.8	n.s.
3 months	81.1 (14.0) 77.9–84.2	76.9 (24.3) 72.3–81.5	
6 months	82.9 (14.9) 79.3–86.4	76.9 (18.9) 72.4–81.4	
12 months	84.7 (11.1) 82.0–87.4	78.9 (17.8) 74.7–83.1	
Mental component score			
Baseline	47.4 (10.4) 45.1–49.7	46.7 (11.5) 44.2–49.2	0.014
3 months	51.7 (8.6) 49.7–53.7	51.9 (11.4) 49.3–54.5	
6 months	53.6 (9.4) 51.3–55.9	51.0 (11.0) 48.3–53.8	
12 months	54.3 (7.4) 52.3–56.2	51.2 (10.0) 48.7–53.7	
Physical component score			
Baseline	41.9 (10.2) 39.6–44.2	43.4 (8.5) 41.5–45.2	n.s.
3 months	45.4 (8.4) 43.4–47.3	45.8 (8.7) 43.8–47.7	
6 months	46.7 (10.2) 44.2–49.2	46.2 (9.1) 43.9–48.5	
12 months	46.9 (10.0) 44.3–49.5	46.0 (10.2) 43.5–48.6	

n.s.: not significant.

has been reported previously, with significant exercise effects measured on SF-36 disappearing over time.[17] However, this supports the contention that the psycho-educational component has a beneficial effect on mental health, since the effect on mental health is significant and increases over time.

Even though SF-36 has often been used in descriptive studies, only one other psycho-educational intervention

trial in ICD patients has used it as an outcome measure. That trial showed no overall effect with significant improvements in patients less than 65 years but not in older patients.[38] Two trials used SF-12 (a shorter form of SF-36) with no significant difference in mental component score.[9,39] These trials were also psycho-educational programmes only and were very short, eight weeks in duration.

No patients experienced ICD shock during exercise training or testing indicating a safe programme. A low rate has been reported previously.[16,37] No significant difference was found in the number of ICD shocks or anti-tachycardia pacing therapy. This is in accordance with previous findings,[8,19] however, Davids et al. found a difference in favour of the intervention group in a smaller exercise training, non-randomised study.[15]

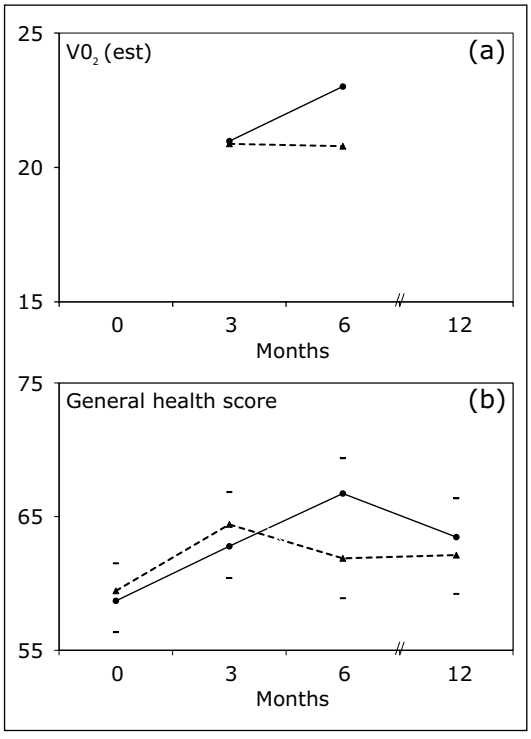

Figure 2. (a) Peak oxygen uptake VO_2 (est.) comparison between rehabilitations and usual-care groups; (b) General health comparison between rehabilitations and usual care-groups. Bold line=intervention, dotted line=control.

Generalisability

External validity is high since this population was included following the new guidelines for ICD implantation from 2006.[1] This means that a higher number in the cohort has heart failure and primary prophylactic ICD indication than would have been the case 10 years ago. However, we only randomised about one-third of potential eligible patients and this may represent bias. The literature reports female gender, age, co-morbidity, socioeconomic burden, distance and disbelief in the beneficial effect as the most important barriers to participation in cardiac rehabilitation.[40–46] We found non-participants to be older which is often associated with higher co-morbidity so a selection bias exists. Half of the eligible patients refused consent with one reason being distance to the hospital. This might be overcome with a local initiative instead of a heart centre set-up. Therefore a larger percentage of participants should be expected if rehabilitation was offered locally as standard treatment. The baseline measures were mostly similar to findings from studies conducted in the United States and Europe.[39,47,48] However, the physical component score in SF-36 is about 10 absolute points higher in our population than found at baseline by Kapa et al. in 2010.[47] This may be due to more patients being in New York Heart Association (NYHA) class III and IV with left ventricular ejection fraction below 35% in the Kapa et al. trial. Kao et al. reported data of five absolute points below our findings in a secondary prophylaxis population with NYHA distribution and systolic function more similar to the current trial.[49] The mental component score seems to be similar to other findings, at about 47.[47,48]

Post-hoc calculation of our power to detect significant differences in our primary outcomes showed this to be above 98% based on an alpha=0.025. We used telephone voice-response as a randomisation method, which increases internal validity.[49] We used blinded-outcome assessment for the estimation of VO_2 (est.) but, due to the design of the trial, subjective outcomes were not blinded. Accordingly, we cannot exclude bias regarding these outcomes.[49]

Table 4. Comparison of implantable cardioverter defibrillator therapy history between comprehensive cardiac rehabilitation patients and control.

Ventricular arrhythmia and ICD therapy count during the 12 months.	Rehabilitation (n=99) mean episodes per patient (±SD) 95% CI	Usual care (n=97) mean episodes per patient (±SD) 95% CI	*p*
VT/VF	3.7 (18.3) 0.80–7.37	10.5 (71.5) 3.87–24.8	0.71
ATP	3.9 (18.4) 0.21–7.55	9.8 (65.5) 0–23.02	0.42
ICD shock	0.20 (0.9) 0.02–0.38	0.43 (2.0) 0.03–0.84	0.76

ATP: anti-tachycardia pacing; CI: confidence interval; ICD: implantable cardioverter defibrillator; SD: standard deviation; VF: ventricle fibrillation; VT: ventricular tachycardia.

Study limitations

Study limitations include the fact that selection bias may exist as we did not include patients if they were already included in other trials. Looking at the baseline measures it seems as the randomisation worked as there are comparable values. A slightly higher number of patients in the usual care group had a history of ischaemic heart disease and NYHA III than in the rehabilitation group; however no difference in 6MWT and VO_2 were seen between groups before the intervention occurred.

The control group might be contaminated by the information given during the project inclusion, suggesting that psycho-educational assistance and exercise training might be beneficial after ICD implantation. This information may have led to control patients seeking rehabilitation elsewhere. Collateral intervention occurred when some patients were offered cardiac rehabilitation at their local hospital, which may have reduced the effects of the experimental intervention, but this would have resulted in more conservative estimations of differences by intervention. Since a Danish law encourages rehabilitation for all cardiac patients, it was not possible to prevent participation in local initiatives. Patients were asked whether they had participated in such activities at the 12-month follow-up. However, we did detect a difference between the groups.

Conclusion

Comprehensive cardiac rehabilitation combining exercise training and psycho-education improves VO_2-uptake and perception of general health compared to patients not receiving rehabilitation. Furthermore, mental health seems improved as a significant difference was found between groups. After exercise training ends, the effect on mental health increases over time, suggesting that the effect is somewhat carried by the psycho-educational intervention that continues. No significant difference was found in the number of ICD shocks or anti-tachycardia pacing therapy. Future studies should also include ICD therapy history and a systematic review with meta-analyses and trial sequential analyses should be planned.

Implications for practice

- Patients with ICDs are in need of rehabilitation and a combined psycho-educative and exercise training intervention seems recommendable.
- Exercise training should be encouraged as it is safe and increases perceived physical health.
- An individualised psycho-educative nursing intervention based on the principle of Human Becoming Theory could be a way to address patients' issues living with an ICD.

Acknowledgements

The authors would like to thank Pernille Preisler, Lone Siersbaek-Hansen, Mette B Hansen and Rune Nielsen for their professional contribution to the intervention and the Pace laboratory staff for conducting the exercise tests. We would also like to thank Katrine Haase, Lene Mackintosh, Anne V Christensen and Karin Jensen for research assistance, and all participating patients for informing the study about very personal matters.

SKB in collaboration with JHS, ADZ, PUP, and BDP designed the study. PW, CG and SKB conducted the statistical analyses. SKB drafted the manuscript. All revised the manuscript critically. All have given their final approval of the version to be published. All authors meet the criteria in the ICMJE authorship guidelines.

Conflicts of interest

The authors declare that there are no conflicts of interest.

Funding

This work was supported by the Novo Nordisk Foundation; the Oticon Foundation; the Danish Heart Foundation; the AP Møller and Chastine Mc-Kinney Møller Foundation; Helsefonden; the Tryg Foundation; the Augustinus Foundation; Krista and the Viggo Petersens Foundation; The Danish Cardiovascular Research School (DaCRA); King Christian X Foundation and Copenhagen University Hospital, Rigshospitalet.

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