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Original Article

Are the group-based interventions improving the functional exercise capacity and quality of life of frail subjects with chronic heart failure?

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Abstract

Objectives: Frail subjects with chronic heart failure (CHF) often demonstrate limited tolerance of exertion, shortness of breath, and reduced walking capacity resulting poor quality of life (QoL). The aim of this study was to quantify the improvements in functional exercise capacity (FEC) and QoL among Bulgarian frail subjects with CHF performed group-based high-intensity aerobic interval training (HIAIT)/m-Ullevaal intervention and to compare it with moderate intensity continuous training (MICT) protocol. **Methods**: One hundred and twenty (n=120) frail subjects with mean age of 63.73±6.68 years, in CHF and NYHA class II-IIIB, were enrolled in the single-center, prospective, two-arm randomized controlled clinical trial conducted at the Medical Center for Rehabilitation and Sports Medicine-I-Plovdiv. The baseline assessment included 6-minute walk test (6MWT), peak oxygen uptake (VO_{2peak}), modified Borg Perceived Exertion Scale (mBPES), and Minnesota living with the Heart Failure Questionnaire (MLHFQ). **Results**: The improvement in 6MWT (P<0.001), VO_{2peak} (P<0.001), mBPES (P<0.001), and MLHFQ (P<0.001) observed among frail subjects performed HIAIT/m-Ullevaal intervention was significantly greater compared to the improvement observed in the subjects performed MICT protocol (P<0.001). **Conclusions**: The group-based HIAIT/m-Ullevaal intervention is a new perspective and challenge for both, Bulgarian cardiac rehabilitation (CR), and frail patients with CHF.

Keywords: Chronic heart failure, Frailty, Group-based, Rehabilitation

Introduction

Frailty is a complex clinical syndrome that precedes disability and is characterized by poor physiological reserves, increased vulnerability to stressors, and adverse health outcomes[1]. It's proven that frailty can robustly quantify the variability in health status of patients of the same age, and may accelerate the prognosis and the treatment approach of several chronic diseases including chronic heart failure (CHF)[2]. An association has been found between frailty and cardiovascular disease, particularly heart failure (HF)[3]. Up to 25% of elderly patients with HF show frailty, and frail patients have an increased risk of developing HF[4]. Frail subjects with CHF often demonstrate limited tolerance of exertion, exhaustion, shortness of breath, loss of body weight and reduced walking capacity resulting poor quality of life (QoL)[5].

QoL is a multidimensional concept that is affected by economic and social factors, life satisfaction, and reflects patients' subjective perceptions about the impact of a clinical condition on their lives[6,7]. Moreover, the poor QoL in patients with CHF is associated with increased hospitalization times and mortality rates, higher costs imposed on health systems, families and patients[8,9]. Despite limitations and the disagreement about the appropriate QoL measures[10], health related QoL (HRQoL)

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	HIAIT/m-Ullevaal (n =60)	MICT (n=60)	P-value
Age (years)	63.65 ±6.71	63.82± 6.71	<0.05
Gender (men/women)	35/25	35/25	<0.05
6MWT (m)	440.58±39.7	442.90±42.5	<0.05
M-Borg Scale	6.60±0.64	6.42±0.62	<0.05
$VO_{2\ peak}$	13.49±3.7	12.51±3.5	<0.05
MLHFQ score	36.88±5.1	37.40±7.7	<0.05
NYHA class II/III	48/12	46/14	
Smoking status			
Never	40 (66. 6%)	38 (63.3%)	<0.05
Ever	17 (28.3%)	18 (30.1%)	<0.05
Current	3 (5.06%)	4 (6.6%)	<0.05
Diagnosis			
Coronary artery disease	36 (60%)	36 (60%)	<0.05
Hypertension	16 (26.7%)	16 (26.7%)	<0.05
Cardiomyopathy	8 (13.3%)	8 (13.3%)	<0.05

Data presented as mean ± SD or number of patients (percent).

Table 1. Demographic and clinical characteristics of the 120 frail subjects with CHF.

is acknowledged as a crucial dimension for health policy design and evaluation of various healthcare interventions as cardiac rehabilitation (CR)[11]. Maintaining or improving HRQoL of frail subjects with CHF is one of the major challenges for health care professionals involved in CR[12].

In this context, CR is recognized as integral and comprehensive intervention in secondary prevention that uses patient education, health behavior modification, and exercise training to improve secondary prevention outcomes in patients with cardiovascular disease[13].

Previous clinical studies[14-15] and Cochrane reviews[16] have focused on the effects of various exercise-based CR interventions for patients with CHF and have found clear benefits from CR, which the National Institute for Health and Care Excellence (NICE) in England have indicated as being highly cost-effective[17,18]. It is noteworthy that frail subjects are at higher risk of adverse outcomes, such as independently, disability[19], mortality and prolonged hospitalizations[20], however, little is known about the impact of CR interventions on functional exercise capacity (FEC) and QoL of frail subjects with CHF[21].

Based on the abovementioned, this study aimed to quantify the improvements on FEC and QoL among Bulgarian frail subjects with CHF performed group-based HIAIT/m-Ullevaal intervention and to compare it with moderate intensity continuous training (MICT) protocol.

Material and Methods

This study is part of another larger-sized single-center, prospective, randomized controlled clinical trial whose methodology has been described elsewhere[21]. One hundred forty-six (n=146) frail subjects with stable CHF, New York Heart Association classes II to IIIB were recruited from the Department of Cardiology at Medical University of Plovdiv and were from the Plovdiv Region which had an estimated population of 683, 027 inhabitants in 2015. Twenty-six (n=26) eligible subjects withdrew for various reasons. Therefore, the final sample study consisted of one hundred and twenty (n=120) frail subjects with CHF (mean age: 63.73±6.68 years), enrolled from the period of 1 January 2012 to 30 June 2015. A flow chart summarizing the distribution of the included subjects during each stage of the study is presented in Figure 1. The general demographic characteristics and the baseline assessment of the study participants are presented in Table 1.

In the present study the NICE guidelines were applied shown in the Table 2[22]. Subjects with decompensated HF, ongoing unstable angina or acute myocardial infarction within 2 days, uncontrolled cardiac arrhythmia with hemodynamic compromise, active endocarditis, symptomatic severe aortic stenosis cardiomyopathy, recent pulmonary embolism, deep vein thrombosis, fever, stroke or transient ischemic attack, disabilities and mental impairments that preclude safe and adequate testing were excluded.

The randomization of included subjects was performed, using stratified block randomization by sex, age, NYHA class, and cause of CHF. Sixty frail subjects (n=60) with stable CHF were allocated to perform the group-based HIAIT/m-Ullevaal, while sixty subjects (n=60) were allocated to perform MICT in electrically braked ergometers (Pure Bike

Indications	Contraindications
Primary: • Detection of coronary artery disease (CAD) in patients with chest pain (chest discomfort) syndromes or potential symptom equivalents • Evaluation of the anatomic and functional severity of CAD • Prediction of cardiovascular events and all-cause death • Evaluation of physical capacity and effort tolerance • Evaluation of exercise-related symptoms • Assessment of chronotropic competence, arrhythmias, and response to implanted device therapy • Assessment of the response to medical interventions **Additional:** • Development of the exercise plan or prescription • Response to medication • Evaluation of perioperative risk for non-cardiac surgery	**Absolute contraindications:** • Acute myocardial infarction within 2 days • Ongoing unstable angina • Uncontrolled cardiac arrhythmia with hemodynamic compromise • Active endocarditis • Symptomatic severe aortic stenosis • Decompensated heart failure • Acute pulmonary embolism, pulmonary infarction, or deep vein thrombosis • Acute myocarditis or pericarditis • Acute aortic dissection • Physical disability that precludes safe and adequate testing **Relative contraindications:** • Known obstructive left main coronary artery stenosis • Moderate to severe aortic stenosis with uncertain relation to symptoms • Tachyarrhythmia with uncontrolled ventricular rates • Acquired advanced or complete heart block • Hypertrophic obstructive cardiomyopathy with severe resting gradient • Recent stroke or transient ischemic attack • Mental impairment with limited ability to cooperate • Resting hypertension with systolic or diastolic blood pressures >200/1 10 mmHg • Uncorrected medical conditions, such as significant anaemia, important electrolyte imbalance, and hyperthyroidism

Table 2. The NICE guidelines.

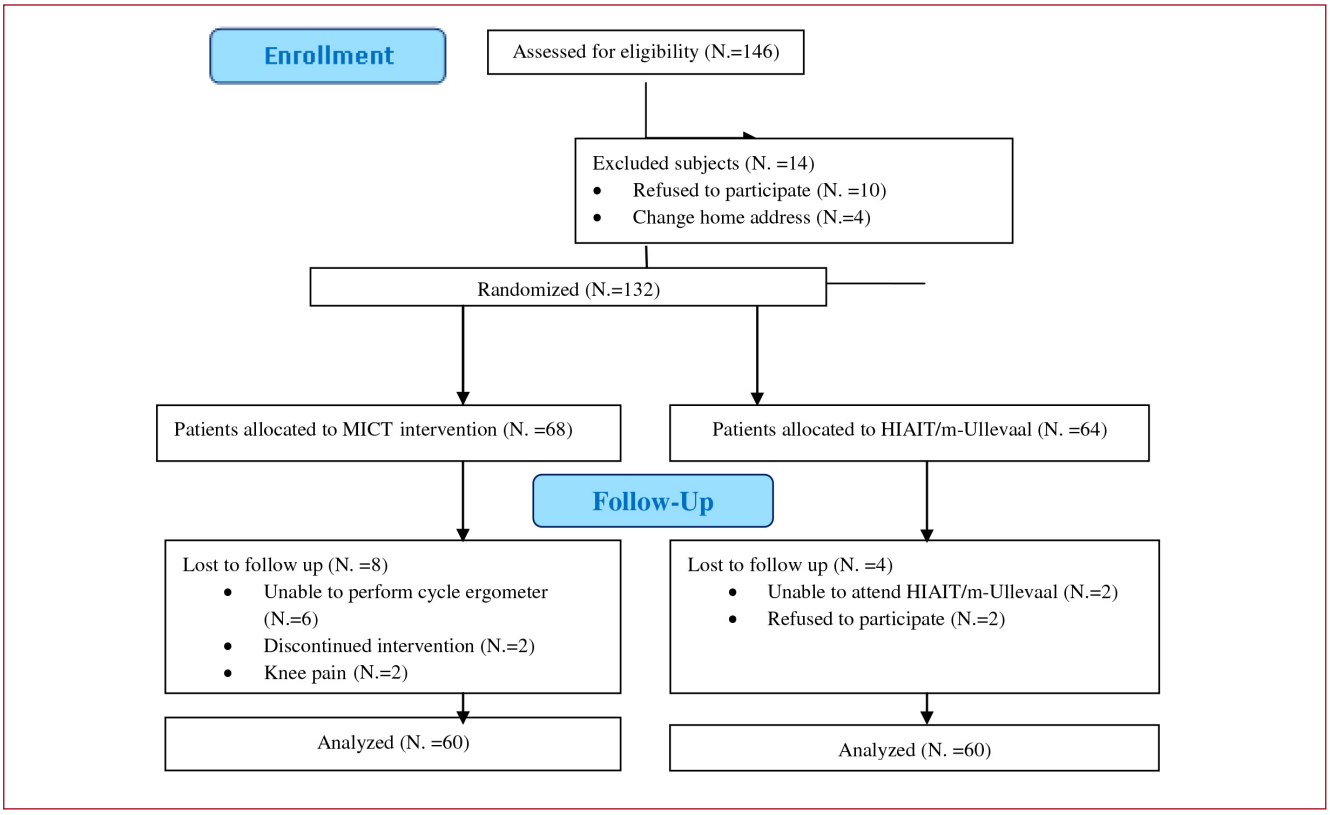

Figure 1. Flow chart of the study.

CR interventions		HIAIT/ m-Ullevaal	Δ (%)	p	MICT		Δ (%)	p	P-value
Variable	Baseline (T1)	Follow-up			Baseline (T1)	Follow-up			
6MWTD (m)	440.58±39.79	513.38±37.73	16.86±6.43	<0.001	442.90±42.53	489.32±43.45	10.58± 2.91	<0.001	<0.001
VO_{2peak}	13,49±3,78	16,97±3,65	29,16±21,77	<0.001	12,51±3,56	14,53±3,09	19,68±21,69	<0.001	<0.001
mBPES	6.60±0.64	4.62±0.61	-29.79±88.8	<0.001	6.42±0.62	4.73±0.66	-25.71±11.29	<0.001	<0.001
MLHFQ score	36.88±5.19	29.80±5.37	-19.46±6.04	<0.001	37.40±7.73	35.65±7.80	-6.41±4.23	<0.001	<0.001

Table 3. 6MWT, VO_{2peak} ,BPES and MLHFQ scores at baseline (T1) and after 24 CR sessions (T2).

4.1, Tunturi, Almere, Finland) over 12 weeks, for a total of 24 training sessions. No adverse effects during the training sessions were observed.

Group-based HIAIT/m-Ullevaal intervention consisting of three high-intensity intervals (HR max: 90%) and two intervals of moderate intensity (HR max: 70%) guided by motivational and melodious music pieces[23]. It includes mainly three different exercise types: muscle-strengthening, flexibility, and endurance/fitness exercise. At baseline the functional exercise capacity (FEC) was estimated through the 6-minute walk test (6MWT) and peak oxygen uptake (VO_{2peak})[24].

The 6MWT was recently introduced as a tool for the assessment of mobility and FEC of frail subjects, as well as those with CHF[25]. Participants performed the 6MWT in the 30-m marked corridor at the Medical Center for Rehabilitation and Sports Medicine-I-Plovdiv, following the most current American Thoracic Society (ATS) guidelines[26].

It's proven that 6MWT is a powerful prognostic indicator of the severity of various cardiac and pulmonary diseases[27]. VO_{2peak} was collected and analyzed by a portable gas analyzer VO2000 (Med Graphis, St Paul, Minnesota, USA).

The perceived exertion of frail subjects was evaluated using the m-Borg's perceived exertion scale (mBPES) which ranges from 0 (nothing at all) to 10 (extremely severe)[28]. Participants were encouraged to achieve 5 to 7 on mBPES during high-intensity intervals of the group-based HIAIT/m-Ullevaal intervention, and 2 to 4 on mBPES (i.e. 70% of the HRmax) during the moderate intensity intervals. The frail subjects randomly assigned to MICT were encouraged to achieve 2 to 4 on mBPES (i.e. 70% of the HRmax).

The study participants were requested to complete the Bulgarian version of Minnesota Living with Heart Failure Questionnaire (MLHFQ)[29] twice, at baseline (T1), and after 24 sessions (T2). The MLHFQ is one of the most widely used validated disease-specific questionnaires for measuring the effects of different rehabilitation interventions among patients with CHF[30].

The MLHFQ assesses the physical and emotional impact of HF on QoL and consists of 21 rated on six-point Likert scales, representing different degrees of impact of HF on HRQoL, from 0 (none) to 5 (very much). It provides a global score (range 0–105, from best to worst HRQoL), as well as scores for two dimensions, physical (8 items, range 0–40) and emotional (5 items, range 0–25). The other eight items (of the total of 21) are only considered for the calculation of the global score.

Ethics

Ethical approval was obtained from the Ethics Committee of the Medical University of Plovdiv under number (approval # R 3/, date 05/07/2015) which was in accordance with the World Medical Association's Code of Ethics (Declaration of Helsinki, 1967). All participants have provided written informed consent[31].

Statistical analysis

Data are presented as mean ± standard deviation (SD) or as percentages (proportions) unless stated otherwise. The Shapiro–Wilk statistic was used to test the normality of the distribution of all variables. A mixed-model ANOVA analysis was performed on outcome measures (6MWT, VO_{2peak}, mBPES, and MLHFQ). In the present study time (levels: T1 and T2) was the within-subjects factor. Frail subjects had been separated into two groups by the type of the applied group-based HIAIT/m-Ullevaal intervention and MICT, i.e. the between-subjects factor was the type of the applied intervention. The statistical significance level was set at $p<0.05$ for both main and interaction effects. All statistical analyses were performed using Statistical Software Package for Social Sciences (SPSS) for windows version 18.0 (SPSS Inc., Chicago, USA).

Results

Significant improvement in FEC was observed among the participants after 24 training sessions. However, the improvement in the 6MWT achieved from the frail subjects performed the HIAIT/m-Ullevaal intervention (73 m) was significantly higher compared to improvement observed among the frail subjects with CHF performed MICT intervention (46 m) [average improvement of baseline 6MWD by 17% vs 11% respectively, $p <0.001$] (Table 3).

VO_{2peak} increased by 29.1% in frail subjects performed

the group-based HIAIT/m-Ullevaal intervention, (13.49±3.78 vs 16.97±3.65 ml/kg/min) (p<0.001), after 24 sessions which was significantly greater than the improvement achieved in subjects performed MICT, respectively 19,68 % (12.51±3,56 to 14.53±3.09, p<0.001), (Table 3). Statistically significant decrease in mBPES was observed among participants performed both CR interventions after 24 training sessions (T2). However, the decrease in mBPES observed among frail subjects performed the group-based HIAIT/m-Ullevaal intervention was significantly higher than these achieved from subjects performed MICT intervention (respectively -29.79±8.88% vs. -25.71±11.29%, P<0.001) (Table 3).

A significant improvement in the MLHFQ scores was observed after 24 sessions (T2) among frail subjects performed both CR interventions (group-based HIAIT/m-Ullevaal and MICT), (Table 2). Specifically, the MLHFQ scores, decreased by -19.46 % in subjects performed the group-based HIAIT/m-Ullevaal intervention and -6.41 % for the subjects performed MICT. The improvement observed in HRQOL is derived from the fact that QoL is inversely proportional to the MLHFQ score. Therefore, the referred score decrease implies QoL improvement. The proportional changes in the 6MWT, VO_{2peak}, BPES and MLHFQ scores are presented in Table 3.

An analysis of the correlation between QoL and changes in other demographic, anthropometric, and functional indicators was carried out.

The mixed ANOVA analysis indicated a significant and strong influence was mainly exerted by the type of CR intervention (r=0.726, p<0.001). Moreover, the single-factor analysis of variance (ANOVA) shows that type of CR intervention was a significant factor influenced the changes in FEC (F = 39.46 P = 0.000), mBPES (F = 9.42, P = 0.003) and MLHFQ (F = 81.22 P = 0.000).

Discussion

This was the first single-center, controlled clinical trial conducted in Bulgaria aimed to quantify the improvements on FEC and QoL in frail subjects with CHF performed group-based CR interventions[21].

The significance and characteristics of frailty in patients with CHF are increasingly recognized. Some authors show that frailty can be diagnosed in subjects who do not demonstrate any chronic illness, whereas others argue that chronic illnesses and frailty share many characteristics, the most commonly being HF[32]. To our knowledge in previous studies and systematic reviews the relationship between the effectiveness of various CR interventions and reducing frailty were investigated[33-36]. Although the duration of the applied rehabilitation interventions were short ranging from three to six weeks, consequently the improvements were less impressive.

Individually supervised rehabilitation is often considered as the "gold standard"therapy for improving physical function and physiologic outcomes for subjects with CHF, however, these interventions is resource-intensive. Group-based interventions are the field of our study that examines the positive and negative forces that reside within groups, which posits that one's interactions with fellow members change both the individual and the group members[21]. Moreover, it's proven that the group-based interventions contributes to the creation of positive social relationships on its members and can exert much influence and motivation for continuous physical activity. Strong evidence suggests that group-based interventions applied in subjects with CHF generally increases both FEC and QoL[23].

The improvement in MLHFQ score observed among participants performed the group-based HIAIT/m-Ullevaal intervention (7.08 points) is considered as a clinically meaningful difference (CMD). The CMD was significantly greater than the improvement observed in MLHFQ score among frail subjects performed MICT protocol resp. 2.32 points (Table 3).

The aforementioned confirms the superiority of the group-based HIAIT/m-Ullevaal intervention in terms of QoL improvement in frail subjects with CHF. Moreover, the reverse correlation between changes in MLHFQ score and changes in FEC (with r=-0.54, p<0.001), were significant indicating that changes in QoL are associated with the FEC in frail subjects performed HIAIT/m-Ullevaal group-based intervention. It's important to be noted that study population was not highly selected, however reflected the poor social and economic status, as well as the low QoL of the Bulgarian pensioners. Frail subjects performed HIAIT/m-Ullevaal protocol reported high satisfaction with the intervention and found it motivating and enjoyable. On the other hand, the poor initial MLHFQ scores are associated with the weaknesses of the Bulgarian healthcare system i.e. limited access to rehabilitation services due to lack of adequate health policy regarding national CR programs. Although, some authors referred relatively low MLHFQ scores, in high-income countries, with more efficient health care system[35].

The search for an optimal rehabilitation intervention for frail subjects with CHF is not merely related to the improvement in these aspects, but also with the magnitude of this improvement. Nilsson et al., have found that CHF patients who received HIAIT present much better outcomes regarding QoL and 6MWTD, than the subjects, which received MICT[14]. Additionally, it has been acknowledged that HIAIT is more effective than MICT, mainly in terms of FEC improvement for CHF patients[37], which is a finding that is also supported by our results. Furthermore, according to Wisloff et al., HIAIT is superior to MICT not only as a means for FEC increase but also from a QoL perspective[38]. Based on the aforementioned results, the group-based HIAIT/m-Ullevaal intervention led to significant improvements on FEC and QoL of frail subjects with CHF.

Effective rehabilitation strategies in frail subjects with

CHF are still evolving, but evidence suggests that supervised group-based interventions including exercise training, education, and psychological care, improves clinical outcomes and reduces costs. Cost-constrained healthcare systems such Bulgarian recently introduced health technology assessment (HTA)[39] in order to evaluate the relationship between clinical effectiveness, safety, and cost-effectiveness of different rehabilitation interventions. A rapid HTA should motivate the health policy-makers, Bulgarian Medical Association (BMA) as well as the National's Health Insurance Fund (NHIF), to introduce this novel intervention in the updated clinical pathway for CR[40], consequently a growing number of Bulgarian frail subjects with CHF can benefit from this effective intervention.

Limitations

The present study has some limitations that need to be addressed. First, the frail subjects included were homogeneous with stable CHF, NYHA classes II to IIIB and were predominately referred from the Cardiology Clinic at the Medical University of Plovdiv. While all the participants were classified as moderate-to-severe CHF, NYHA classes, both group-based interventions improved significantly the FEC and QoL of the subjects. We hypothesize that stricter inclusion criteria, e.g. ejection fraction <30% or including subjects with slow walking speed, significantly low FEC, and/or exhaustion, might lead to different results. The lack of validated frailty assessment instruments applied in the study population was another limitation. However, the 6MWT was used for both, to assess the FEC of the participants, as well as a valid measure of frailty. Further research on the development and validation of clinically relevant frailty assessment instrument across different cultural contexts, including adaptation for use in Bulgarian language is necessary.

Conclusions

The group-based HIAIT/m-Ullevaal intervention is a new perspective and challenge for Bulgarian CR as well in rehabilitation for frail individuals with CHF. There is strong evidence that this intervention is highly effective regarding the improvement observed in FEC and QoL among this population. These promising results should motivate the Bulgarian health policy-makers to include the group-based HIAIT/m-Ullevaal intervention in the updated CR clinical pathway.

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