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A randomized study examining the effects of mild-to-moderate group exercises on cardiovascular, physical, and psychological well-being in patients with heart failure

Laura S. Redwine, Ph.D.[1], **Kathleen S. Wilson, M.S.**[2], **Meredith A. Pung, Ph.D.**[2], **Kelly Chinh, B.S.**[1], **Thomas Rutledge, Ph.D.**[1], **Paul J. Mills, Ph.D.**[1,2], **Barbara Smith, RN, PhD, FACSM, FAAN**[3]

[1]Department of Psychiatry, University of California, San Diego, CA

[2]Department of Family Medicine and Public Health, University of California, San Diego, CA

[3]College of Nursing, University of South Florida, Tampa, FL

Abstract

Purpose: To compare two mild-to-moderate group exercises and treatment as usual (TAU) for improvements in physical function and depressive symptoms.

Methods: Patients with heart failure (HF) (n = 70, mean age = 66 yr, range = 45 – 89 yr) were randomized to 16-wk of Tai Chi (TC), resistance band (RB) exercise, or TAU.

Results: Physical function differed by group from baseline to follow-up, measured by distance walked in the 6-min walk test (6MWT) (F = 3.19, $P = .03$). TC demonstrated a non-significant decrease of 162 ft [95% CI, 21 to −345, $P = .08$] while RB's distance walked remained stable with a non-significant increase of 70 ft [95% CI, 267 to −127, $P = .48$]. TAU significantly decreased by 205 ft [95% CI, −35 to −374, $P = .02$] and no group differences occurred over time in end systolic volume (ESV) ($P = .43$) and left ventricular function (LVEF) ($P = .67$). However, groups differed over time in the Beck Depression Inventory (BDI) (F = 9.2, $P < .01$). Both TC and RB groups improved (decreased) by 3.5 points [95% CI, 2 - 5] ($P < .01$). TAU decreased insignificantly 1 point [95% CI, −1 to 3] ($P = .27$).

Conclusions: TC and RB participants avoided a decrease in physical function decrements as seen with TAU. No groups changed in cardiac function. TC and RB groups both saw reduced depression symptoms compared with TAU. Thus, both TC and RB avoided a decrease in physical function and improved their psychological function when compared to TAU.

Condensed Abstract:

Tai Chi (TC), resistance band (RB) exercise, and treatment as usual (TAU) were compared in 70 heart failure patients. TC and RB group's physical function remained stable, while TAU showed declines. TC and RB groups had reduced depression symptoms compared with TAU. None of the groups changed in cardiac function.

Correspondence: Laura Redwine, PhD, College of Nursing, University of South Florida, 12901 Bruce B. Downs Blvd., MDC22, Tampa, Florida, 33612-4766, lredwine@health.usf.edu.

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Heart failure (HF) is a worldwide public health problem associated with considerable morbidity, mortality and diminished quality of life.[1] Although medications can improve some symptoms, individuals with HF with either preserved or reduced ejection fraction (HFpEF, HFrEF) continue to experience debilitating symptomatology, including exercise intolerance. In addition to physical symptoms, depressive symptoms are present in up to 30% of HF patients,[2, 3] and are associated with increased mortality, clinical events, hospitalization, and general health care use.[4] Yet the efficacy of antidepressant therapy in patients with coronary heart disease has been limited.[5] The goal of exercise interventions in this chronic disease group is primarily to improve symptoms and the quality and duration of life [6]. Research literature suggests vigorous exercise improves cardiorespiratory fitness [7], and can produce substantial reductions in depression symptoms in patients with HF [8–10]. However, many exercise intervention studies consist of participants that are younger than the typical HF patient, with little comorbidity. The HF-ACTION study included participants with a median age of 59 yr (range 51-67 yr), and excluded patients with major comorbidities or limitations that could interfere with exercise training and/or with devices that limited the ability to achieve target heart rates [11]. Meanwhile, over 80% of HF patients are > 65 yr of age and approximately 50% are > 80 yr [12]. Many patients with HF have limited capacity for vigorous exercise due to comorbidities such as sarcopenia [13], anemia, [14] obesity, diabetes, chronic obstructive lung disease (COPD), peripheral artery disease, and advanced age [15, 16].

In contrast to conventional exercise, tai chi (TC) is composed of low-impact, mindfully meditative movements with integrated breathing techniques that generate a mild to moderate workout [17]. Many TC interventions have been studied specifically in elderly and frail cohorts and are well tolerated across fitness levels [18]. Research suggests that practicing TC is effective for reducing depression symptoms in a broad range of patients with HF, as compared to treatment as usual [17, 19]. Meanwhile, resistance exercise is effective for increasing muscle strength, endurance, physical function (six minute walk test [6MWT]), and promoting favorable arterial remodeling [20]. However, there are few if any studies that have examined resistance exercise for effects on depression symptoms in patients with HF

Moreover, few studies have investigated whether TC differs from more conventional exercises for reducing depression symptoms, particularly in patients with HF. A small study (n = 16) examined effects of TC versus aerobic exercise in patients with HF and HFpEF, finding that TC was more effective in reducing depression symptoms [21].

The overall goal of this investigation was to compare TC, RB exercise, and TAU for changes in physical, cardiac, and psychological function. Associated with the primary aims of our investigation, we hypothesized that mild-to-moderate exercise practices including TC and RB would be more effective in improving physical and cardiac function compared with TAU but would not differ from each other. Associated with our secondary aim, we hypothesized that TC would be more effective than RB and TAU for reducing depressive symptoms.

METHODS

This study was approved by the VA San Diego Healthcare System (VASDHS) and University of California at San Diego (UCSD) Institutional Review Boards, and informed

consent was obtained from all participants included in the study. All procedures performed were in accordance with the 1964 Helsinki declaration and its later amendments. Patients were recruited from VASDHS and UCSD Healthcare System (between 2010 – 2015). At baseline and immediately after the 16-wk intervention, physical and cardiac function, and depression symptoms were measured. This was a randomized trial and the study coordinator determined group allocation using computer generated randomization algorithms and was responsible for all patient correspondence such as group assignment and testing appointments. Recruitment, and assessment personnel were naïve to participant group assignment. Our original study protocol compared TC with health education. However, in response to NIH grant reviewers' suggestions and discussions with the NIH granting agency the health education group was replaced with another mild exercise intervention, to examine whether TC practice went beyond conventional exercise for outcomes, including depression symptoms. We also included a treatment as usual control group in the study design as a comparator of the typical disease course, in the absence of these interventions.

PARTICIPANTS

Inclusion criteria were diagnosis with American Heart Association/ American College of Cardiology Classification Stage C symptomatic HF (both HFpEF and HFrEF) for at least 3 mo, clinically stable (not having been hospitalized for a 3-mo period), on stable doses of neurohormonal blocking agents and diuretics for at least 3 mo, no cardiac surgeries for at least 6 mo, not in an exercise program, ≥40 yr of age. Exclusion criteria included presence of a psychiatric diagnosis other than major depression including psychosis, bipolar disorder and practicing TC within the previous year.

ASSESSMENTS

The following assessments were administered pre- and post-intervention period. Six-minute walk-test was used to assess physical functional capacity. It is a reliable and reproducible method to assess the severity of heart failure in patients, having high predictive value [22]. Patients were instructed to walk as far as possible within 6-min in a straight corridor. The task was performed in a 25-ft walkway, blocked off from foot-traffic. This method has been regularly used by our group for similar studies [17, 23]. Research assistants blinded to the participant's group assignment remained at one end of the hall recording the distance. Standardized encouragement was given at 3-min into the task, i.e. "you are doing good"; "you have 3 more minutes left". Echocardiography was performed by blinded assessors at UCSD Medical Center. All pre- and post-intervention echocardiograms were quantitatively analyzed by the same physician, who was also blinded to group allocation. Briefly, pulsed doppler spectral recordings were obtained from 4 X 4-mm sample volume placed at the tips of the mitral leaflets and in the pulmonary vein and that were adjusted to yield the maximal amplitude velocity signals. Images were digitized to obtain endocardial contours and LV cavity areas at end systole from the apical 4- and 2-chamber views. This method has been shown to be a reliable method of assessing LV function and predicting mortality in patients with HF.[24] Ejection fractions were derived from biplane apical (2- and 4-chamber) views with use of modified Simpson's rule algorithm [25]. Depression symptoms were assessed with the 21-item Beck Depression Inventory −1A (BDI), which is recommended for measurement of depression in patients with cardiovascular disease, with reliability and capacity to

discriminate between depressed and non-depressed participants with broad applicability for research and clinical practice [26]. Cronbach's alpha = .86 for the current study.

GROUP INTERVENTIONS

The intervention groups were Yang-style Tai Chi Chuan-Short Form (first third), and RB training (based on the Center for Disease Control's "Move" program). RB exercise was chosen as a comparison to TC due to the psychosocial and mild-to-moderate physical exertion level similarities. Both exercises can be led by an experienced instructor, performed in a group, and provided at medical care or senior centers with minimal equipment and thus easily disseminated. Participants attended TC or RB training twice/wk for 60 min/session for 16-wk. TC and RB participants were asked to practice at home for 10-20 min/day, on non-class days. Descriptions of TC and RB class content are provided (SDC1). The TC instructor is a certified holistic health practitioner with > 10 yr of experience teaching TC to chronically ill and older adults. The RB instructor has her master's degree in nutrition and taught physical fitness for 10 yr. Both groups were asked to exercise at a perceived exertion rating of "moderate difficult", according to the Borg scale [27]. Classes for the 2 groups were held on different days of the week at different locations within the University to avoid cross-contamination. Written materials were provided to support home practice for both groups. All participants continued to receive usual care, including regular visits to their cardiologist, primary care physicians, and other health specialists. TAU participants did not receive an active intervention.

STATISTICAL ANALYSES

Analyses were performed using SPSS version 24 (IBM Corp). Skewed data distribution was determined by the Kolmogorov-Smirnov test. All continuous variables approximated a normal distribution with skewness and kurtosis < 1.0. Baseline differences between groups were examined using analysis of variance for continuously measured variables and $\chi 2$ statistics for non-continuous variables. Mixed-effects models were used to analyze the efficacy of TC compared with RB exercises and TAU over 16 wk of treatment [28]. The analysis for each outcome consisted of a model that included treatment, time, and treatment × time interaction as fixed effects with a heterogeneous covariance matrix. Post hoc analyses were performed to make specific group comparisons with repeated measures ANCOVA using estimated mean imputation.

RESULTS

Of 135 individuals screened for eligibility (see Figure 1, flow diagram) 70 patients were enrolled into the study with a median age of 66 yr (range, 45 – 89 yr) and 89% were male. BDI scores averaged 10 ± 7.3 suggesting that the cohort's scores were at the cut-off for clinically significant elevation of depression symptoms ($\geq$ 10) [29]. Participants were assigned to TC (n = 25), RB training (n = 22) or TAU groups (n = 23) (Table 1).

TREATMENT FIDELITY AND ADHERENCE

Of 70 participants enrolled, 16% dropped out (TC: n = 4; RB: n = 3; TAU: n = 4) and 59 participants completed the study (n = 21, 19 and 19 respectively). There were no group

differences in drop-out rates ($P = .81$). TC participants attended a median of 87% of classes (28 sessions), and practiced a median of 74 min/wk. Whereas, the RB group attended a median of 81% of classes (26 classes) and practiced a median of 61 min/wk. There were no differences between the two active intervention groups for class attendance ($P = .76$) or practice time outside of class ($P = .86$). There were no differences in age, sex, %LVEF, 6MWT, HFpEF or HFrEF sub-types, BDI, scores between those who dropped out from those who completed the study (P's > .10). There were no serious adverse events associated with the study.

PHYSICAL AND CARDIAC FUNCTION

Fixed effect group differences from pre- to post-intervention period were found with a mixed model analysis, with 6MWT as the dependent variable (group x time interaction, F = 3.19, $P = .03$) (Figure 2). Estimated fixed effects revealed TAU significantly declined in distance walked by 205 ft [95% CI, −35 to −374, $P = .02$] and the RB group with a slight increase of 70 ft [95% CI, 267 to −127, $P = .48$] and TC trending for a significant decrease of 162 ft [95% CI, 21 to −345, $P = .08$]. Post hoc analyses revealed only RB and TAU group differences ($\eta^2 = .087$, $P = .05$). There were no differences between RB and TC ($\eta^2 = .023$, $P = .33$), or between TC and TAU ($\eta^2 = .009$, $P = .51$). Also, there were no fixed effect group differences over time in cardiac function measured with ESV ($P = .43$) and %LVEF ($P = .67$).

DEPRESSION SYMPTOMS

There were fixed effect group differences over time for BDI scores (group x time interaction, F = 9.2, $P < .01$) (Figure 3). Estimated fixed effects revealed a decrease in BDI scores by TC [95% CI, 2 - 5, $P < .01$] and RB groups [95% CI, 1 to 5, $P < .01$] of 3.5 points, while the TAU group decreased by 1 point [95% CI, −1 to 3] ($P = .27$). Post hoc analyses revealed both TC ($\eta^2 = .096$, $P = .039$) and RB ($\eta^2 = .11$, $P = .034$) groups differed from TAU over time. There were no differences between TC and RB ($\eta^2 = .014$, $P = .45$).

DISCUSSION

The present investigation sought to compare TC, RB exercise, and TAU for changes in physical, cardiac, and psychological function. Over the 16-wk study, attrition was 18% which was slightly better than the 20% drop-out rate that was predicted. There were no differences in drop-out rates among the 3 groups, and no differences between intervention groups in class attendance or practice times, with median class attendance > 80%, and reported median practice times of > 1 hr/wk. There were no serious adverse events associated with the study. The median age of the participants was 66 yr, an age group representative of most HF patients.

From our primary aims, we hypothesized that mild exercise practices including TC and RB would be more effective in improving physical and cardiac function compared with TAU but would not differ from each other. However, at the end of 16 wk we failed to see improvements from baseline in physical function, measured with the 6MWT by any of the groups. Instead, we found physical function did not decline in the TC and RB group, and

that RB and TAU differed significantly from each other over time. This may suggest that RB can hamper HF related physical function decline. Our findings illustrate that the intensity and mode of exercise used in this study does not generate the level of effect on exercise capacity that has been seen in studies with higher intensity aerobic exercise [30]. Our findings correspond with Yeh et al, (2011) whose study included 100 patients with HF and found no significant differences in change in 6MWT distance when comparing TC with a health education control group [31]. Also, our results corresponded with the literature in that RB had better outcomes on the 6MWT then TAU controls [32]. Of note, the RB group had a lower functional capacity (6MWT) at baseline (albeit not significantly lower) than TAU and TC, and thus the magnitude of improvement by the RB group may have been influenced by a lower baseline state.

Our hypothesis that TC and RB would improve cardiac function compared with TAU was also not supported, since there were no changes in %LVEF and ESV in any of the groups over time. This agrees with the literature suggesting that more vigorous exercise interventions have a greater likelihood of improving cardiovascular function [7]. Our physical and cardiac function findings should be replicated due to the small sample size, but particularly regarding physical function which may be impacted by the older age of the participants and acute and chronic HF comorbidities (e.g. claudication, COPD, diabetic neuropathy) that can impact 6MWT results.

From our secondary aim, we hypothesized that TC would be more effective than RB and TAU for reducing depressive symptoms. This hypothesis was partially supported in that TC was superior to TAU for reducing depressive symptoms over time. This is consistent with our previously published work and findings from other investigators, observing that TC practice is associated with depression symptom reductions in patients with HF [17, 33]. However, RB was also superior to TAU and did not differ from TC in reducing depressive symptoms. The present investigation extends prior research by including RB as a conventional exercise condition and suggests that various mild-to-moderate exercises can reduce symptoms of depression in patients with heart failure. These findings may be clinically relevant since elevated depression symptoms in cardiovascular diseases such as HF are related to greater risk of cardiovascular hospitalization and mortality [34, 35];[36]. More study is needed to determine the influence of exercising in groups on depression, since both interventions were group based.

A main limitation of the study includes a modest sample size resulting in limited statistical power. This precluded the inclusion of important covariates that may also influence physical and cardiac function, depression symptoms, and ultimately lessens the certainty of the findings presented. Also, because of the small sample-size we could not adequately address differences between HFpEF and HFrEF. However, both groups are known to experience reduced physical function [37] and depression [38]. Therefore, the findings relating to physical function and depression are likely relevant to both groups. Other limitations include, lack of measures for range of motion and exercise progression. Also, we had a small number of women in our study, since most patients were recruited from the Veterans hospital. Additionally, it is unclear from patient records specifically how many were taking anti-depressants.

CONCLUSION

In sum, this study found that 2 different types of mild-to-moderate exercise training was associated with reduced depression symptoms and a potential reduction of functional decline. Importantly, patients were willing to come into a facility for group exercise when specifically recruited from cardiac clinics. Future research is needed to replicate and expand upon our findings to more fully understand the mechanisms by which mild-to-moderate exercise may reduce functional decline and depression symptoms.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments:

The protocol for the parent study can be found at clinicaltrial.gov Clinical Trial number: NCT01625819. ORCID#: 0000-0001-7633-2034

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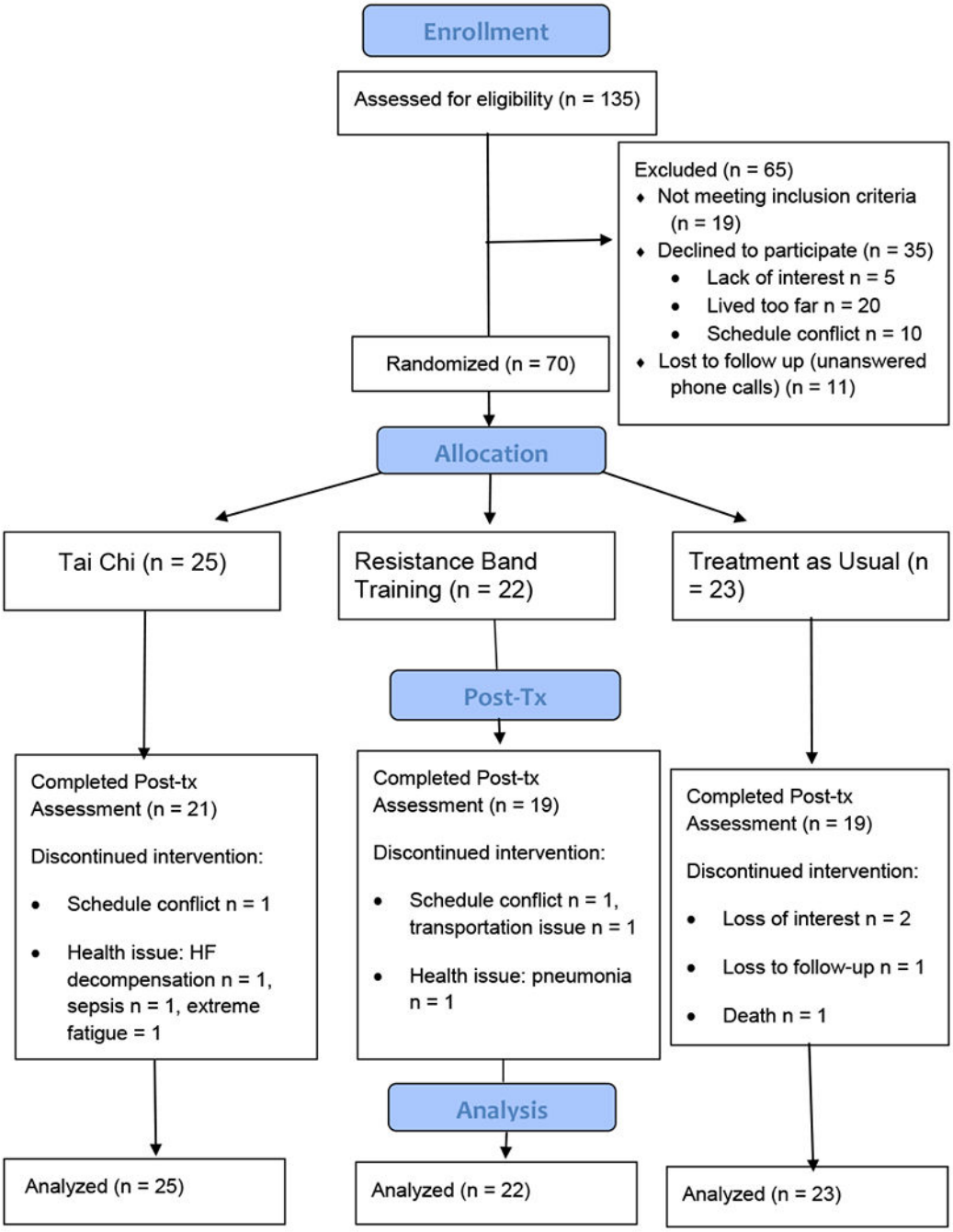

Figure 1:
Participant Flow Diagram

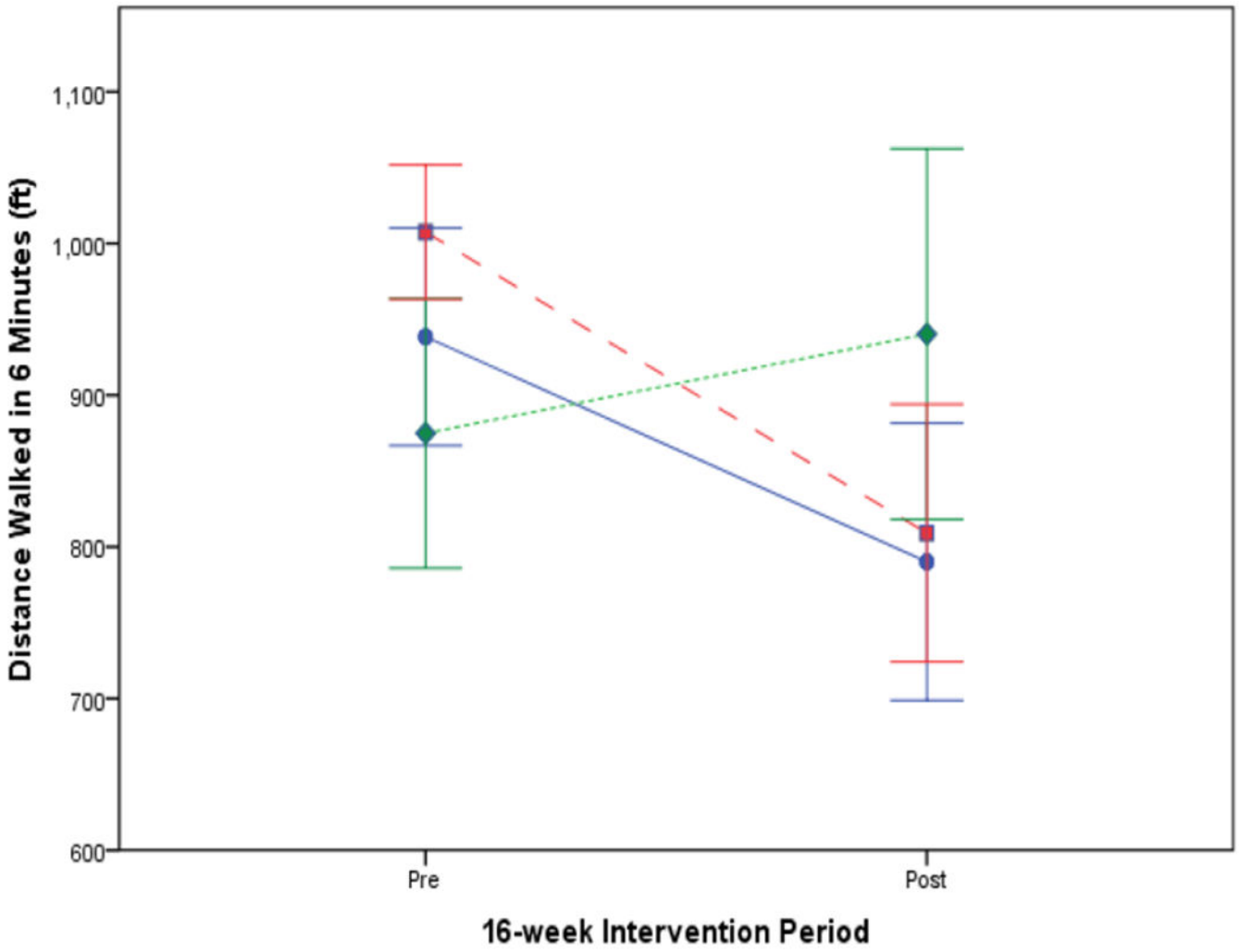

Figure 2.

Changes in 6-min walk test (mean ± SE) from baseline to post-16-wk intervention period in patients with heart failure trained in tai chi (TC) (circles), resistance bands (RB) (diamonds) exercise or treatment as usual (TAU) controls (squares).

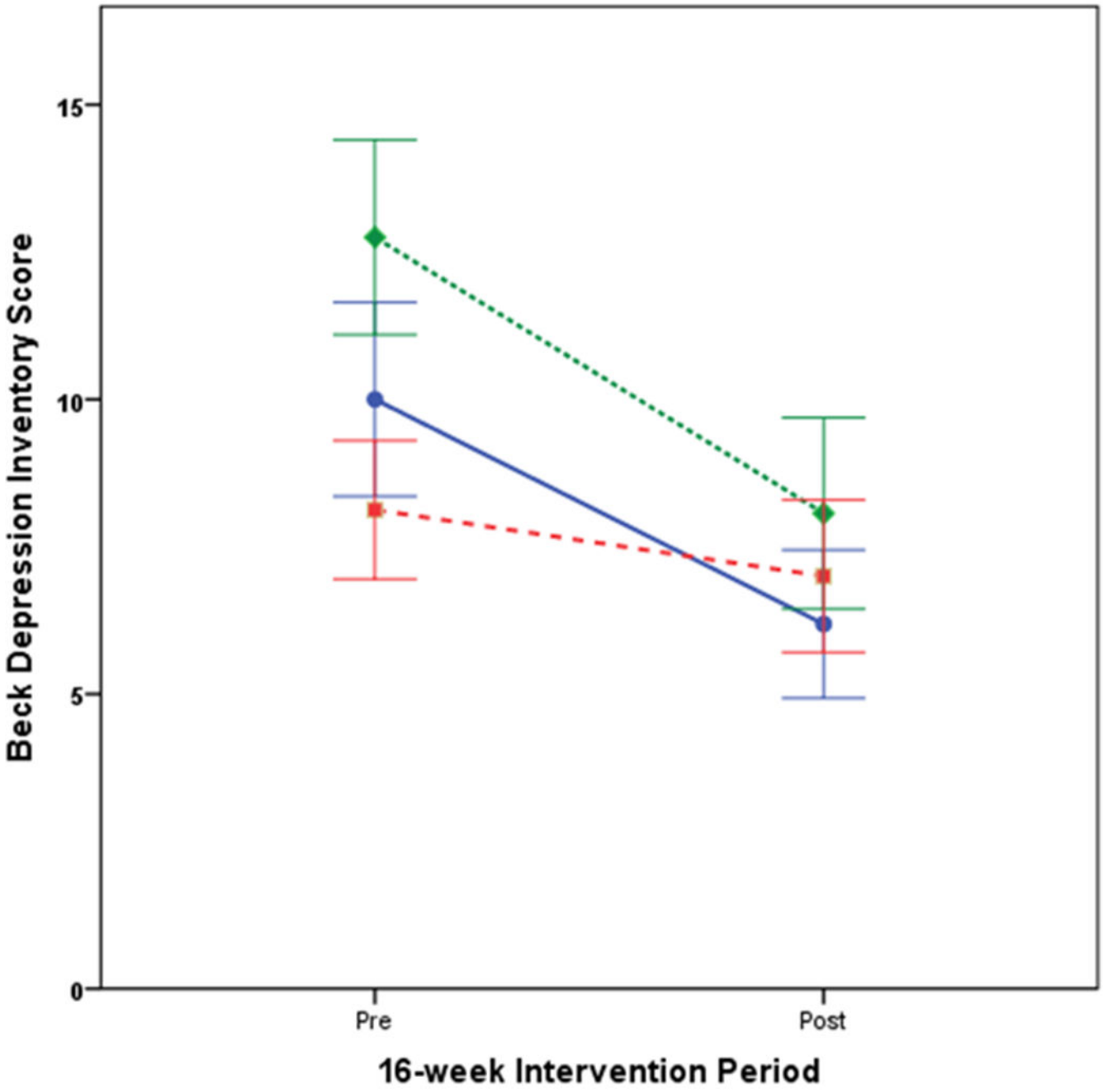

Figure 3.

Changes in Beck Depression Inventory-IA scores (mean ± SE) from baseline to post-16-wk intervention period in patients with heart failure trained in tai chi (TC; circles), resistance band (RB; diamonds) exercise or treatment as usual (TAU; squares).

Table 1.

Baseline Subject Characteristics

	Total	**TC**	**RB**	**TAU**	***P* value**
n	**70**	**25**	**22**	**23**	
Age, yr	66 ± 10	63 ± 9	65 ± 9	67 ±7	.52
Sex, male	89	92	86	87	.81
Race, white	68	68	82	54	.29
LVEF	46 ± 14	44 ± 13	46 ± 14	46 ± 12	.85
HFpEF, n	43	44	45	37	.79
BMI, kg/m^2	32 ± 8	32 ± 8	33 ± 8	31 ± 6	.64
Marital, married	30	32	23	29	.57
6MWT, ft	943 ± 336	938 ± 359	875 ± 407	1011 ± 336	.41
BDI	9 ± 7	10 ± 6	12 ± 8	8 ± 6	.17

Abbreviations: BDI = Beck Depression Index; BMI = body mass index; HFpEF = heart failure with preserved ejection fraction; LVEF = left ventricular ejection fraction; 6MWT = six-minute walk test; RB, resistance band; tai chi; TAU; TC, treatment as usual.

Data are reported as mean ± SD or n (%).

Independent t-tests and Kruskal-Wallis tests were used to evaluate group differences.