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ORIGINAL ARTICLE
Cardiac Rehabilitation

Effects of Phase II Cardiac Rehabilitation on Physical Function and Anxiety Levels in Frail Patients

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Background: Frailty is an important prognostic factor in patients with cardiovascular diseases (CVD), and patients with CVD have a high rate of concurrent psycho-emotional stress, as well as depressive mood and anxiety symptoms. Despite this, few reports have examined the effects of the efficacy of Phase II cardiac rehabilitation (CR) in frail patients, including improvements in anxiety levels.

Methods and Results: In all, 137 patients (mean [±SD] age 65.8±13.0 years; 71% male) who participated in Phase II CR and were assessed after CR completion were included in this study. Patients were evaluated using the Kihon Checklist (KCL) form at the beginning of CR and were divided into the 3 groups according to KCL scores: frail (n=34, 25%), pre-frail (n=40, 29%), and non-frail (n=63, 46%). Physical function and anxiety levels were compared among the 3 groups. The pre-frail and frail groups had significantly higher state anxiety and trait anxiety than the non-frail group ($P<0.01$). At the end of Phase II CR, all 3 groups showed significant improvements in the 6-min walking distance ($P<0.05$). State anxiety improved significantly in the non-frail and pre-frail groups, whereas trait anxiety only improved in the non-frail group.

Conclusions: Physical function was improved in frail patients who participated in Phase II CR. However, there was no significant improvement in their level of anxiety.

Key Words: Anxiety; Cardiac rehabilitation; Frailty; Physical function

Frailty is defined as a "biologic syndrome of decreased reserve and resistance to stressors, resulting from cumulative declines across multiple physiologic systems, and causing vulnerability to adverse outcomes".[1] Frailty consists of multiple problems, such as physical problems, psychiatric disorders, cognitive impairment, depression, and social problems.[2] Frailty is an important prognostic factor in community-dwelling individuals and those with cardiovascular disease.[3,4]

Individuals with physical frailty have an 8-fold increased risk of cognitive impairment or dementia and are at a high risk of depression[5] compared with those without physical frailty.[6] Frail patients not only have depression and cognitive decline, but are also at a high risk of apathy and anxiety.[7] In a previous study, we demonstrated that frail patients had lower levels of physical function and significantly higher levels of anxiety than non-frail patients among those undertaking Phase II cardiac rehabilitation (CR).[8]

Comprehensive CR is a multifaceted intervention that aims to improve physical, psychological, and social states and to ameliorate arteriosclerosis in patients with cardiovascular disease.[9,10] Moreover, CR has been reported to improve not only exercise tolerance, but also long-term prognosis.[11] However, only a few studies have examined the effects of CR, including on anxiety, in frail patients.

Therefore, the aim of the present study was to investi-

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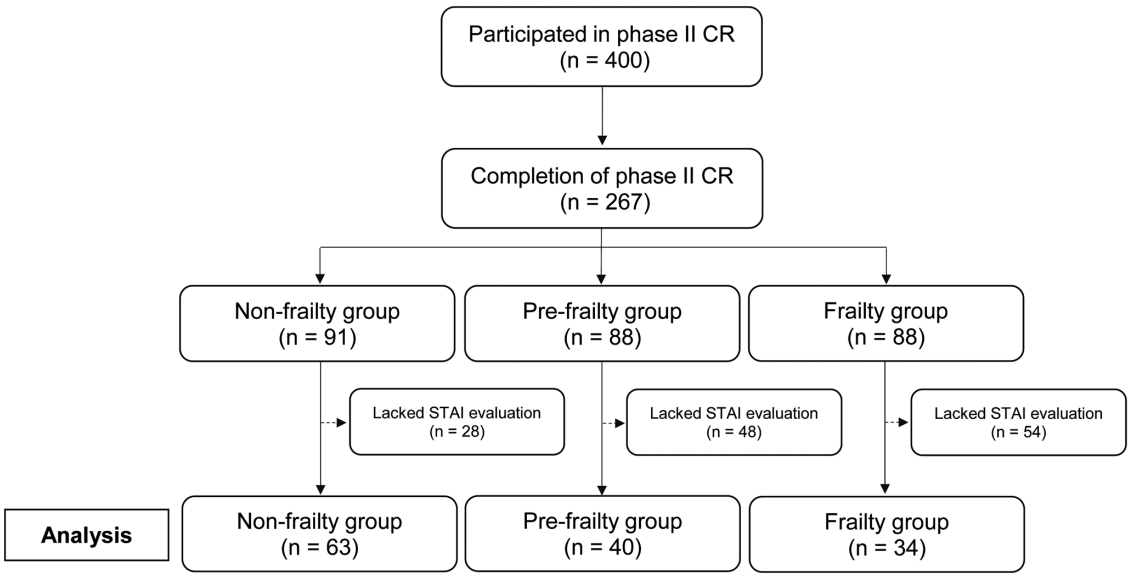

Figure 1. Study flow chart. Based on Kihon Checklist scores, patients were divided into 3 groups: non-frail (0–3 points), pre-frail (4–7 points), and frail (>8 points). CR, cardiac rehabilitation; STAI, State Trait Anxiety Inventory.

gate the effects of Phase II CR on physical function and anxiety levels based on the prevalence of frailty.

Methods

Study Population

In all, 400 patients who participated in early Phase II CR between November 2015 and August 2017 at Juntendo University Hospital were enrolled. These patients were evaluated for clinical indices, including coronary risk factors, physical function, and anxiety levels, at the beginning of CR. Of the 400 patients, 267 completed Phase II CR, but evaluation data at the end of Phase II CR were lacking for 130. This left 137 patients who met all the eligibility criteria and were included in this study. These patients were divided into 3 groups (non-frail, pre-frail, and frail groups) on the basis of Kihon Checklist (KCL) scores (**Figure 1**).

Patients were informed as to the purpose and details of this study before they provided their consent to participate, in accordance with the provisions of the Declaration of Helsinki. The items related to this study were studied retrospectively. This study was approved by the Ethics Review Board of Juntendo University Hospital (Approval no. 13-058).

Data Collection and Measurements

Age, sex, underlying diseases, coronary risk factors, left ventricular ejection fraction, body composition, muscle strength, 6-min walking distance (6MWD), KCL, and State Trait Anxiety Inventory (STAI) form were assessed at the beginning and end of CR, as described previously.[8,12] Anthropometric parameters, including percentage body fat, lean body mass, and muscle mass, were measured using bioelectrical impedance analysis (MC-780A; TANITA, Tokyo, Japan). The grip strength of both hands was measured in participants in a standing position, with the higher grip strength value of the 2 hands used in analyses. The 6MWD test was performed as described previously.[3] For blood biochemistry, parameters such as hemoglobin, albumin, creatinine, triglyceride, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, HbA1c, and B-type natriuretic peptide concentrations, estimated glomerular filtration rate (eGFR), and the geriatric nutritional risk index (GNRI) were measured.[13]

KCL

The KCL is a 25-item self-administrated questionnaire developed by the Japanese Ministry of Health, Labour and Welfare for older individuals who are at risk of requiring new certification for long-term care insurance.[14] The KCL comprises 7 types of questions that aim to assess the instrumental activities of daily living, physical function, nutritional status, oral function, social activities of daily living, cognitive function, and depressive mood of participants. Thus, the KCL is a comprehensive evaluation method that focuses on social and psychological aspects, in addition to physical aspects, of frailty. Given its ability to assess frailty across multiple domains, the KCL is regarded as an effective screening tool.[14] The questions on the KCL require a simple "yes" or "no" answer, and are scored as 1 or 0 points, respectively.

Patients in the present study were classified into 3 groups based on the KCL. Patients with a score ≥8 points (out of a maximum of 25) on the KCL were categorized as frail, those with a score of 4–7 points were categorized as pre-frail, and those with a score ≤3 points were categorized as non-frail.[14]

Anxiety Levels

Anxiety levels were evaluated using a self-administered STAI form.[15] This form is an inventory consisting of 40 state-

Table 1. Clinical Characteristics of the Study Participants

	Non-frail (n=63)	Pre-frail (n=40)	Frail (n=34)	P value
Age (years)	63.5±12.9	66.8±12.4	69.0±13.2	0.12
Male sex	50 (79)	26 (65)	21 (62)	0.12
BMI (kg/m^2)	23.5±2.6	24.2±3.6	22.4±3.1	0.05
Lean body mass (kg)	49.9±8.9	46.4±8.4	43.5±9.0	<0.01
Hypertension	40 (63)	28 (70)	25 (74)	0.56
Dyslipidemia	32 (51)	21 (53)	19 (56)	0.89
Diabetes (%)	15 (24)	7 (18)	8 (24)	0.75
Current smoker	8 (13)	7 (18)	1 (3)	0.19
CVD at the beginning of CR				
Myocardial infarction	12 (19)	1 (3)	2 (6)	
Angina pectoris	6 (10)	2 (5)	2 (6)	
Chronic heart failure	12 (19)	13 (33)	9 (26)	
Open heart surgery	29 (46)	18 (45)	18 (53)	
Coronary artery bypass grafting	9 (31)	6 (15)	8 (42)	0.14
Valvular surgery	19 (30)	10 (25)	10 (29)	
Other open-heart surgery	1 (2)	2 (5)	0 (0)	
Aortic disease	2 (3)	5 (13)	2 (6)	
Peripheral artery disease	2 (3)	1 (3)	1 (3)	
Laboratory data				
Hemoglobin (g/dL)	13.7±1.7	13.4±2.1	12.3±1.9*	<0.01
Albumin (g/dL)	3.9±0.5	3.9±0.5	3.8±0.6	0.35
Creatinine (mg/dL)	0.79±0.3	1.14±1.2	1.24±1.5	0.08
eGFR (mL/min/1.73 m^2)	79.8±26.1	67.1±25.3	61.9±25.9*	<0.01
TG (mg/dL)	124.9±89.5	125.4±59.3	119.9±55.9	0.50
HDL-C (mg/dL)	49.7±15.5	48.6±18.7	48.2±12.4	0.89
LDL-C (mg/dL)	99.1±27.9	99.9±32.7	98.1±23.2	0.97
HbA1c (%)	6.2±1.0	5.9±0.6	6.1±0.8	0.37
BNP (pg/mL)	108.5±139.4	240.6±385.3	237.9±633.4	0.16
GNRI	110.2±8.3	102.2±19.1*	103.7±8.3*	<0.01
LVEF (%)	59.7±13.1	58.3±15.4	62.2±11.4	0.45
Medications				
ACEI	18 (29)	5 (13)	3 (9)	0.03
ARB	11 (17)	5 (13)	10 (29)	0.17
β-blocker	52 (83)	30 (75)	24 (71)	0.37
CCB	10 (16)	8 (20)	9 (26)	0.46
Diuretic	37 (59)	32 (80)	26 (76)	0.04
Statin	39 (62)	24 (60)	23 (68)	0.78
OHA	9 (14)	5 (13)	6 (18)	0.82
Insulin	2 (3)	3 (8)	3 (9)	0.46
Anxiolytic	1 (2)	1 (3)	5 (15)	0.01
Sleeping pills	0 (0)	3 (8)	0 (0)	0.02
No. late Phase II CR participation	12±1	11±1	12±1	0.70

Unless indicated otherwise, data are given as the mean±SD or n (%). *P<0.05 compared with the non-frail group. ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; BMI, body mass index; BNP, B-type natriuretic peptide; CCB, calcium channel blocker; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LVEF, left ventricular ejection fraction; OHA, oral hypoglycemic agent; TG, triglycerides.

ments about the feelings of the participant, divided into 2 parts. In Part I (consisting of 20 statements), patients are instructed to indicate the intensity of their feelings of anxiety at a particular moment (indicating state anxiety), using scores ranging from 1 (absolutely not) to 4 (very much). In Part II (another 20 statements), patients describe how they generally feel (indicating trait anxiety) by reporting the frequency of their symptoms of anxiety, again using scores ranging from 1 (hardly ever) to 4 (often). The total score for each part can range between 20 and 80, with higher scores indicating higher levels of anxiety. In the present study, we used the Japanese version of the STAI.[16]

Comprehensive CR Program

Comprehensive CR consists of patient risk stratification, exercise therapy, education for secondary prevention, and

Table 2. KCL Scores at the Beginning of Phase II CR in the Non-Frail, Pre-Frail, and Frail Groups

	Non-frail (n=63)	Pre-frail (n=40)	Frail (n=34)	P value
KCL items				
Instrumental ADL	0.2±0.5	0.5±0.8	1.6±0.2	<0.01
Physical function	0.3±0.6	1.3±0.9	2.0±1.2	<0.01
Nutritional status	0.3±0.1	0.6±0.1	0.6±0.1	0.04
Oral function	0.2±0.1	1.1±0.1	1.5±0.8	<0.01
Social ADL	0.1±0.4	0.3±0.5	0.7±0.7	<0.01
Cognitive function	0.1±0.4	0.6±0.7	0.9±1.0	<0.01
Depressive mood	0.3±0.6	1.3±1.2	3.0±1.4	<0.01
Total KCL score	1.6±1.2	5.6±1.2	10.2±2.3	<0.01

Data are presented as the mean±SD. ADL, activities of daily living; CR, cardiac rehabilitation; KCL, Kihon Checklist.

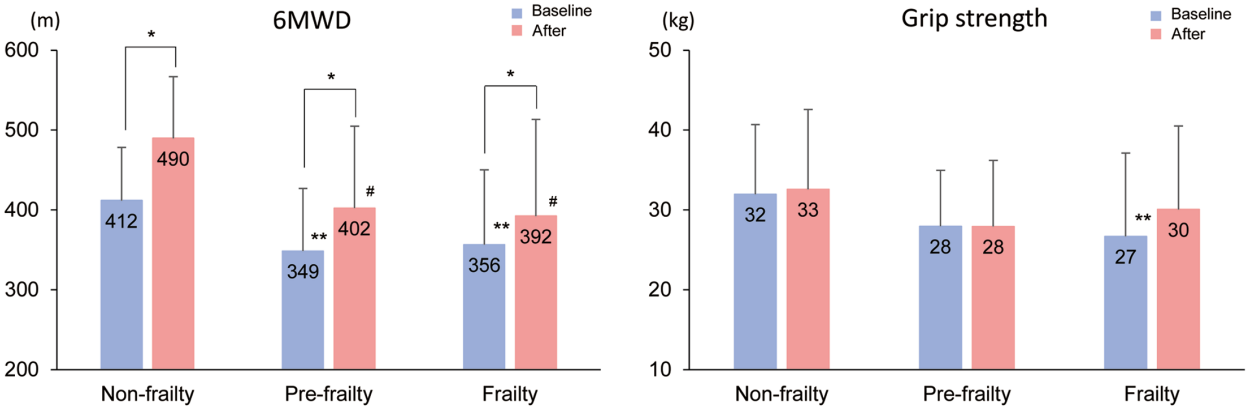

Figure 2. Comparison of changes in physical function in the non-frail, pre-frail, and frail groups from the beginning to the end of Phase II cardiac rehabilitation (CR). Data are the mean±SD. *P<0.05. **P<0.05 compared with the non-frail group at baseline; #P<0.05 compared with the non-frail group at the end of Phase II CR. 6MWD, 6-min walking distance.

support for psychosocial factors.[17] The CR program consists of warm-up stretching, aerobic exercise, resistance training, and a cool-down period, and was scheduled once or twice weekly for 150 days from the beginning of CR.[18] Aerobic exercise consisted of a cycle ergometer, treadmill, and walking on an indoor track for a total duration of approximately 60 min. Exercise intensity was prescribed individually at the anaerobic threshold level, as measured by an ergometer test using expiratory gas analysis or a rating of 11–13 on a standard Borg's rating of perceived exertion scale. In addition, except for the day of visit, we individually recommended a voluntary training plan at home. Moreover, doctors, nurses, and CR staff provided lifestyle guidance and consultations regarding risk factors for cardiovascular disease.[17]

Statistical Analysis

Continuous variables are presented as the mean±SD. Differences among the 3 groups were analyzed using one-way analysis of variance followed by Tukey's honestly significant difference test. The χ^2 test was used to compare categorical variables. Differences were considered significant at 2-sided P <0.05. Statistical analyses were performed using JMP14.0 (SAS Institute, Cary, NC, USA).

Results

Clinical Characteristics

The clinical characteristics of patients in each of the 3 groups are presented in **Table 1**. The mean age of the entire cohort was 65.8±13.0 years, and 97 (71%) were men. In all, 34 patients were classified as frail (25%), 40 were classified as pre-frail (29%), and 63 were classified as non-frail (46%). There were no significant differences among the groups in age, sex, indications for CR in cardiovascular disease, coronary risk factors, left ventricular ejection fraction, or the number of Phase II CR implementation. Both hemoglobin and eGFR were significantly lower in the frail than non-frail group (both P<0.01). At the beginning of CR, the pre-frail and frail groups had significantly lower lean body mass and GNRI than the non-frail group (both P<0.01). In addition, the prescription rate of anxiolytics was significantly higher in the frail than non-frail and pre-frail groups (P<0.05). Furthermore, the rate of sleeping pill prescriptions was significantly higher in the pre-frail than non-frail and frail groups (P<0.05). A comparison of KCL subitems among the 3 groups showed significant differences for all items of instrumental activities of daily living, physical function, nutritional status, oral function, social

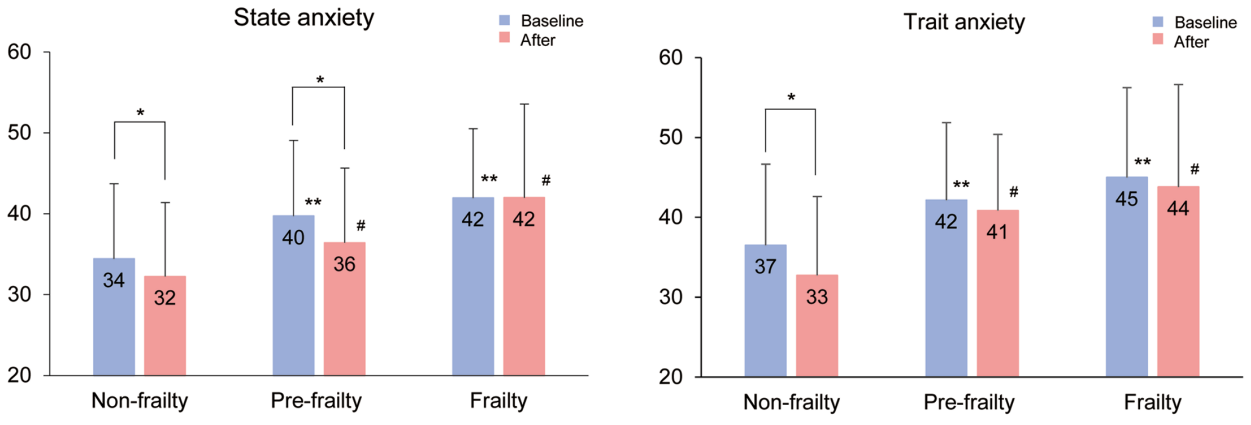

Figure 3. Comparison of changes in anxiety scores in the non-frail, pre-frail, and frail groups from the beginning to the end of Phase II cardiac rehabilitation (CR). Data are the mean±SD. *P<0.05. **P<0.05 compared with the non-frail group at baseline; #P<0.05 compared with the non-frail group at the end of Phase II CR.

activities of daily living, cognitive function, and depressive mood (**Table 2**).

Changes in Physical Function After Phase II CR

Physical function at the beginning and end of Phase II CR among the 3 groups is shown in **Figure 2**. At the beginning of CR, 6MWD was significantly lower in the pre-frail and frail groups than in the non-frail group (412±67 and 349±78 vs. 356±94 m, respectively; P<0.01). Furthermore, grip strength was significantly lower in the frail than non-frail and pre-frail groups (32±9 vs. 28±7 and 27±10 kg, respectively; P=0.03). At the end of CR, none of the groups showed significant improvements in grip strength; however, there were significant improvements in the 6MWD: from 412±67 to 492±77 m (P<0.01) in the non-frail group; from 349±78 to 402±103 m (P<0.01) in the pre-frail group; and from 356±94 to 392±121 (P=0.01) in the frail group (**Figure 2**). Moreover, at the end of CR, 6MWD was significantly lower in the pre-frail and frail groups than in non-frail group (490±77 and 402±103 vs. 392±121 m, respectively; P<0.01).

Changes in Anxiety Levels After Phase II CR

Figure 3 shows anxiety levels in each of the 3 groups. State anxiety scores at the beginning of CR were significantly higher in the pre-frail and frail groups than in the non-frail group (34±9 and 40±9 vs. 42±9, respectively; P<0.01). State anxiety scores at the end of CR improved significantly compared with those at the beginning of CR in the non-frail (from 34±9 to 32±9; P=0.04) and pre-frail (from 40±9 to 36±9; P<0.01) groups, but not in the frail group (from 42±9 to 42±12; P=0.99).

Like state anxiety scores, trait anxiety scores at the beginning of CR were significantly higher in the pre-frail and frail groups than in the non-frail group (37±10 and 42±10 vs. 45±11, respectively; P<0.01). Trait anxiety scores at the end of CR improved significantly compared with those at the beginning of CR in the non-frail group (from 37±10 to 33±10; P<0.01). However, similar improvements in trait anxiety scores were not observed in the pre-frail (from 42±10 to 41±10; P=0.20) and frail (from 45±11 to 44±13; P=0.42) groups.

Discussion

This study investigated the effects of Phase II CR on physical function and anxiety based on the prevalence of frailty. CR improved physical function, such as 6MWD, but not anxiety levels in frail patients. To the best of our knowledge, this is the first study to demonstrate the efficacy of Phase II CR in frail patients, including an examination of anxiety levels.

To date, exercise therapy has been shown to improve physical function, 6MWD, and the Short Physical Performance Battery in frail patients.[19–21] Furthermore, recent studies in Japan have suggested that a 3-month CR program for frail older adults with cardiovascular disease may significantly improve walking speed, grip strength, and lower limb muscle strength.[22] In the present study, a significant improvement in 6MWD at the end of CR was also observed, suggesting that a CR program that includes exercise therapy improves exercise tolerance in frail patients.

In elderly patients with cardiovascular disease, the incidence of physical frailty, cognitive impairment, and social frailty has been reported to be 56.6%, 36.9%, and 66.4%, respectively.[23] There are also notable overlaps between the areas of frailty, and frail patients in multiple frailty domains have been shown to have higher mortality and rates of rehospitalization for heart failure, indicating the importance of a comprehensive approach.[23]

CR has been shown to improve physical function, anxiety, depression, and quality of life.[9] Acquiring the habit to exercise was reported to improve biopsychological responses to psychological stress, as well as to ease symptoms in patients with depression and alleviate trait anxiety.[24]

Conversely, a 3-month exercise program resulted in improvements in lower limb muscle strength, but that had no effect on anxiety, depression symptoms, and psychophysical factors in pre-frail and frail older adults.[25] Furthermore, patients who had severe anxiety at the beginning of CR remained anxious after a 3-week CR program.[26] A home-based physiotherapy program for community-dwell-

ing older adults improved functional impairment scores in older adults with moderate frailty; however, the effects of the intervention were limited for older adults who had severe frailty.[27] Moreover, CR was associated with favorable outcomes in patients with heart failure with mild and moderate frailty, but not relevant to favorable outcomes for patients with heart failure with severe frailty.[28]

Recent studies reported that a multiple-intervention program consisting of exercise, nutritional interventions, and psychotherapy or cognitive therapy was more effective than a single-intervention program in improving physical or cognitive frailty.[29,30] Furthermore, participation in cultural or community activities and engaging in volunteer work, as well as maintaining physical activity, have been suggested to prevent frailty. In an aging society, a multifaceted regional social prescription is required, including social participation, social contribution, and interaction with other generations.[31]

For frail patients, it may be necessary to implement a comprehensive and long-term CR program with multidisciplinary interventions.[25] In addition, aggressive and preventive intervention is crucial even before the progression to frailty.

There are several limitations to this study. First, it was based on data collected from a small sample in a single center; thus, outcomes should be generalized with caution. Second, we enrolled patients who completed Phase II CR. Therefore, the results may not necessarily be representative of all Phase II CR patients. In a future study we need to investigate patients who dropped out of Phase II CR. Third, we did not survey physical activity, social activity, and lifestyle habits during Phase II CR. Therefore, home-based life-space assessments have not been reflected in the results. Fourth, the rate of collection of STAI forms at the end among patients who completed Phase II CR was 51%. A comparison of the 137 patients for whom STAI data could be collected with 130 patients for whom these data were not available showed no significant differences in age, sex, the total KCL score, subscale scores on the KCL, or in the proportion of pre-frail and frail patients (data not shown); however, there was a significant difference in the number of Phase II CR participants between these 2 groups (11.8±7.3 vs. 9.5±6.7, respectively; $P<0.05$). Therefore, the patients who completed Phase II CR may have been motivated.

Fifth, the trait anxiety score at the beginning of CR tended to be significantly higher in women than in men (43.0±11.1 vs. 39.1±10.6, respectively; $P=0.05$). Previous studies have also reported that anxiety levels in patients with heart disease are higher among women than men.[32] In the future, it will be necessary to increase the number of samples and verify the effect of improving anxiety according to sex.

Finally, the KCL is an effective screening tool for multiple areas of frailty. However, because some individuals in this study did not meet the criteria of frailty proposed by Fried et al,[1] the physical impairment in the frailty group may have been relatively mild.

Conclusions

Frail patients who participated in Phase II CR showed improvements in physical function. However, no significant improvement was observed in their anxiety levels, suggesting the importance of a multidisciplinary program including psychological interventions for frail patients.

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Disclosures

T.A., H.D. are members of *Circulation Reports*' Editorial Team. The remaining authors have no conflicts of interest to declare.

IRB Information

The study protocol was approved by Juntendo Hospital Ethics Committee (No. 13-058) and the ethics committees of participating institutions.

Data Availability

The datasets will not be publicly available because patient consent at Juntendo Hospital does not allow for such publication. The corresponding author will respond to inquiries regarding data analyses.

References

1. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al. Frailty in older adults: Evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001; **56:** M146–M156.
2. Arai H, Satake S. English translation of the Kihon Checklist. *Geriatr Gerontol Int* 2015; **15:** 518–519.
3. Cacciatore F, Abete P, Mazzella F, Viati L, Della Morte D, D'Ambrosio D, et al. Frailty predicts long-term mortality in elderly subjects with chronic heart failure. *Eur J Clin Invest* 2005; **35:** 723–730.
4. Boxer R, Kleppinger A, Ahmad A, Annis K, Hager D, Kenny A. The 6-minute walk is associated with frailty and predicts mortality in older adults with heart failure. *Congest Heart Fail* 2010; **16:** 208–213.
5. Makizako H, Shimada H, Doi T, Yoshida D, Anan Y, Tsutsumimoto K, et al. Physical frailty predicts incident depressive symptoms in elderly people: Prospective findings from the Obu study of health promotion for the elderly. *J Am Med Dir Assoc* 2015; **16:** 194–199.
6. Kulmala J, Nykänen I, Mänty M, Hartikainen S. Association between frailty and dementia: A population-based study. *Gerontology* 2014; **60:** 16–21.
7. Hiriscau EI, Bodolea C. The role of depression and anxiety in frail patients with heart failure. *Diseases* 2019; **7:** 45.
8. Honzawa A, Nishitani-Yokoyama M, Shimada K, Kunimoto M, Yamada M, Matsubara T, et al. Relationship between Kihon Checklist score and anxiety levels in elderly patients undergoing early Phase II cardiac rehabilitation. *Cardiol Res* 2020; **11:** 405–411.
9. Leon AS, Franklin BA, Costa F, Balady GJ, Berra KA, Stewart KJ, et al. Cardiac rehabilitation and secondary prevention of coronary heart disease: An American Heart Association scientific statement from the Council on Clinical Cardiology (Subcommittee on Exercise, Cardiac Rehabilitation, and Prevention) and the Council on Nutrition, Physical Activity, and Metabolism (Subcommittee on Physical Activity), in collaboration with the American Association of Cardiovascular and Pulmonary Rehabilitation. *Circulation* 2005; **111:** 369–376.
10. Nishitani-Yokoyama M, Miyauchi K, Shimada K, Yokoyama T, Ouchi S, Aikawa T, et al. Impact of physical activity on coronary plaque volume and components in acute coronary syndrome patients after early Phase II cardiac rehabilitation. *Circ J* 2018; **83:** 101–109.
11. Linden W, Stossel C, Maurice J. Psychosocial interventions for patients with coronary artery disease: A meta-analysis. *Arch Intern Med* 1996; **156:** 745–752.
12. Nishitani-Yokoyama M, Miyauchi K, Shimada K, Miyazaki T,

Ogita M, Okazaki S, et al. Effects of Phase II comprehensive cardiac rehabilitation on coronary plaque volume after acute coronary syndrome. *Int Heart J* 2015; **56:** 597–604.
13. Sugita Y, Miyazaki T, Shimada K, Shimizu M, Kunimoto M, Ouchi S, et al. Correlation of nutritional indices on admission to the coronary intensive care unit with the development of delirium. *Nutrients* 2018; **10:** 1712.
14. Satake S, Senda K, Hong YJ, Miura H, Endo H, Sakurai T, et al. Validity of the Kihon Checklist for assessing frailty status. *Geriatr Gerontol Int* 2016; **16:** 709–715.
15. Spielberger CD, Gorsuch RL, Lushene RE. Manual of the State Trait Anxiety Inventory. Palo Alto: Consulting Psychologists Press, 1983.
16. Hidano T, Fukuhara M, Iwawaki S, Soga S, Spielberger CD. State Trait Anxiety Inventory (Form JYZ) test manual. Tokyo: Jitsumu Kyoiku Shuppan, 2000.
17. Nishitani M, Shimada K, Masaki M, Sunayama S, Kume A, Fukao K, et al. Effect of cardiac rehabilitation on muscle mass, muscle strength, and exercise tolerance in diabetic patients after coronary artery bypass grafting. *J Cardiol* 2013; **61:** 216–221.
18. Nohara R, Adachi H, Goto Y, Hasegawa E, Ishihara S, Itoh H, et al; JCS Joint Working Group. Guidelines for cardiac rehabilitation in patients with cardiovascular disease (JCS2012). http://www.j-circ.or.jp/guideline/pdf/JCS2012_nohara_h.pdf (accessed March 25, 2000).
19. Witham MD, Gray JM, Argo IS, Johnston DW, Struthers AD, McMurdo ME. Effect of a seated exercise program to improve physical function and health status in frail patients >or=70 years of age with heart failure. *Am J Cardiol* 2005; **95:** 1120–1124.
20. Uehara A, Obata H, Watanabe H, Izumi Y, Suzuki Y, Izumi T. The baseline speed of 10-m gait predicts ambulatory discharge for hospitalized frail elderly after DOPPO rehabilitation. *Int J Rehabil Res* 2018; **41:** 331–336.
21. Molino-Lova R, Pasquini G, Vannetti F, Paperini A, Forconi T, Polcaro P, et al. Effects of a structured physical activity intervention on measures of physical performance in frail elderly patients after cardiac rehabilitation: A pilot study with 1-year follow-up. *Intern Emerg Med* 2013; **8:** 581–589.
22. Ushijima A, Morita N, Hama T, Yamamoto A, Yoshimachi F, Ikari Y, et al. Effects of cardiac rehabilitation on physical function and exercise capacity in elderly cardiovascular patients with frailty. *J Cardiol* 2021; **77:** 424–431.
23. Matsue Y, Kamiya K, Saito H, Saito K, Ogasahara Y, Maekawa E, et al. Prevalence and prognostic impact of the coexistence of multiple frailty domains in elderly patients with heart failure: The FRAGILE-HF cohort study. *Eur J Heart Fail* 2020; **22:** 2112–2119.
24. Petruzzello SJ, Landers DM, Hatfield BD, Kubitz KA, Salazar W. A meta-analysis on the anxiety-reducing effects of acute and chronic exercise. Outcomes and mechanisms. *Sports Med* 1991; **11:** 143–182.
25. Dziubek W, Pawlaczyk W, Stefańska M, Waligóra J, Bujnowska-Fedak M, Kowalska J. Evaluation of psychophysical factors in individuals with frailty syndrome following a 3-month controlled physical activity program. *Int J Environ Res Public Health* 2020; **17:** 7804.
26. Szczepanska-Gieracha J, Morka J, Kowalska J, Kustrzycki W, Rymaszewska J. The role of depressive and anxiety symptoms in the evaluation of cardiac rehabilitation efficacy after coronary artery bypass grafting surgery. *Eur J Cardiothorac Surg* 2012; **42:** e108–e114.
27. Gill TM, Baker DI, Gottschalk M, Peduzzi PN, Allore H, Byers A. A program to prevent functional decline in physically frail, elderly persons who live at home. *N Engl J Med* 2002; **347:** 1068–1074.
28. Kamiya K, Sato Y, Takahashi T, Tsuchihashi-Makaya M, Kotooka N, Ikegame T, et al. Multidisciplinary cardiac rehabilitation and long-term prognosis in patients with heart failure. *Circ Heart Fail* 2020; **13:** e006798.
29. Dedeyne L, Deschodt M, Verschueren S, Tournoy J, Gielen E. Effects of multi-domain interventions in (pre)frail elderly on frailty, functional, and cognitive status: A systematic review. *Clin Interv Aging* 2017; **12:** 873–896.
30. Cameron ID, Fairhall N, Langron C, Lockwood K, Monaghan N, Aggar C, et al. A multifactorial interdisciplinary intervention reduces frailty in older people: Randomized trial. *BMC Med* 2013; **11:** 65.
31. Yoshizawa Y, Tanaka T, Takahashi K, Fujisaki M, Iijima K. The associations of frailty with regular participation in physical, cultural, and community social activities among independent elders in Japan. *Nihon Koshu Eisei Zasshi* 2019; **66:** 306–316 (in Japanese).
32. Guzelhan Y, Conkbayir C, Ugurlucan M, Yildiz CE, Alpagut U, Bozbuga N. Gender difference in patients with anxiety after coronary after bypass surgery. *Heart Surg Forum* 2018; **21:** E165–E169.