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
Cardiac Rehabilitation and Anxiety Levels

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. 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. 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.

KCL
The KCL is a 25-item self-administered 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. 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. The questions on the KCL require a simple “yes” or “no” answer, and are scored as 1 or 0 points, respectively.

Anxiety Levels
Anxiety levels were evaluated using a self-administered STAI form. This form is an inventory consisting of 40 state-
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...
Cardiac Rehabilitation and Anxiety Levels

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

| Table 2. KCL Scores at the Beginning of Phase II CR in the Non-Frail, Pre-Frail, and Frail Groups |
|----------------------------------------|-----------------|-----------------|-----------------|-----------------|
| KCL items                | Non-frail (n=63) | Pre-frail (n=40) | Frail (n=34) | P value |
| 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.

Results

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 X² 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).
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 m and 349±78 m 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 m (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±2, 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. 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. 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. 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.

CR has been shown to improve physical function, anxiety, depression, and quality of life. 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. 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. Furthermore, patients who had severe anxiety at the beginning of CR remained anxious after a 3-week CR program. 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. 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. 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. 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.

For frail patients, it may be necessary to implement a comprehensive and long-term CR program with multidisciplinary interventions. 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. 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., 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.

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