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Effects of exercise intensity on nutritional status, body composition, and energy balance in patients with COPD: a randomized controlled trial

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Abstract

Background High-intensity exercise is recommended for the pulmonary rehabilitation of patients with chronic obstructive pulmonary disease (COPD); however, it can cause an energy imbalance due to increased energy expenditure. Here, we aimed to explore the effect of reducing exercise intensity on energy balance in patients with COPD experiencing high-intensity training-induced weight loss.

Methods All participants underwent high-intensity endurance and resistance training for a 2-week preliminary period. Those who lost more than 1% of their weight were then randomized to either continue high-intensity exercise (AA group) or switch to low-intensity exercise (AB group) for another 2 weeks (experimental period).

Results The analysis included 30 participants (AA, $n=15$; AB, $n=15$). The AA group showed significant increases in body composition, dietary intake, nutritional status, muscle strength, and exercise capacity at week 4 than at week 2, with no significant changes in the AB group. After the experimental period, a greater proportion of the AA group had energy intake exceeding expenditure than did the AB group (80% vs. 40%).

Conclusions In patients with COPD who lost body weight during pulmonary rehabilitation with high-intensity exercise, continuing this exercise had a more positive effect on body composition, nutritional status, physical function, and energy balance than did reducing exercise intensity. These results suggest the importance of continuing high-intensity exercise, while taking into consideration energy intake and nutritional therapy, even when body weight loss occurs during pulmonary rehabilitation in patients with COPD.

Trial registration This study was retrospectively registered on the UMIN-CTR as UMIN000050976 on May 5, 2023.

Keywords Chronic obstructive pulmonary disease, Exercise therapy, Nutritional status, Weight loss

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Background

Chronic obstructive pulmonary disease (COPD) is a leading cause of death worldwide and is characterized by persistent airflow limitation and systemic inflammation. According to the Global Initiative for Chronic Obstructive Lung Disease (GOLD), an international guideline for COPD, 30–60% of hospitalized patients with COPD are considered malnourished, and 50% of patients are below 90% of their ideal weight [1]. Low body weight is a prognostic factor that is independent of COPD severity [2]. Moreover, malnourished patients with COPD are reported to have higher healthcare costs than non-malnourished patients with COPD, owing to more frequent hospitalizations for acute exacerbations and longer hospital stays [3]. Therefore, preventing weight loss in patients with COPD is important for disease management and healthcare economics.

Pulmonary rehabilitation, consisting of exercise training, education, and self-management interventions aimed at behavior change, is the most effective therapeutic intervention for reducing dyspnea, improving physical performance, and improving quality of life [1]. Exercise training is the cornerstone of pulmonary rehabilitation, which requires energy intake to exceed energy expenditure for effective exercise training [4]. However, patients with COPD show lower dietary intake than healthy participants [2], and resting energy expenditure increases to approximately 140% of the predicted values in underweight patients with COPD [3, 4]. Thus, the energy balance is expected to be skewed toward consumption in patients with COPD and weight loss. Patients with COPD with a low body weight show poor responsiveness to pulmonary rehabilitation [5]. Consequently, health care providers should consider maintaining positive energy balance during pulmonary rehabilitation in these populations.

High-intensity exercise is recommended for the pulmonary rehabilitation of COPD because it is more effective [6]. However, high-intensity exercise may cause an energy imbalance because it increases energy expenditure [7], which can lead to weight loss during pulmonary rehabilitation. Thus, it is necessary to consider adding interventions to correct energy imbalance in patients who lose body weight during pulmonary rehabilitation with high-intensity exercise. Several studies have shown the positive effects of nutritional supplements on increasing energy intake during pulmonary rehabilitation in patients with COPD [8]. However, no studies have focused on reducing energy expenditure by adjusting exercise intensity (i.e., mitigating exercise intensity) during pulmonary rehabilitation to regulate energy imbalance. This study aimed to investigate the effects of reducing exercise intensity on nutritional status, body composition, and energy balance in patients with COPD who had lost body weight with high-intensity exercise training. We hypothesized that reducing exercise intensity would correct the energy balance of patients with COPD who lost body weight during pulmonary rehabilitation, prevent weight loss, and enhance the effect of pulmonary rehabilitation.

Participants and methods

Participants

Patients with stable COPD without acute exacerbations for the past 4 weeks who were admitted to receive an educational and/or pulmonary rehabilitation program at the Kirigaoka Tsuda Hospital, Japan from December 2017 to August 2021 were recruited. COPD was diagnosed according to the Japanese Respiratory Society COPD guidelines [9]. Participants were included if they had no significant diseases that limited the evaluation of pulmonary rehabilitation (i.e., cerebrovascular, musculoskeletal, or cardiovascular diseases, malignancy, or cognitive dysfunction), no dietary restrictions, and a body mass index (BMI) < 25 kg/m^2. In addition, participants who did not consent, were not able to complete the 4 weeks of pulmonary rehabilitation, or had not lost at least 1% of their body weight during the 2-week preliminary period were excluded.

Ethics, consent and permissions

The study was reviewed and approved by the Ethics Committee of Kibi International University (IRB number: 17–69) and performed in accordance with the Declaration of Helsinki. All the participants provided written, informed consent. This study was retrospectively registered on the UMIN-CTR (https://center6.umin.ac.jp/cgi-bin/ctr/ctr_reg_rec.cgi) as UMIN000050976 on May 5, 2023.

Study design and protocol

This was a randomized controlled trial with an AB design conducted in accordance with the CONSORT statement (Additional file 1). Participants who met the inclusion criteria were enrolled in the study within 3 days of admission. The study consisted of a 4-week inpatient pulmonary rehabilitation period, including a 2-week preliminary and a subsequent 2-week experimental period (Fig. 1). All participants underwent high-intensity endurance and resistance training during the initial 2-week preliminary period. Once the preliminary period was completed, participants who lost more than 1% of their weight were included for an additional 2-week period (the experimental period). In the subsequent 2-week experimental period, eligible participants

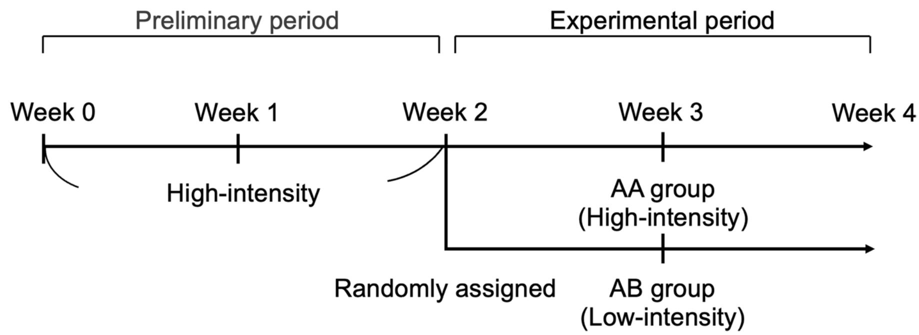

Fig. 1 Overview of the 4-week pulmonary rehabilitation period

Table 1 Time schedule for the evaluation

	W0	W1	W2	W3	W4
Body composition*1	○	○	○	○	○
Pulmonary function	○	—	—	—	—
Biochemical tests	○	—	—	—	○
6MWT	○	—	○	—	○
Muscle strength	○	—	○	—	○
mMRC	○	—	○	—	○
HR-QOL	○	—	○	—	○
Anxiety and depression	○	—	○	—	○
Energy expenditure*2	→	→	→	→	→
Dietary intake*2	→	→	→	→	→

*1Height was assessed only during the initial evaluation

*2Energy expenditure and dietary intake were recorded daily

W0 week 0, *W1* week 1, *W2* week 2, *W3* week 3, *W4* week 4, *HR-QOL* health-related quality of life, *mMRC* modified Medical Research Council dyspnea scale, *6 MWT* 6-minute walk test were randomized to maintain high-intensity exercise (AA group) or adjust to low-intensity exercise (AB group). The amount of food served during pulmonary rehabilitation (i.e., both preliminary and experimental periods) was calculated based on the predicted energy expenditure for COPD and provided in amounts not less than the predicted daily energy consumption of COPD [10]. The dietitians interviewed the patients as needed to change their dietary intake upon request.

Randomization

A random number table was created using JMP 15.0 (SAS Institute, Cary, NC, USA), and the participants were simply randomized 1:1 to the AA and AB groups based on the random number table. Allocations were made by those unrelated to the experiment. The experimenters and participants were aware of the study groups to which they were assigned.

Data collection

Eligible participants underwent the following assessments at week 0 (beginning of the preliminary period), week 2 (beginning of the experimental period), and week 4 (post-intervention). Details of the time schedule are presented in Table 1.

Study outcomes

Primary outcome

The primary outcome measure was BMI.

Secondary outcomes

Pulmonary function and computed tomography Pulmonary function was assessed by spirometry (CHESTGRAPH Jr. HI-101; CHEST, Tokyo, Japan) in accordance with published guidelines [11]. The severity of emphysema was assessed by three-dimensional computed tomography analysis and is indicated as the percentage (%) of low attenuation area to the lung field cross-sectional area [12].

Dyspnea, health-related quality of life, anxiety, and depression The effect of dyspnea on daily activities was assessed using the modified Medical Research Council (mMRC) dyspnea scale. Health-related quality of life (HR-QOL) was assessed using the COPD Assessment Test (CAT) [13]. Anxiety and depression were assessed using the Hospital Anxiety and Depression Scale (HADS) [14].

Functional exercise capacity and muscle strength A 6-min walk test (6MWT) was conducted according to the European Respiratory Society /American Thoracic Society technical standard [15] with the distance walked (6MWD) used as the measure of functional exercise capacity. Quadriceps muscle strength (QMS) was measured in the sitting position with the knee flexed 90º using a hand-held dynamometer with a fixing belt (ANIMA, μ-Tas, Japan). [16], which has been validated in COPD [17].

Body composition, nutritional features, and blood tests Body fat mass was measured using bioelectrical impedance analysis [18] and corrected for height to calculate the fat mass index (FMI), expressed in kg/m^2 (InBody 270, InBody Japan, Tokyo). Fat-free mass (FFM) was calculated by subtracting the amount of fat mass from the body weight. The FFM was corrected for height to produce the fat-free mass index (FFMI), which is expressed in kg/m^2. All participants refrained from eating or drinking 4 h prior to testing and measurements were taken between 11:30 and 12:00 am [19]. The Geriatric Nutritional Risk Index (GNRI) [20] was calculated using body weight and albumin levels. Controlling Nutritional Status (CONUT) [21] calculated from albumin, total cholesterol, and lymphocyte counts, was used. In addition, serum albumin as an indicator of nutritional status and C-reactive protein (CRP) as a marker of inflammation were evaluated.

Dietary intake and energy expenditure Dietary intake was calculated by visual inspection using a dietary record method [22] to determine the percentage of food consumed from the amount provided. The average value of these data over the 3-day period was used as a measure of dietary intake. Meals served no less than the energy requirement, calculated by multiplying the Harris–Benedict equation by the stress factor and activity coefficient [23]. The provision of meals is done on a daily basis and takes into consideration both dietary intake and the balance of nutrients. Daily low fat and high protein meals were planned by dietitians based on the dietary reference intake for Japanese and in consideration of COPD [24]. Snacks were consumed freely and were included in the intake calculations. Daily meal (kcal/day) servings were increased through a multidisciplinary conference if participants wished to have more.

Energy expenditure was assessed using a uniaxial accelerometer (SUZUKEN, Lifecorder®, Japan), which has been validated in COPD [25]. Participants were instructed to wear the accelerometers over 7 consecutive days, and the average values of the 7-day period were recorded [25]. Energy expenditure calculated by the accelerometer did not consider metabolic stress from respiratory diseases in the basal metabolic rate; therefore, it was adjusted by metabolic stress for Harris–Benedict. The metabolic stress in COPD was calculated to be 1.3 [4]. Although energy expenditure during resistance training was not measured, the energy expenditure of resistance training (energy expenditure [kcal] = metabolic equivalents [METs] × body weight [kg] × time [h] × 1.05) was added to the energy expenditure obtained from the accelerometer to record the total energy expenditure for the day. METs were used to calculate energy expenditure during resistance training [26]. At 70% of one repetition maximum (1RM), 3.5 METs were used, and at 40%, 2.4 METs were used [27]. Energy intake minus expenditure was defined as the energy balance (*energy intake – energy expenditure*).

Pulmonary rehabilitation program

The pulmonary rehabilitation program consisted of endurance training, resistance training, self-management education, nutritional management, and psychosocial support provided by physicians, physical therapists, nurses, dietitians, medical social workers, and clinical psychologists for 4 weeks. Exercises were performed under the supervision of a physical therapist with individualized goal settings and repeated feedback. All exercises were performed at the pulmonary rehabilitation center of the Kirigaoka Tsuda Hospital. During the preliminary period, all participants underwent endurance training with 20 min of treadmill (SportsArt Fitness, T652 TREADMILL, Japan) walking at 70% intensity based on the 6MWD (e.g., walking speed [m/h] = 6 MWD [m] × 10 × 0.7 [15, 28]). Resistance training consisted of trunk flexion and extension, rowing, leg pressing, and leg flexion and extension using machine-based exercises (Platz, Rest Rehabilitation, Japan). Resistance training consisted of 10–15 repetitions at a 70% intensity of 1RM [29]. 1RM was assessed as the maximum amount a participant could lift in one movement cycle of the exercise under the physical therapist's supervision. Exercise intensity started at 70% intensity for all participants for both endurance and resistance training. The AA group continued the same intensity of endurance and resistance training as in the preliminary period during the experimental period, whereas the AB group decreased exercise intensity to 40% of walking speed during the 6MWT and 40% of 1RM. The exercise frequency was two sessions per day and 6 days per week in both groups. Breaks were taken as needed to accommodate dyspnea and fatigue, and some exercised in the AM and PM if it was difficult to exercise continuously. Participants who completed at least 80% of the sessions in this study were considered to have completed the program.

Sample size

The sample size was calculated using G*Power with a Wilcoxon-signed rank test, effect size of 0.83, alpha of 0.05, and power of 0.90 based on previous studies in which pulmonary rehabilitation increased BMI [6]. The required sample size was 30 (15 patients in each group), and the 1% weight loss rate after the start of exercise was 40% for COPD admitted to our hospital for pulmonary rehabilitation in the past year. The dropout rate was set at 20%, for a total sample size of 93.

Statistical analyses

Continuous variables are presented as medians and 25–75% percentiles. Categorical variables are expressed as frequencies and percentages. Baseline characteristics between the AA and AB groups were compared using the Mann–Whitney U test. BMI, body composition, mMRC, HR-QOL, HADS, dietary intake, 6MWD, and QMS were compared between weeks 2 and 4 using a Wilcoxon signed-rank test. Nutritional assessments and CRP levels were compared between weeks 0 and 4 using the Wilcoxon signed-rank test. The Mann–Whitney U test was used to compare the changes before and after intervention between the AA and AB groups. Furthermore, the chi-square test was used to compare the number of participants in the AA and AB groups whose energy intake exceeded expenditure at weeks 0, 2, and 4. The extent of the of between weeks 2 and 4 differences were reported as effect size; in the Wilcoxon signed-rank test, effect size r was calculated as $z/\sqrt{N}$ [30].

Statistical significance was defined as $p < 0.05$. All statistical analyses were conducted using JMP 15.0 (SAS Institute, Cary, NC, USA).

Results

Participants and baseline characteristics

Figure 2 shows a flowchart of the selection of the study participants. Of the 93 participants, 56 were excluded (body weight did not decrease by more than 1% [$n = 53$], consent was not obtained [$n = 2$], and exercise was no longer possible owing to a fall [$n = 1$]) during the preliminary period. Three participants withdrew their consent at the time of allocation. Two participants, each from the AA and AB groups, were excluded during the experimental period because of acute exacerbations. All other participants were able to perform endurance and strength training according to the protocol and completed pulmonary rehabilitation with an attendance rate of > 80%. No adverse events attributable to exercise were observed in this study. Finally, 30 participants were included in the analysis (AA [$n = 15$] and AB [$n = 15$]). Participant characteristics at baseline did not differ significantly between the two groups. (Table 2).

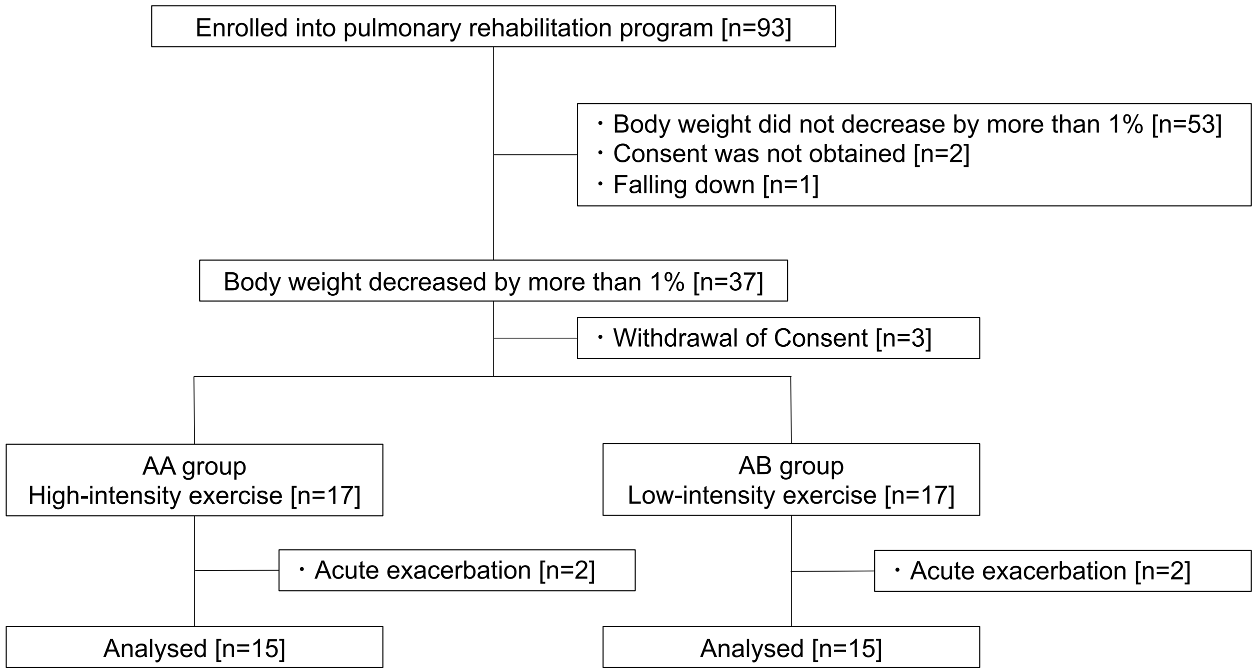

Fig. 2 Consolidate standards of reporting trials (CONSORT) flow diagram of the trial design

Primary outcome

The degree of change in BMI between weeks 2 and 4 was significantly higher in the AA group than in the AB group (0.8 [0.7–1.2] vs. 0.0 [−0.3–0.4], $p<0.001$) (Table 3). Regarding within-group change, the AA group had significantly higher BMI at week 4 than at week 2, whereas the AB groups showed no significant changes (AA group: 20.1 [18.7–22.4] vs. 20.5 [19.2–22.6], $p<0.001$; AB group: 19.5 [18.6–21.1] vs. 19.5 [18.7–21.0], $p=0.850$).

Secondary outcomes

Dyspnea, health-related quality of life, anxiety, and depression

The mMRC and HADS scores showed no significant changes between weeks 4 and 2 in either group AA or AB. mMRC and HADS score changes as measured before and after the experimental period, also showed no significant differences between the AA and AB groups (Table 3). The AB group showed a significant worsening of the CAT scores between weeks 2 and 4, whereas the AA group showed no change (AB group: 13 [12–19] vs. 16 [13–20], $p=0.039$; AA group: 16 [13–21] vs. 14 [9–21], $p=0.148$). The extent of change between weeks 2 and 4 was significantly higher in the AA group than in the AB group (−2 [−3–0] vs. 0 [0–3], $p=0.009$).

Functional exercise capacity and muscle strength

The 6MWD (360 [329–378] vs. 375 [352–417], $p<0.001$) and QMS (29 [24–35] vs. 31 [27–36], $p=0.002$) scores were significantly improved in the AA group, whereas no significant differences were observed in the AB group (Table 3). The extent of change between weeks 2 and 4 was also significantly higher in the AA group than in the AB group (20 [15–28] vs. −2 [−17–7], $p<0.001$).

Body composition, nutritional features, and blood tests

The AA group showed significantly higher FMI and FFMI scores at week 4 than at week 2, whereas the AB group showed no significant changes in these scores. Dietary intake increased significantly in the AA group (1800 [1775–1945] vs. 1900 [1800–2008], $p=0.049$) but not in the AB group. The change in FFMI between weeks 2 and 4 was also significantly higher in the AA group than in the AB group (0.19 [0.08–0.36] vs. −0.04 [−0.08–0.00], $p<0.001$) (Table 3). The CONUT improved significantly in the AA group (2 [1–3] vs. 0 [0–2], $p=0.004$) but remained the same as the baseline in the AB group (1 [0–3] vs. 0 [0–1], $p=0.766$). The AA group showed significantly higher improvement than the AB group (−1 [−2–0] vs. 0 [0–0.5], $p=0.008$). Albumin (4.0 [3.7–4.2] vs. 4.0 [3.9–4.3], $p=0.056$) and GNRI (97.1 [91.3–103.0]

Table 2 Characteristics of participants in the AA and AB groups

	Total (*n* = 30)	**AA group (*n* = 15)**	**AB group (*n* = 15)**	***p*-value**
Age, years	75.5 [72.0-82.3]	76.0 [72.5-81.0]	75.0 [71.5-84.0]	0.884
Sex, male	25 (83)	13 (87)	12 (80)	
Body composition				
Body weight, kg	53.4 [46.8-57.2]	54.5 [50-58.1]	49.0 [43.5-56.8]	0.305
BMI, kg/m^2	20.5 [19.0-21.7]	20.6 [19.0-22.7]	19.7 [18.9-21.6]	0.561
FMI, kg/m^2	5.2 [4.6-6.7]	5.2 [4.6-6.3]	5.9 [4.3-7.0]	0.740
FFMI, kg/m^2	14.7 [13.2-15.6]	15.4 [14.3-16.0]	14.5 [13.0-15.5]	0.300
Nutritional features				
Albumin, g/dL	4.0 [3.6-4.1]	4.0 [3.7-4.2]	4.0 [3.7-4.1]	0.917
GNRI	96.8 [91.2-102.5]	97.1 [91.3-103.0]	96.7 [90.8-100.0]	0.648
CONUT	2 [1-2]	2 [1-3]	1 [1-2]	0.166
Dietary intake, kcal	1625 [1494-1835]	1800 [1624-1840]	1533 [1366-1715]	0.101
Energy expenditure, kcal	1782 [1609-1901]	1820 [1740-1929]	1665 [1509-1821]	0.056
Physical function				
6MWD, m	318 [286-349]	323 [304-344]	309 [255-355]	0.590
QMS, kgf	24 [20-31]	26 [22-32]	21 [15-29]	0.067
Pulmonary function				
FEV_1, L	1.15 [0.84-1.69]	1.20 [0.90-1.65]	1.10 [0.81-1.68]	0.981
FEV_1, % predicted	53.5 [36.5-75.2]	57.4 [35.4-74.2]	53.5 [38.4-77.4]	0.751
FEV_1/FVC, %	53.1 [42.2-68.2]	54.0 [45.7-63.5]	52.1 [41.6-76.1]	1.000
Dyspnea, anxiety, depression and HRQOL				
mMRC, 0/1/2/3/4	0/6/11/8/5	0/3/6/4/2	0/3/5/4/3	0.364
HADS anxiety	7 [4-8]	7 [4-7]	6 [4-10]	0.530
HADS depression	7 [5-10]	7 [6-10]	9 [5-11]	0.617
CAT	17 [13-20]	17 [15-22]	15 [13-18]	0.360
Blood test				
CRP, mg/dL	0.11 [0.05-0.30]	0.20 [0.09-0.30]	0.07 [0.04-0.23]	0.229
Computed tomography				
LAA, %	28.9 [16.9-42.7]	28.3 [13.3-43.6]	29.50 [17.1-40.1]	1.000

The data are presented as medians and 25–75% percentiles or n (%)

BMI body mass index, *CAT* COPD Assessment Test, *CONUT* Controlling Nutritional Status, *CRP* C-reactive protein, *FEV_1* forced expiratory volume in 1 s, *FFMI* fat-free mass index, *FMI* fat mass index, *FVC* forced vital capacity, *GNRI* Geriatric Nutritional Risk Index, *HADS* Hospital Anxiety and Depression Scale, *HR-QOL* health-related quality of life, *LAA* low attenuation area, *mMRC* modified Medical Research Council dyspnea scale, *QMS* quadriceps muscle strength, *6 MWD* 6-minute walk distance

vs. 101.3 [94.9–103.1], $p = 0.073$) showed improvement trends in the AA group but did not in the AB group (Table 4). When comparing the changes before and after the experimental period, albumin level (0.2 [0.0–0.3] vs. −0.1 [−0.4–0.2], $p = 0.041$) and GNRI (3.2 [0.1–4.8] vs. −1.2 [−5.5–1.0], $p = 0.023$) also showed significant higher improvement in the AA group. CRP levels were significantly lower in the AA group at week 4 than at week 0; however, they showed no statistical significance in the AB group (AA group: 0.20 [0.09–0.30] vs. 0.10 [0.03–0.14], $p = 0.004$; AB group: 0.07 [0.04–0.23] vs. 0.09 [0.07–0.21], $p = 0.680$). A comparison between the two groups before and after the experimental period also showed significantly higher improvement in the AA group than in the AB group (−0.07 [−0.15–0.02] vs. 0.00 [−002–0.06], $p = 0.023$) (Tables 3 and 4).

Dietary intake and energy expenditure

Figure 3 shows that the balance between energy expenditure and energy intake changed during the study period. Energy expenditure exceeded energy intake during the preliminary period in both AA and AB groups. However, during the experimental period, energy intake exceeded expenditure in the AA group, whereas the AB group showed inconsistent results. The AB group showed inconsistent energy balance results with an approximately equal number of participants showing negative, positive, and unchanged values. Figure 4 shows the proportion of participants whose energy intake exceeded expenditure during

Table 3 Comparison of body composition, nutritional features, physical function, dyspnea, and HR-QOL

	AA group ($n = 15$)					
	W2	**W4**	**change[a]**	**ES**	***p*-value[b]**	
Body composition						
Body weight, kg	53.9 [49.5 - 57.9]	54.7 [50.8 - 58.5]	0.8 [0.7 - 1.2]	0.84	<0.001	
BMI, kg/m^2	20.1 [18.7 - 22.4]	20.5 [19.2 - 22.6]	0.30 [0.25 - 0.45]	0.84	<0.001	
FMI, kg/m^2	4.6 [4.3 - 5.7]	4.8 [4.4 - 5.8]	0.11 [-0.02 - 0.35]	0.59	0.019	
FFMI, kg/m^2	15.4 [14.4 - 16.5]	15.7 [14.8 - 16.5]	0.19 [0.08 - 0.36]	0.66	0.009	
Nutritional features						
Dietary intake, kcal	1800 [1775 - 1945]	1900 [1800 - 2008]	25 [-16 - 83]	0.51	0.049	
Energy expenditure, kcal	1850 [1740 - 1954]	1865 [1777 - 1977]	13 [-9 - 51]	0.46	0.083	
Physical function						
6MWD, m	360 [329 - 378]	375 [352 - 417]	20 [15 - 28]	0.85	<0.001	
QMS, kgf	29 [24 - 35]	31 [27 -36]	2 [1 - 3]	0.81	0.002	
Dyspnea, anxiety, depression and HRQOL						
mMRC, 0/1/2/3/4	0/3/6/4/2	0/4/5/5/1	0 [0 - 0]	0.37	0.500	
HADS anxiety	4 [3 - 7]	4 [2 - 7]	0 [-2 - 2]	0.01	1.000	
HADS depression	7 [4 - 9]	7 [4 - 8]	0 [-1 - 0]	0.17	0.594	
CAT	16 [13 - 21]	14 [9 - 21]	-2 [-3 - 0]	0.04	0.148	
	AB group ($n = 15$)					
	W2	**W4**	**change[a]**	**ES**	***p*-value[b]**	***p*-value[c]**
Body composition						
Body weight, kg	47.9 [43.5 - 55.9]	48.0 [43.2 - 55.4]	0.0 [-0.3 - 0.4]	0.06	0.814	<0.001
BMI, kg/m^2	19.5 [18.6 - 21.1]	19.5 [18.7 - 21.0]	0.00 [-0.12 - 0.13]	0.06	0.850	<0.001
FMI, kg/m^2	5.6 [4.3 - 6.8]	5.6 [4.4 - 7.1]	0.03 [0.00 -0.16]	0.32	0.240	0.345
FFMI, kg/m^2	14.7 [12.7 - 15.3]	14.7 [12.8 - 15.3]	-0.04 [-0.08 - 0.00]	0.30	0.266	<0.001
Nutritional features						
Dietary intake, kcal	1607 [1552 - 1873]	1600 [1548 - 1888]	-7 [-47 -18]	0.25	0.347	0.035
Energy expenditure, kcal	1582 [1549 - 1853]	1591 [1525 - 1795]	5 [-25 - 21]	0.03	0.923	0.126
Physical function						
6MWD, m	330 [291 - 380]	335 [275 - 380]	-2 [-17 - 7]	0.18	0.498	<0.001
QMS, kgf	25 [18 - 32]	25 [18 -31]	0 [-1 - 0]	0.35	0.181	0.002
Dyspnea, anxiety, depression and HRQOL						
mMRC, 0/1/2/3/4	0/3/5/4/3	0/3/6/4/2	0 [0 - 0]	0.00	1.000	0.539
HADS anxiety	7 [5 - 9]	7 [5 - 10]	0 [0 - 1]	0.20	0.469	0.935
HADS depression	8 [5 - 10]	8 [5 - 11]	0 [0 - 2]	0.16	0.574	0.267
CAT	13 [12 - 19]	16 [13 - 20]	0 [0 - 3]	0.54	0.039	0.009

Data are presented as medians and 25–75% percentiles

W2 week 2, *W4* week 4, *BMI* body mass index, *CAT* COPD assessment test, *ES* effect size, *FFMI* fat-free mass index, *FMI* fat mass index, *HADS* Hospital Anxiety and Depression Scale, *HR-QOL* health-related quality of life, *mMRC* modified Medical Research Council dyspnea scale, *QMS* quadriceps muscle strength, *6MWD* six-minute walk distance

[a] difference between week 2 and week 4, [b]within-group comparison *p*-value, [c]difference in change between the AA and AB groups

the study period. In the preliminary period, fewer participants in both groups had energy intake exceeding expenditure, and there was no significant difference between the two groups (13% in the AA group vs. 27% in the AB group, $p=0.326$). At week 2, the number of participants whose energy intake exceeded expenditure increased but did not differ between the two groups (47% in the AA group vs. 60% in the AB group, $p=0.464$). At week 4, the number of participants whose energy intake exceeded their expenditure was significantly higher in the AA group than in the AB group (80% in the AA group vs. 40% in the AB group, $p=0.025$).

Table 4 Comparison of nutritional features and blood tests

	AA group ($n = 15$)					
	W0	**W4**	**change**[a]	**ES**	***p*-value**[b]	
Nutritional features						
Albumin, g/dL	4.0 [3.7 - 4.2]	4.0 [3.9 - 4.3]	0.2 [0.0 - 0.3]	0.50	0.056	
GNRI	97.1 [91.3 - 103.0]	101.3 [94.9 - 103.1]	3.2 [0.1 - 4.8]	0.47	0.073	
CONUT	2 [1 - 3]	0 [0 - 2]	-1[-2 - 0]	0.69	0.004	
Blood test						
CRP, mg/dL	0.20 [0.09 - 0.30]	0.10 [0.03 - 0.14]	-0.07 [-0.15 - -0.02]	0.71	0.004	
	AB group ($n = 15$)					
	W0	**W4**	**change**[a]	**ES**	***p*-value**[b]	***p*-value**[c]
Nutritional features						
Albumin, g/dL	4.0 [3.7 - 4.1]	3.8 [3.6 - 4.2]	-0.1 [-0.4 - 0.2]	0.26	0.334	0.041
GNRI	96.7 [90.8 - 100.0]	95.1 [87.0 - 99.8]	-1.2 [-5.5 -1.0]	0.34	0.208	0.023
CONUT	1 [0 - 3]	0 [0 - 1]	0 [0 - 0.5]	0.13	0.766	0.008
Blood test						
CRP, mg/dL	0.07 [0.04 - 0.23]	0.09 [0.07 - 0.21]	0.00 [-002 - 0.06]	0.11	0.680	0.015

Data are presented as medians and 25–75% percentiles

W0 week 0, *W4* week 4, *CONUT* Controlling Nutritional Status, *CRP* C-reactive protein, *ES* effect size, *GNRI* Geriatric Nutritional Risk Index

[a] difference between week 2 and week 4, [b]within-group comparison *p*-value, [c]difference in change between the AA and AB groups

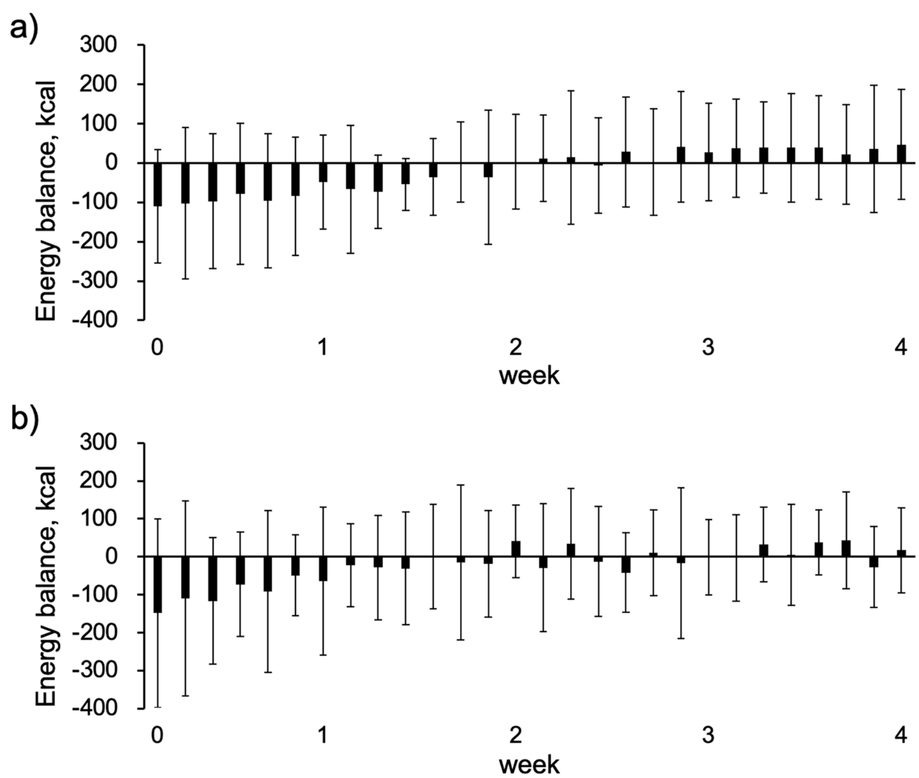

Fig. 3 Transition of energy balance in the AA (**a**) and AB groups (**b**) during the study period. Energy balance is calculated by the equation: *energy intake – energy expenditure*

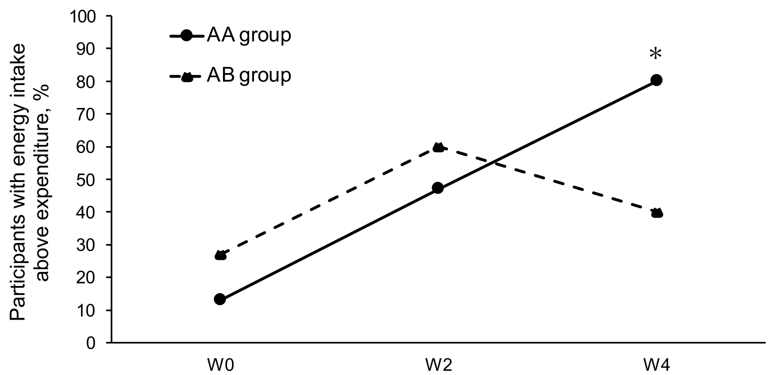

Fig. 4 Percentage of participants whose energy intake exceeded expenditure. Data are presented as percentages. W0, week 0; W2, week 2; W4, week 4; *, $p<0.01$

Discussion

To the best of our knowledge, this is the first study to examine the effect of modifying exercise intensity on nutritional features in patients with COPD who lost body weight during pulmonary rehabilitation. The main findings of this study were as follows: 1) participants who lost body weight in the first 2 weeks could increase their dietary intake and gain weight as they continued their high-intensity training; 2) the high-intensity group completed the study and demonstrated more positive effects of exercise training on body composition, nutritional status, and physical and psychological functions than did the low-intensity exercise group.

The AA group showed improvements in BMI, FMI, and FFMI after pulmonary rehabilitation, whereas the AB group showed no change in these parameters. As a positive correlation between energy balance and body weight has been reported [31], it is reasonable to assume that the changes in BMI, FMI, and FFMI in the AA group resulted from an improved energy balance. These changes are consistent with a previous report that BMI increased more during moderate- and high-intensity exercises than during low-intensity exercise [6]. Considering that FFMI also increases with high-intensity exercise [32], the lack of changes in BMI, FMI, and FFMI in the AB group in this study may be due to insufficient exercise intensity.

Notably, during the 2-week experimental period, dietary intake in the AB group remained the same as that during the preliminary period, whereas it significantly increased in the AA group. Although an increase in dietary intake has been reported after exercise in low-body-weight COPD [5], the present study suggests that dietary intake was particularly improved by high-intensity exercise. With this increased energy intake, the energy balance improved in the AA group but not in the AB group. In addition, since energy expenditure remained unchanged in both groups, increase in energy intake was independent of energy expenditure. Neunhauserer et al. [33] demonstrated that leptin level, an appetite-suppressing hormone, was reduced by exercise training in patients with COPD, especially at high intensities. As dietary intake is negatively correlated with leptin in patients with COPD [34], leptin might have contributed to the increased dietary intake in the AA group. Further studies are required to clarify the effects of appetite-suppressing hormones on dietary intake after pulmonary rehabilitation in patients with COPD.

A significant improvement in the CONUT and a trend toward improvements in GNRI and albumin levels were observed in the AA group but not in the AB group. These results support the idea that an improvement in energy balance contributes to improved nutritional status and body composition. Furthermore, as higher CRP levels are related to higher energy expenditure and lower weight gain [35], it is likely that the reduced CRP levels in the AA group also contributed to improved energy balance and weight gain. Generally, despite a lack of evidence, healthcare providers consider stopping or decreasing the intensity of exercise if patients experience weight loss during exercise [5]. However, our results suggest that continued high-intensity exercise is effective in improving body composition, even if weight loss is observed during exercise training. However, these results were based on appropriate nutritional supplementation.

Notably, the 6MWD and QMS scores in the AA group were significantly improved, even though participants were originally recruited from among those who lost body weight during the preliminary pulmonary rehabilitation period. In contrast, Slinde et al. [5] demonstrated that multidisciplinary pulmonary rehabilitation improved the 6MWD score in normal-weight patients with COPD but not in those who were underweight. However, in that study, exercise training was suspended if participants with COPD lost body weight during pulmonary rehabilitation. Furthermore, the CAT score showed a more positive change in the AA group than in the AB group. These results are consistent with those of a previous report showing that high-intensity exercise improved HR-QOL more than low-intensity exercise did [36]. Taken together, continued high-intensity exercise training with appropriate nutritional supplementation is important for maintaining and improving physical function and HR-QOL, even if weight loss occurs during the initial weeks of pulmonary rehabilitation. However, the CAT score improved more than the minimal clinically important difference (MCID) (2 points [37]), whereas improvements in 6MWD and QMS did not reach the MCID (26 m [38] and 3.3 kgf [39]). This may be attributed to the short experimental period of this study at 2 weeks. Further studies are needed to clarify the reason for the insufficient effect in physical function.

Although the participants in the AB group reduced exercise intensity during the experimental period to decrease energy expenditure, there were no significant changes in energy expenditure in either group. This may be because energy expenditure is related to activities of daily living (i.e., amount of daily physical activity) rather than exercise intensity during pulmonary rehabilitation. Further studies are needed to clarify why energy expenditure did not change in the AB group despite the change to lower exercise intensity.

This study has a few limitations. First, the study was conducted at a single institution; therefore, it is unknown whether the results can be used in a widespread clinical setting. Second, as energy intake was measured using dietary intake as a guide, there may have been errors in energy intake. Third, this study was based only on data from Japanese patients. As Japanese patients with COPD are believed to be more underweight than their Western counterparts [9], it is unknown whether the results of this study can be applied to other countries and ethnic groups. Fourth, the researchers were not blinded to allocation to the AA and AB groups as the type of rehabilitation performed by the participants was visible to all. Fifth, since we calculated exercise intensity from the 6MWT in this study, the intensity of exercise may have been lower than that calculated from maximum oxygen consumption. Another consideration is that because pulmonary rehabilitation was performed for a short duration, its long-term effects are unknown.

Conclusions

This study demonstrated that continued high-intensity exercise improved BMI, FMI, FFMI, 6MWD, QMS, HR-QOL, and CONUT scores in patients with COPD despite decreased body weight during pulmonary rehabilitation. These results underscore the importance of continuing high-intensity exercise even if weight loss occurs during pulmonary rehabilitation in patients with COPD. Further investigations are required to clarify the mechanisms underlying the increase in dietary intake caused by high-intensity exercise.

Abbreviations

BMI	Body mass index
CAT	COPD Assessment Test
CONUT	Controlling Nutritional Status
COPD	Chronic obstructive pulmonary disease
CRP	C-reactive protein
CT	Computed tomography
FFMI	Fat-free mass index
FMI	Fat mass index
GNRI	Geriatric Nutritional Risk Index
GOLD	Global Initiative for Chronic Obstructive Lung Disease
HADS	Hospital Anxiety and Depression Scale
HR-QOL	Health-related quality of life
METs	Metabolic equivalents
mMRC	Modified Medical Research Council dyspnea scale
1RM	One repetition maximum
QMS	Quadriceps muscle strength
6MWD	Six-minute walking distance
6MWT	Six-minute walk test

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12890-024-03448-1.

Supplementary Material 1.

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Author contributions

TI: conceptualization, methodology, formal analysis, investigation, data curation, writing (original draft, review, and editing), management, and coordination responsibility for research activity planning and execution. KS: formal analysis, writing the original draft, writing the review, and editing. KI: resources, writing (original draft, review, and editing). TJ: resources, writing (original draft, review, and editing). TK: resources, writing (original draft, review, and editing). KK: resources, writing (original draft, review, and editing). TT: conceptualization, methodology, resources, writing (original draft, review, and editing), and supervision.

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Data availability

The datasets in this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Kibi International University (IRB number: 17-69) and conducted in accordance with the ethical standards set forth in the 1964 Declaration of Helsinki and subsequent amendments. Written informed consent was obtained from all the participants.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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