Effect of Intradialytic Supine Ergometer Exercise on Hemodialysis Patients with Different Nutritional Status

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ABSTRACT. Objective: It is important for hemodialysis patients to exercise while their nutritional status is being monitored. This study aimed to examine the difference in physical exercise function and the effect of exercise intervention in hemodialysis patients who were divided into two groups (high-nutrition and low-nutrition groups) based on the serum albumin levels.

Method: A total of 26 outpatients (18 men and 8 women) undergoing hemodialysis (age: 66 ± 10 years) were included in this study. The patients’ body composition data (weight, body mass index, percentage of body fat, fat-free mass, and total body water) and physical functions (grip strength, knee extensor strength, open-eyed one-legged standing time, long sitting trunk anteflexion, and 6-minute walking distance [6MWD] test) were measured. The intervention was supine ergometer exercise during hemodialysis, and the patients exercised for 30 minutes during hemodialysis thrice a week. The intervention period was three months.

Results: Compared to the high-nutrition group, the low-nutrition group showed a significant decrease in muscle strength. Furthermore, long sitting trunk anteflexion in the high-nutrition group and 6MWD in the low-nutrition group improved significantly after the intervention.

Conclusion: The result of this study may indicate that 6MD can be improved by exercise during dialysis, regardless of nutritional status. It is said that low nutritional status has a negative impact on survival rate; thus, considering the impact on survival rate, it is hemodialysis patients with a low nutritional status that should be considered to introduce more active exercise during dialysis.

Key words: Intradialytic exercise, Renal rehabilitation, Serum albumin, Muscle strength, 6-minute walking distance

Since the 1990s, the number of dialysis patients in Japan has been increasing in tandem with the number of patients with diabetes. According to a report by the Japanese Society for Dialysis Therapy, there were more dialysis patients aged ≥65 years than those aged ≤64 in 2017. In older patients undergoing hemodialysis, there is a decline in physical function or increased mortality due to sarcopenia and cachexia. The high mortality rate and decreased physical function in dialysis patients can be improved by a variety of exercise programs. Therefore, exercise intervention is important, and it needs to be supported by appropriate nutritional support. Further, serum albumin level, which is an indicator of nutritional status, is negatively affected by inflammation, and the effect is said to be greater in long-term dialysis patients; hence, it is a valuable indicator in hemodialysis patients. Various studies have reported hypoalbuminemia to be a strong predictor of mortality in dialysis patients. Therefore, it is important to maintain a high serum albumin level in hemodialysis patients. In a study of hemodialysis patients by Johansen et al., frailty scores decreased as serum albumin levels increased, and patients whose serum albumin levels increased over time were less likely to...
become frailty\(^8\). Serum albumin levels have a positive impact on frailty scores; thus, further verification of the association between albumin levels and exercise is needed. A systematic review examining the combined effects of exercise and nutrition in healthy older adults found that exercise had a positive effect on muscle strength and muscle mass in many studies and that nutrition had a positive effect in some studies\(^9\). A meta-analysis examining the effects of oral nutritional supplements on muscle fitness of dialysis patients reported that supply of a mixture of macronutrients and an intervention duration of 48 weeks had some effects on increasing lean body mass\(^10\).

As mentioned above, there have been studies that have looked at combined nutrition and exercise interventions, but it is not known whether the original nutritional status affects exercise function or the effectiveness of exercise. If the effect of exercise intervention changes depending on the original nutritional status, then the exercise interventions recommended for hemodialysis patients may change dramatically. In the exercise prescription for dialysis patients, there are various intervention methods such as exercise during dialysis and individual rehabilitation outside of dialysis\(^11\). However, there are still many unanswered questions about the ideal design of the exercise intervention for hemodialysis patients, such as what kind of exercise program should be prescribed and for which patients. The hypothesis of this study is that dialysis patients with higher nutritional status will have higher exercise capacity and will respond better to exercise interventions.

Therefore, the purpose of this study was to determine the difference in physical exercise function and the effect of exercise intervention in hemodialysis patients who were divided into two groups based on the serum albumin levels and to examine the design of exercise prescription as influenced by nutritional status.

### Method

#### Study design and participants

The study design was a controlled before-and-after trial conducted to compare exercise function before and after a 12-week exercise intervention during hemodialysis. The participants were approximately 200 outpatients from two dialysis centers in Ishikawa Prefecture, Japan. We recruited participants by making announcements and distributing flyers in the dialysis center. Finally, 30 participants (20 men and 10 women) aged 67±10 years were included in the study. The sample size was set at 30 patients or more based on previous studies and the number of patients at the study sites. The physical therapists in the study team explained the details of the study and ethics to the participants when they applied for participation. Four participants dropped out after the intervention started, and the final number of participants was 26 (age 66 ±10 years, 18 males and 8 females) (Fig. 1). The four dropouts were due to discontinuation of the exercise intervention due to ill health (1), insufficient number of interventions (1), and death (1). Twenty-six eligible participants were divided into two groups: a high nutrition group (HN group) with a serum al-
bumin level of 3.6 g/dl or higher and a low nutrition group (LN group) with a serum albumin level of less than 3.6 g/dl. This study was started after confirming that the participants had no serious complications prior to the study and after obtaining permission for exercise intervention from their physicians. The study was conducted in compliance with the principles of the Declaration of Helsinki and was approved by the Research Ethics Committee of Mizuho Medical Corporation (approval No. 6).

**Physical therapy assessment**

The participants’ body composition data were measured as the basic information. The body composition data included weight, body mass index (BMI), percentage of body fat (%BF), fat-free mass (FFM), and total body water (TBW). These were measured using a body fat analyzer (TB-310, Tanita Corporation, Tokyo, Japan). Serum albumin levels were collected from the medical records as an indicator of nutritional status. The participants’ physical functions (grip strength, knee extensor strength (KES), open-eyed one-legged standing time, long sitting trunk anteflexion, and 6-minute walking distance [6MD] test) were measured before and after the intervention. All measurements were taken by more than one physical therapist. The measurement method was standardized through a manual and prior practice. A digital grip strength meter (Grip-D TKK5401, Takei Kiki Kogyo, Niigata, Japan) was used to measure grip strength. Grip strength of both hands was measured twice with participants in the standing position, and the maximum value was taken as the representative value. A hand-held dynamometer (μ-TAS F-1, Anima Co., Ltd., Tokyo, Japan) was used to measure KES. Measurements were taken with participants in the sitting position on a training bed, with the upper limbs folded in front of the chest, the belt attached to the foot of the bed to secure the lower limbs, and the attachment placed on the front of the lower leg. The measurement results were expressed in kilograms and divided by the distance from the knee axis to the attachment (kg/m). The one-leg standing time was measured from the time when both upper limbs were placed on the hips and one leg was raised from the floor until the raised leg touched the floor or the contralateral leg. The maximum measurement time for the one-leg standing time was 60 s. The long sitting trunk anteflexion was performed on a bed in the rehabilitation room. Two measurements were taken, and the maximum value was used as the representative value. The 6MD was measured as the maximum distance walked in 6 min, although rest was allowed if the participant became fatigued during that time.

**Exercise Intervention**

The method of exercise and discontinuation criteria were prototyped in accordance with the American College of Sports Medicine exercise guidelines and renal rehabilitation guidelines. The exercise intervention consisted of a supine ergometer exercise during dialysis for 12 weeks. The exercise equipment used was an electric cycle machine Escargot PBE-100 (Meisei Co., Ltd., Tokyo, Japan). The physical therapists set up the equipment and checked the physical condition of the patients each time. The exercise was performed for 30 minutes during the first half of dialysis. The participants were instructed to row to a metronome at 120 beats per minute for the rotation speed, and a drive of 60 rotations per minute was used as the standard. Participants rowed 1800 revolutions/30 minutes based on 60 rotations/minute for 30 minutes and recorded the actual number of rotations they were able to drive on that day after exercise of each day. During the exercise, patients were allowed to train independently. Blood pressure and pulse rate were measured before and after each exercise intervention using a dialysis machine. The number of interventions and the number of rotations on the ergometer were also recorded during the intervention period. After the exercise, the rating of perceived exertion (RPE) during exercise was measured using the Borg Scale.

**Statistical analysis**

The data obtained in this study were presented as mean ± standard deviation. The gender ratio between the HL and LN groups was tested for bias by Fisher’s exact test. Normality of all data was calculated using the Shapiro-Wilk test. A two-way analysis of variance was conducted to compare the two factors before and after the intervention and the two levels of the HN and LN groups, respectively. In addition, the data between the two groups were compared using the two-sample t-test and Mann-Whitney U-test. The pre- and post-intervention groups were compared using the paired t-test and Wilcoxon signed-rank sum test. SPSS Statistics version 25.0 (IBM Corp., Armonk, NY, USA) was used for all statistical analyses. The significance level was set at 5%.

**Results**

The characteristics of the participants are listed in Table 1. There were no significant differences in age, weight, BMI, %BF, FFM, or TBW between the two groups. The implementation records during exercise intervention are presented in Table 2. The number of exercise interventions during 12 weeks was approximately 36 in both groups. The amount of exercise per session was approximately 1600 revolutions/30 minutes in the HN group and approximately 1400 revolutions/30 minutes in the LN group, a difference of approximately 200 revolutions per minute (rpm). The post-exercise RPE was approximately 10, and the exercise intensity was low to moderate.

The physical functions of the HN and LN groups are shown in Table 3. A two-way analysis of variance showed...
and after the intervention (p<0.05). In comparison before
higher in the HN group than in the LN group both before
these analyses. Grip strength and KES were significantly
after the intervention, a non-parametric test was used for
standing time before and after the intervention and the KES
there was no normal distribution for open-eyed one-legged
Since the results of the Shapiro-Wilk test assumed that
no interaction between pre- and post-intervention and nutri-
tional status, and grip strength, KES, and 6MD were found
tional status, and grip strength, KES, and 6MD were found
to have significant differences between HN and LN groups.
Since the results of the Shapiro-Wilk test assumed that
there was no normal distribution for open-eyed one-legged
standing time before and after the intervention and the KES
after the intervention, a non-parametric test was used for
these analyses. Grip strength and KES were significantly
higher in the HN group than in the LN group both before
and after the intervention (p<0.05). In comparison before
and after the intervention, long sitting trunk anteflexion im-
proved significantly after the intervention in the HN group
(p<0.05), and the 6MD improved significantly after the in-
tervention in the LN group (p<0.05).

Discussion

The results of this study revealed that grip strength and
KES were significantly lower in patients with low nutri-
tional status than in those with high nutritional status. A

| Table 1. Characteristics of participants |
|----------------------------------------|
| HN group n=13                          | LN group n=13                          | p value |
| Male:Female                            | 10 : 3                                 | 8 : 5    | p=0.05 |
| Age (years)                            | 63 ± 9                                 | 68 ± 10  | p=0.05 |
| Body weight (kg)                       | 59.05 ± 9.16                          | 55.78 ± 11.11 | p=0.05 |
| BMI (m/²)                              | 21.67 ± 3.73                          | 22.24 ± 3.66 | p=0.05 |
| %BF (%)                                | 19.11 ± 8.21                          | 22.31 ± 9.46 | p=0.05 |
| FFM (kg)                               | 47.45 ± 6.97                          | 42.88 ± 7.19 | p=0.05 |
| TBW (kg)                               | 34.72 ± 5.11                          | 31.37 ± 5.26 | p=0.05 |

HN group: high-nutrition group; LN group: low-nutrition group; BMI: body mass index; %BF: percentage of body fat; FFM: fat-free mass; TBW: total body water

| Table 2. Exercise intervention data |
|-------------------------------------|
| HN group                             | LN group                             | p value |
| Number of exercise intervention (time) | 36.54 ± 1.266                       | 36.92 ± 1.32 | p>0.05 |
| Number of ergometer rotation (time)  | 1616.15 ± 433.09                     | 1462.81 ± 406.85 | p>0.05 |
| RPE in respiratory discomfort        | 10.31 ± 1.89                         | 10.92 ± 2.02 | p>0.05 |
| RPE in leg fatigue                   | 10.69 ± 2.32                         | 10.92 ± 2.02 | p>0.05 |
| Pre-exercise systolic blood pressure (mmHg) | 143.68 ± 9.52                    | 147.70 ± 18.36 | p>0.05 |
| Post-exercise systolic blood pressure (mmHg) | 144.28 ± 8.41                   | 148.00 ± 15.15 | p>0.05 |
| Pre-exercise diastolic blood pressure (mmHg) | 79.64 ± 8.41                      | 77.00 ± 10.03 | p>0.05 |
| Post-exercise diastolic blood pressure (mmHg) | 78.88 ± 7.29                     | 77.15 ± 9.40  | p>0.05 |
| Pre-exercise pulse beat (bpm)         | 67.35 ± 12.03                        | 67.16 ± 7.32 | p>0.05 |
| Post-exercise pulse beat (bpm)        | 70.33 ± 12.09                        | 69.02 ± 6.74 | p>0.05 |

HN group: high-nutrition group; LN group: low-nutrition group; RPE: rating of perceived exertion; bpm: beats per minute

| Table 3. Results of physical functions |
|---------------------------------------|
| HN group                              | LN group                              |
| Grip strength (kg)                    | 31.38 ± 8.75                          | 22.92 ± 9.95*                         | 22.58 ± 9.37*                         |
| Knee extensor strength (kg)           | 27.99 ± 13.63                         | 17.11 ± 7.90*                         | 18.91 ± 6.67*                         |
| One leg standing time (s)             | 33.85 ± 24.93                         | 26.42 ± 22.74                         | 24.96 ± 22.30                         |
| Long sitting trunk anteflexion (cm)   | 31.65 ± 9.82                          | 28.50 ± 17.39                         | 29.65 ± 14.86                         |
| 6MD (m)                               | 459.85 ± 146.37                       | 374.69 ± 127.01                       | 406.85 ± 124.64*                      |

Compared between pre and post intervention: *p<0.05. Compared between HN group and LN group: <p<0.05
HN group: High nutrition group; LN group: Low nutrition group; 6MD: 6-minute walking distance test
previous study examining the effects of exercise on the nutritional status and body composition of hemodialysis patients reported that physical activity could have a beneficial impact on the nutritional status of hemodialysis patients and help prevent sarcopenia[17]. Although this study only investigated albumin levels before the intervention, it was found that dialysis patients with originally high albumin levels maintained high muscle strength after the intervention. This study may have a positive effect on sarcopenia in terms of muscle strength.

As for the exercise intervention, the number of driving rotations for the supine ergometer during 30 minutes of intradialytic exercise was approximately 1600 in the HN group and approximately 1400 in the LN group. Souweine et al. discovered a relationship between physical activity, serum albumin levels, and quadriceps muscle weakness[15]. Therefore, this difference in the number of driving rotations may be attributed to the difference in original muscle strength, which had a significant effect on the driving force. Silva et al. reported that biarticular muscles such as quadriceps and biceps femoris have a significant influence on lower limb movements during cycling[6]. It is suggested that the difference in the strength of the quadriceps muscle, which is a knee extensor, had a significant effect on this driving force. In the future, maintaining a high nutritional status and training the quadriceps and other biarticular muscles of the lower extremities may lead to more effective supine ergometer exercise during dialysis.

In the comparison before and after the intervention, long sitting trunk anteflexion in the HN group improved significantly after the intervention. Reportedly, ergometer exercises during dialysis improved flexibility which is similar to the present study[17]. Studies that looked at the effects of cycling on spastic muscles such as cerebral palsy and spinal cord injury showed a decrease in muscle tone[8,10]. In the present study, it is possible that the bicycle ergometer exercise reduced muscle tone in the lower limb muscles. In particular, the improvement was observed in the HN group, suggesting that the nutritional status and the amount of exercise may affect the improvement. Furthermore, 6MD in the LN group improved significantly after the intervention. Long-term nutritional supplementation has been reported to increase skeletal muscle anabolic effects, thigh fat cross-sectional area, and skeletal muscle mitochondrial content[30]. Therefore, we hypothesized that a more effective exercise effect would be obtained in the HN group. However, 6MD significantly improved even in patients with low nutritional status. This may indicate that 6MD can be improved by exercise during dialysis, regardless of nutritional status. It has been reported that 6MD is related to the survival rate of hemodialysis patients and that every 100 m of walking is associated with approximately 5.3% of life expectancy[31]. It is said that low nutritional status has a negative impact on survival rate; thus, considering the impact on survival rate, it is hemodialysis patients with a low nutritional status that should be considered to introduce more active exercise during dialysis.

This study has some limitations. The first limitation was the small number of participants. This was a limitation of recruiting participants from a small dialysis center. Dialysis patients tend to be particularly reluctant to participate in exercise interventions. In order to increase the number of participants in the future, we need to recruit a wider range of participants and conduct a multicenter collaborative study. The second limitation was that the nutritional status was only checked at the beginning of the study; the nutritional status during and after the intervention should have been checked as well. This would have allowed us to examine the relationship between nutritional status and motor function in more detail. However, despite these limitations, we were able to verify a certain effect of exercise intervention in hemodialysis patients. The exercise intervention is expected to require 1400-1600 revolutions/30 minutes, i.e., 46-53 rpm, and driving at an average speed of 50 rpm may result in improved physical function.

**Conclusion**

Hemodialysis patients with low nutritional status had decreased physical functions compared to those with high nutritional status. The HN group showed more improvement in long sitting trunk anteflexion with exercise intervention during dialysis, and the 6MD improved significantly in the LN group. This may indicate that 6MD can be improved by exercise during dialysis, regardless of nutritional status. It is said that low nutritional status has a negative impact on survival rate; thus, considering the impact on survival rate, it is hemodialysis patients with a low nutritional status that should be considered to introduce more active exercise during dialysis.

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