

Research article

# How much do disuse syndrome patients improve with convalescent rehabilitation? Assessment of improvement

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**Abstract:** The purpose of this study is to determine characteristics of FIM gain after rehabilitation for patients with disuse syndrome and what factors are beneficial for increasing FIM gain. The subjects were 168 patients (87 males and 81 females). We investigated the relationship between the degree of FIM gain and etiology, age, sex, gender, history of cerebrovascular disease, dementia, body weight, body mass index (BMI), hemoglobin, protein, albumin, prognostic nutritional index, malnutrition, and dysphagia. The primary etiologies that resulted in disuse syndrome were COVID-19, respiratory disease, gastrointestinal disease, urinary disease, cardiovascular disease, and others. The average FIM-total gain by age decreased as age increased. FIM-total gain was 8.0 for patients in their 90s. FIM-total gain was 13.8 for patients with no past incident of cerebrovascular diseases, 7.6 for one past incident, and 4.0 for two or more past incidents. FIM-total gain of the patients of severe dysphagia was significantly lower than that of the patients of normophagia / mild or moderate dysphagia. There was a mild correlation between FIM-total gain and gain of body weight ( $r=0.21$ ) and between FIM-total gain and gain of BMI ( $r=0.21$ ). Patients with disuse syndrome over 90 or with two or more incidents of cerebrovascular diseases should be treated, not in rehabilitation but in nursing care.

**Keywords:** Disuse syndrome; Rehabilitation; Malnutrition; Dysphagia; Functional independence measure (FIM)

## 1. Introduction

Disuse syndrome is defined as a "secondary disorder caused by a state of inactivity" (1). Many human functions are weakened due to bed rest, even if they are not due to disease, and further rest leads to pathological functional decline, resulting in a secondary complication.

Aging populations worldwide are increasing, and older adults account for more than 25% of the population in Japan. Everyone wishes for a healthy retirement, but people spend more than a few years at the end of their lives being bedridden. It is essential for everyone needs to spend those years with peace of mind. Many older adults suffer from disuse syndrome at the end of life. It is caused by immobility and nutritional deficiencies, and those patients need rehabilitation. Malnutrition is not particular in patients with the disuse syndrome (2). For patients with disuse syndrome it is essential to improve not only early mobilization and functional training but also their nutritional condition. It is essential to know the characteristics of disuse syndrome and to prevent disuse syndrome. With the development of medical research in space in correlation with NASA since the 1960s, symptoms such as orthostatic low pressure, decreased cardiopulmonary function, and osteoporosis, similar to the disuse syndrome after long-term bed rest, have appeared

after short-term spaceflights (1). The adverse effects of not exercising have been demonstrated (1).

Rehabilitation is not always beneficial for some patients with disuse syndrome. Such patients require not rehabilitation but nursing care. The effects of rehabilitation for disuse syndrome in older adults requiring severe care, we can consider an indication of the rehabilitation and also an indication of nursing care. The functional independence measure (FIM) is the most widely used and essential for rehabilitation in the world.

In this article, we determined characteristics of FIM gain after rehabilitation for patients with disuse syndrome and what factors are beneficial for increasing FIM gain.

## 2. Materials and Methods

This study was approved by the Shimada Hospital Ethics Committee (No.2209). It was a retrospective cohort study and conducted at a single institution for patients with disuse syndrome who were hospitalized from May 2020 to November 2023. In this paper, to know the overall picture of patients with disuse syndrome, we had correlated and analyzed all cases treated for rehabilitation in one private convalescent hospital during a three and a half year period. This retrospective study was using the data of 168 registered subjects. Inclusion criteria for this study were a diagnosis of the disuse syndrome and age older than 20 yrs. There were no exclusion criteria. Finally, 168 patients were registered in the study.

All patients received intensive rehabilitation by qualified physical therapists, qualified occupational therapists and qualified speech-language-hearing therapists. Patients were treated in the full-time integrated treatment (FIT) program (3) managed by rehabilitation 7 days/wk, encouragement of daytime activity, and enhanced communication and collaboration amongst staff sharing in detail patients treatment and progression. Patients who were 78 years or younger had 3 hours of rehabilitation (physical therapy 1 hour, occupational therapy 1 hour, speaking therapy 1 hour), and patients who were 79 years or older had 2 hours of rehabilitation (physical therapy 40 minutes, occupational therapy 40 minutes, speaking therapy 40 minutes). When occupational therapy or speaking therapy was not necessary for patients, physical therapy was given instead. Several members of a nutrition support team (NST) improved the nutritional condition of the patients with disuse syndrome. Nutritional status was assessed at referral by collecting data on hemoglobin, total protein, albumin, and BMI. This data was used to determine the amount calories and the nutrients that should be consumed by each patient.

Clinical and demographic features including primary etiology, sex, age, history of cerebrovascular diseases, dementia, body weight (Kg), body mass index (BMI), serum hemoglobin [Hb (g/dl)], serum total protein [TP (g/dl)], serum albumin [Alb (g/dl)], prognostic nutritional index (PNI), malnutrition and dysphagia were analyzed. PNI was calculated by  $10 \times \text{Alb (g/dl)} + 0.005 \times \text{total lymphocyte count (/mm}^3)$  (4). Dysphagia is classified as follows: normophagia / mild dysphagia suggests that a patient can have a total oral diet at admission. Moderate dysphagia suggests that a patient cannot have a total oral diet at admission but can have it at discharge. Severe dysphagia suggests that a patient cannot have a total oral diet at admission and cannot have a total oral diet at discharge as well. Presence of malnutrition were defined as meeting one or more of a BMI<18.5 kg/m<sup>2</sup>, Hb level<10.0 g/dl, Alb level<3.0 g/dl, or total lymphocyte count<1200 cells/mm<sup>3</sup> (2).

Functional status was assessed by using the functional independence measure (FIM). FIM was calculated every week and evaluated at admission, 4 weeks, 8 weeks after admission, and discharge. The FIM items are classified into total, motor and cognitive categories (FIM-total, FIM-motor, and FIM-cognition). FIM scores were assigned according to a 7-point scale, and the score indicated the amount of assistance required to perform each item (7 = totally independent and 1 = dependent or not testable) (5).

### Statistical Analysis

The data is presented as the mean  $\pm$  standard deviation. A non-parametric test (Mann–Whitney U test) was applied to compare the mean values of the two groups. The statistical analyses were performed based on StatView for Windows (Version 5.0; SAS Institute Inc. Cary, NC, USA). A  $p$ -value of  $< 0.05$  was defined as statistically significant.

### 3. Results

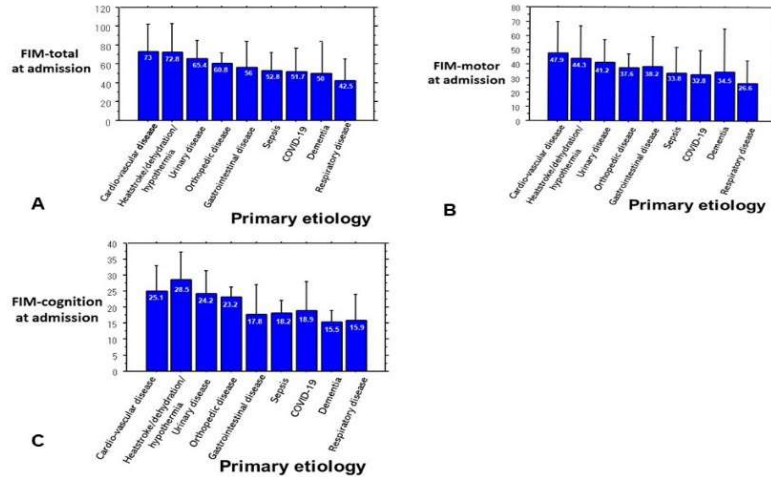
Eighty-seven patients were male and 81 were female (Table 1). Their mean age was  $83.2 \pm 8.7$  (range 44 to 99). Primary etiologies of disuse syndrome were COVID-19 in 13 cases, respiratory disease in 91 cases, gastrointestinal disease in 24 cases, urinary disease in 13 cases, cardiovascular disease in 11 cases, sepsis in 5 cases, orthopedic disease in 5 cases, heatstroke/dehydration/hypothermia in 4 cases, and dementia in 2 cases.

**Table 1.** Patients characteristics

Age		44 ~ 99 ( Mean $\pm$ S.D. : 83.2 $\pm$ 8.7 )			
Sex	Male	87	History of cerebrovascular disease	No incidence	124
	Female	81		One time incidence	42
Primary Etiology	COVID-19	13	Dementia	Two or more times incidence	2
	Respiratory disease	91		Positive	75
	Gastrointestinal disease	24	Negative	93	
	Urinary disease	13	Discharge	Home	94
	Cardiovascular disease	11	Hospital, Nursing home	73	
	Sepsis	5	Death	1	
	Orthopedic disease	5			
	Heatstroke/dehydration / hypothermia	4			
	Dementia	2			

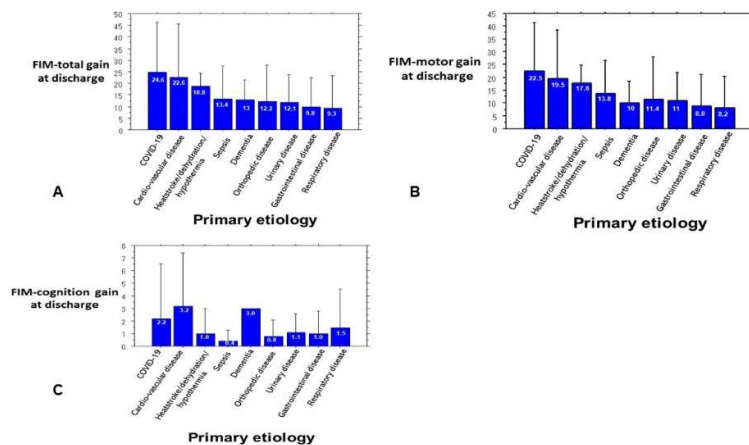
The days until the start of rehabilitation were  $6.8 \pm 9.5$  (range 0 to 62), and the days of hospitalization in convalescent hospital were  $51.9 \pm 19.6$  (range 7 to 100). At admission, FIM-total of all patients was  $50.6 \pm 25.3$  (range 18 to 112), FIM-motor was  $32.3 \pm 18.3$  (range 13 to 79), and FIM-cognition was  $18.2 \pm 8.7$  (range 5 to 35). At discharge, FIM-total gain was  $12.1 \pm 15.5$  (range -18 to 80), FIM-motor gain was  $10.9 \pm 13.7$  (range -16 to 65), and FIM-cognition gain was  $1.5 \pm 2.9$  (range -4 to 17).

The averages of FIM-total by primary etiology were  $73.0 \pm 28.6$  for cardiovascular disease,  $72.8 \pm 29.9$  for heatstroke/dehydration/hypothermia,  $65.4 \pm 19.4$  for urinary diseases,  $60.8 \pm 10.5$  for orthopedic diseases,  $56.0 \pm 28.1$  for gastrointestinal diseases,  $52.8 \pm 19.0$  for sepsis,  $51.7 \pm 24.5$  for COVID-19,  $50.0 \pm 33.9$  for dementia, and  $42.5 \pm 22.6$  for respiratory diseases (Figure 1A). Patients with cardiovascular disease or heatstroke/dehydration/hypothermia had higher FIM-total at admission. The averages of FIM-motor and FIM-cognition by primary etiology were presented in Figure 1B and 1C.



**Figure 1.** A: FIM-total at admission based on primary etiology B: FIM-motor at admission based on primary etiology C: FIM-cognition at admission based on primary etiology

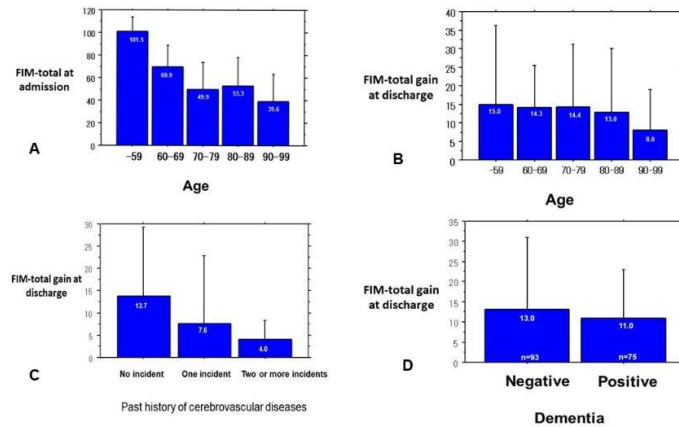
At admission, the average was  $47.4 \pm 12.5$  for body weight,  $19.8 \pm 4.2$  for BMI,  $11.5 \pm 1.7$  for Hb,  $6.5 \pm 0.7$  for TP,  $3.0 \pm 0.6$  for Alb, and  $36.6 \pm 6.2$  for PNI. The averages of FIM-total gain at discharge by primary etiology were  $24.6 \pm 21.8$  for COVID-19,  $22.6 \pm 23.0$  for cardiovascular disease,  $18.8 \pm 5.7$  for heatstroke/dehydration/hypothermia,  $13.4$  for sepsis,  $13.0 \pm 14.2$  for dementia,  $12.2 \pm 15.6$  for orthopedic diseases,  $12.1 \pm 11.5$  for urinary diseases,  $9.8 \pm 12.5$  for gastrointestinal diseases and  $9.3 \pm 14.1$  for respiratory diseases (Figure 2A). Patients with COVID-19 or cardiovascular disease had higher FIM-total gain at discharge. The averages of FIM-motor gain and FIM-cognition gain at discharge by primary etiology were presented in Figure 2B and 2C. Patients with cardiovascular disease or dementia had higher FIM-cognition gain of 3 or more at discharge.



**Figure 2.** A: FIM-total gain at discharge based on primary etiology B: FIM-motor gain at discharge based on primary etiology C: FIM-cognition gain at discharge based on primary etiology

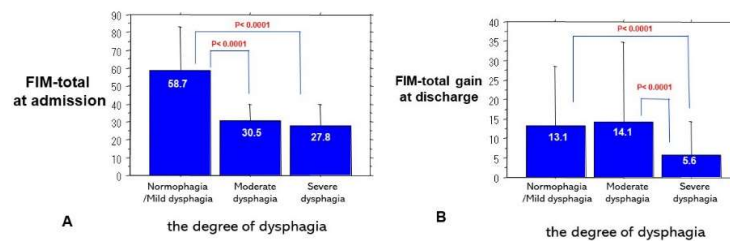
The average FIM-total at admission by age was 101.5 for patients in their 40s - 50s, 69.9 for those in their 60s, 49.9 for those in their 70s, 53.3 or those in their 80s, and 39.6 for those in their 90s, decreasing as age increased (Figure 3A). The average FIM-total gain by age was 15.0 for patients in their 40s - 50s, 14.3 for those in their 60s, 14.4 for those in their 70s, 13.0 for those in their 80s, and 8.0 for those in their 90s, decreasing as age increased (Figure 3B). The average FIM-cognition gain by age was 0.5 for patients in their 40s - 50s, 1.3 for those in their

60s, 1.3 for those in their 70s, 1.9 for those in their 80s, and 1.0 for those in their 90s. FIM-total gain of the females was  $12.9 \pm 14.9$ , which is not significantly better than that ( $11.4 \pm 16.1$ ) of the males. ( $p=0.546$ ). Regarding the history of cerebrovascular diseases, FIM-total gain was 13.7 for patients with no incident, 7.6 for one incident, and 4.0 for two or more incidents (Figure 3C); the more the history of cerebrovascular diseases, the lower the FIM-total gain. The average of FIM-total gain for the 75 patients with dementia was 11.0, which tended to be lower than the 13.0 for the 93 patients without dementia (Figure 3D). 139 patients (83%) were diagnosed with malnutrition. FIM-total gain at discharge of 139 patients with malnutrition was  $11.8 \pm 15.9$ , which was likely to be worse than that ( $13.9 \pm 13.9$ ) of the 29 patients without malnutrition, but there was not a significant difference ( $r=0.496$ ).



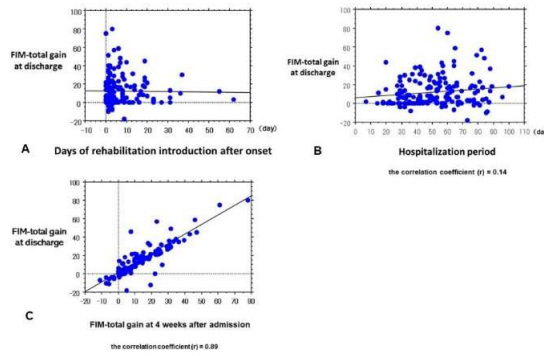
**Figure 3** A: FIM-total at admission based on age. B: FIM-total gain at discharge based on age. C: Past history of cerebrovascular diseases. D: FIM-total gain at discharge based on dementia

Concerning the degree of dysphagia, FIM-total at admission of the patients of normophagia / mild dysphagia was  $58.7 \pm 24.5$ , which was significantly higher than that ( $30.5 \pm 9.2$ ) of the patients with moderate dysphagia or that ( $27.8 \pm 12.1$ ) of the patients with severe dysphagia (Figure 4A). FIM-total gain at discharge of the patients with severe dysphagia was  $5.6 \pm 8.8$ , which was significantly lower than that ( $13.1 \pm 15.3$ ) of the patients with normophagia / mild dysphagia or that ( $14.1 \pm 20.8$ ) of the patients with moderate dysphagia (Figure 4B).



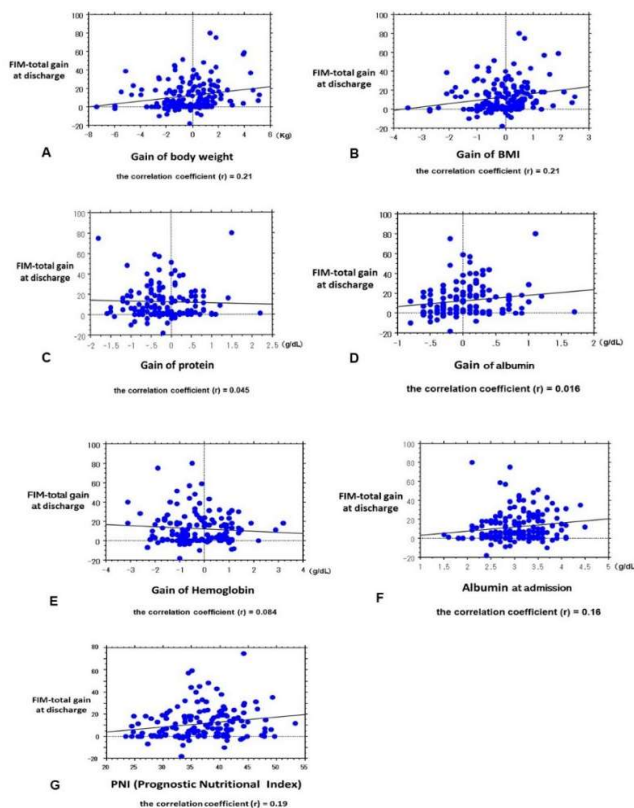
**Figure 4.** A: FIM-total at admission based on the degree of dysphagia. B: FIM-total gain at discharge based on the degree of dysphagia

There was a tendency for cases in which rehabilitation was introduced earlier to have a higher FIM-total gain (Figure 5A). A tendency was observed that the longer the hospitalization period, the higher FIM-total gain (Figure 5B). There was an excellent relationship between FIM-total gain at discharge and FIM-total gain at 4 weeks after admission ( $r=0.89$ ) (Figure 5C).



**Figure 5.** A: FIM-total gain at discharge and days of rehabilitation introduction after onset B: FIM-total gain at discharge and hospitalization period C: FIM-total gain at discharge and FIM-total gain at 4 weeks after admission

There were mild correlations between FIM-total gain and gain of body weight ( $r=0.21$ ) (Figure 6A), and between FIM-total gain and gain of BMI ( $r=0.21$ ) (Figure 6B). There were not significant correlations between FIM-total gain and gain of TP ( $r=0.045$ ) (Figure 6C) or between FIM-total gain and gain of Alb ( $r=0.016$ ) (Figure 6D). There were no significant correlations between FIM-total gain and gain of Hb ( $r=0.084$ ) (Figure 6E). There were no significant correlations between FIM-total gain and body weight at admission ( $r=0.13$ ), or between FIM-total gain and Alb at admission ( $r=0.16$ ) (Figure 6F). There was a tendency of a mild correlation between FIM-total gain and PNI ( $r=0.19$ ) (Figure 6G).



**Figure 6.** A:FIM-total gain at discharge and gain of body weight B: FIM-total gain at discharge and gain of body BMI (Body Mass Index) C: FIM-total gain at discharge and gain of protein D: FIM-total gain at discharge and gain of protein E: FIM-total gain at discharge and gain of hemoglobin F: FIM-total gain at discharge and albumin at admission G: FIM-total gain at discharge and PNI (prognostic nutritional index)

#### 4. Discussion

To know the overall picture of patients with disuse syndrome, we had correlated and analyzed all cases treated for rehabilitation in one private convalescent hospital during a three year and a half period. Our cases would represent the broader population with disuse syndrome. For improving the rehabilitation for patients with disuse syndrome, it is essential to understand the details of FIM gain based on the etiology and clinical factors. Barthel index (6) is also useful for rehabilitation, but the evaluation of Barthel index is rough and does not lend itself to detailed analysis.

##### *Early rehabilitation*

There was a tendency for cases where rehabilitation was introduced earlier to have a higher FIM-total gain. Nutritional and exercise therapy should be started very early after admission and adjusted to the level of inflammation and disease status (7). Early rehabilitation was beneficial treatment for osteoporotic vertebral fractures to reduce the risk for disuse syndrome, maintain pre-injury ADL status, and minimize the medical costs (8). Early rehabilitation was already recommended to be effective for stroke patients (9). The Intercollegiate Stroke Working Party (ICSWP) recommended that stroke rehabilitation should begin 24-48 hours after a stroke and should be reviewed at six months (10). Although patients with an early rehabilitation start had lower FIM admission scores than patients with a late start, patients with an early rehabilitation start experienced more remarkable functional improvement (11). There was a relationship between the early rehabilitation start and better functional improvement (12).

##### *Characteristics of factors:*

A tendency was observed that the longer the hospitalization period, the higher the FIM-total gain. There was an excellent relationship between FIM-total gain at discharge and FIM-total gain at 4 weeks after admission ( $r=0.89$ ). FIM-total gain at 4 weeks after admission was revealed to be a prognostic predictor of patients with disuse syndrome. At admission, patients with cardiovascular disease or heatstroke/dehydration/hypothermia are revealed to have higher FIM-total compared to other etiology. And the average FIM-total at admission by age reveals decreased according to age increase. Patients with COVID-19 or cardiovascular disease, having higher FIM-total gain at discharge, were good candidates for rehabilitation of disuse syndrome. The average of FIM-total gain by age was decreased as age increased. FIM-total gain of the patients with dementia tended to be lower than that of the patients without dementia. FIM gain decreased according to repeating incidents of cerebrovascular diseases. Patients with no previous cerebrovascular disease were good candidates for rehabilitation of disuse syndrome.

##### *Malnutrition*

Wakabayashi H, et al. (2) reported that 91% of patients with disuse syndrome were malnourished. In our series, 83% of patients were malnourished. Malnutrition is common in patients with disuse syndrome. Rehabilitation outcome was worse in malnourished patients than patients with normal nutrition (relative risk: 0.72,  $p=0.04$ ) (2), although our data did not show a significant difference. There was not a significant correlation between FIM-total gain and gain of Hb ( $r=0.084$ ) in this study. Still hemoglobin levels were reported to be associated independently with rehabilitation outcomes (odds ratio 2.34,  $p=0.005$ ) (2). Patients with low hemoglobin levels and PNI at referral are more likely to have a poor rehabilitation outcome (2). In our study, there were mild correlations between FIM-total gain and gain of body weight ( $r=0.21$ ), between FIM-total gain and gain of BMI ( $r=0.21$ ), and between FIM-total gain and PNI ( $r=0.19$ ). However, there were no significant correlations between FIM-total gain and gain of protein ( $r=0.045$ ), between FIM-total gain and gain of albumin ( $r=0.016$ ), between FIM-total gain and body weight at admission ( $r=0.13$ ) or between FIM-total gain and albumin at admission ( $r=0.16$ ).

*Dysphagia:*

Dysphagia is one of the most prevalent and distressing symptoms among palliative care patients (13). Dysphagia was found to be closely associated with malnutrition and sarcopenia (14). A combination of a decrease in activity of daily living (ADL) and cognitive dysfunction influence the outcome of dysphagia (15). In this study the patients of normophagia / mild dysphagia had  $58.7 \pm 24.5$  of FIM-total at admission and get  $13.1 \pm 15.3$  of FIM-total gain at discharge. The patients of moderate dysphagia had  $30.5 \pm 9.2$  of FIM-total at admission, and  $14.1 \pm 20.8$  of FIM-total gain at discharge. However the patients of severe dysphagia had  $27.8 \pm 12.1$  of FIM-total at admission, but got only  $5.6 \pm 8.8$  of FIM-total gain at discharge. Our data revealed that improving dysphagia is essential for patients with disuse syndrome.

*Sarcopenia:*

Secondary sarcopenia is often observed in disuse syndrome. Evaluation and treatment of sarcopenia are also necessary. In 2010, the European Working Group on Sarcopenia in Older People published the following statement: "Sarcopenia is a syndrome characterized by a progressive and generalized loss of skeletal muscle mass and strength, with a risk of adverse outcomes, such as physical disability, poor quality of life and death" (16). The Asian Working Group for Sarcopenia (AWGS) 2014 consensus defined sarcopenia as "age-related loss of muscle mass, plus low muscle strength, and/or low physical performance" (17). Subsequently, in October 2016, sarcopenia was included in the ICD-10 (M62.84) and was internationally recognized as a disease (18). The term, sarcopenia, is a combination of the Greek word sarx, meaning muscle, and penia, meaning to lose. Muscle mass is reduced by about 1%–2% every year after age 50 (19,20). Nutritional management and exercise are crucial for the prevention and treatment of sarcopenia (7). Excessive bed rest and mismanagement of nutrition in medical facilities can lead to iatrogenic sarcopenia (16). It has been reported that 14.7% of older patients who did not have sarcopenia before hospitalization had new-onset sarcopenia at discharge (21). In recent years, "sarcopenia and dysphagia" have become a hot topic in several academic meetings and conferences of medical and healthcare professionals. The expression "dysphagia due to sarcopenia" was first introduced in 2005 (22), whereas the term "sarcopenic dysphagia" was first used in the paper published by Kuroda et al. in 2012 (23). The prevalence of malnutrition and sarcopenia in physically disabled elderly patients who undergo rehabilitation is high (24).

*Osteoporosis:*

Greenleaf et al. (25) found that long-term bed rest reduces stress on bones in the longitudinal direction, allowing the body to interpret this as a state in which bone mass is no longer needed, promote the excretion of calcium and phosphorus, and initiate bed rest. It states that a decrease in bone density occurs after two weeks.

*Indication of nursing care*

From the viewpoint of cost benefit, 90 or more year-old patients with disuse syndrome, whose FIM-total gain was 8.0, could be treated in nursing care, not rehabilitation. Patients who had two or more incidents of cerebrovascular diseases with disuse syndrome, whose FIM-total gain was 4.0, could also be treated in nursing care, not rehabilitation.

Clinical practice for patients with disuse syndrome should start as soon as possible after its onset. Nutritional status and swallowing function are key factors for improving disuse syndrome. But patients with disuse syndrome over 90 or with two or more incidents of cerebrovascular diseases should be treated, not in rehabilitation but in a nursing home.

The average age of our patients was  $83.2 \pm 8.7$  (range 44 to 99), which represented older patients. Younger patients with disuse syndrome achieved better FIM gain than older patients. Average FIM-total gain by age was 15.0 for patients in their 40s - 50s, 14.3 for those in their 60s, 14.4 for those in their 70s, 13.0 for those in their 80s, and 8.0 for those in their 90s, decreasing as age increased. For future research, a study of younger patients with disuse syndrome has high value and would be beneficial.



A healthcare team consists of not only doctors, nurses, and therapists, but also medical social workers, care managers and facility staff. Relationships among them are essential for improving quality of life of patients with disuse syndrome.

**Study limitations** We have to keep in mind that the research had five limitations. First, it was a retrospective research project and was conducted at a single institution. Second, the number of patients of disuse syndrome was only 168. For a more accurate assessment, additional patients with disuse syndrome and more extended follow-up studies are necessary. Third, this study did not have a control group. In a private convalescent hospital, it is rather difficult to add a control group with disuse syndrome for comparison to a study group. In the control group patients cannot get rehabilitation. Most patients with disuse syndrome want to get rehabilitation because there is evidence of the efficacy of this treatment. Fourth, after discharge from our hospital, most patients underwent follow-up observation at their family doctors, while others were admitted to other hospitals or nursing homes. Long term outcomes of rehabilitation for disuse syndrome are not clear yet, so we have work with their home doctors, hospitals and nursing homes, and evaluate the long-term outcomes. Fifth, selection bias might be present in the study. These patients with disuse syndrome would be more interested in healthcare and want to get rehabilitation compared to the broader population with disuse syndrome.

## 5. Conclusions

To increase the degree of FIM improvement in patients with disuse syndrome, it is essential to start rehabilitation early after the onset of symptoms. A sufficient hospitalization period is required, and it is desirable to improve body weight and BMI through dietary intake. Improving of dysphagia is essential for the patients with disuse syndrome. Patients with disuse syndrome over 90 years old or with two or more incidents of cerebrovascular diseases should be treated, not in rehabilitation but in nursing care.

**Supplementary Materials:** none

**Author Contributions:** Conceptualization, Usuda K. and Uesaka T.; methodology, Okubo T.; software, Takeda M.; validation, Yokoyama K., Shimizu M., and Kitagawa K.; formal analysis, Shimada T. and Shimada C.; investigation, Ito H.; data curation, Itamoto N.; writing—original draft preparation, Usuda K.; writing—review and editing, Usuda K.; visualization, Douko N. and Aoki T.; supervision, Shimada O. All authors have read and agreed to the published version of the manuscript.

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**Informed Consent Statement:** An informed consent was obtained from each patient participating in the study.

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**Conflicts of Interest:** The authors declared no conflict of interest.

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