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REVIEW

Medical Rehabilitation Need, Case Complexity, and Related Issues among Patients in an Acute Stroke Rehabilitation Setting

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ABSTRACT. This narrative review introduces case complexity and medical rehabilitation needs in a stroke rehabilitation setting, and proposes methods to more efficiently enhance functional recovery in the acute stage after stroke onset. Therapists may measure a construct of individual need complexity around and beyond the basic and common needs for medical necessity, and thereby screen acute patients who could benefit more from additional rehabilitation inputs. This review also describes the clinical significance of medical rehabilitation needs and challenges for efficient stroke rehabilitation. Overall, we propose that challenging research trials should be conducted to compare the effectiveness of the arrangement of rehabilitation service allocation based on needs assessment after stroke with the usual care pathway.

Key words: Medical rehabilitation, Needs assessment, Case complexity, Acute stroke rehabilitation

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Stroke is one of the most common causes of complex disabilities. The number of independent factors of poorer functional gain and rehabilitation effectiveness in stroke is much greater than that in post-hip fracture arthroplasty and the general elderly population[1]. Clinicians and therapists have been attempting to start rehabilitation services as early as possible after admission. This is because the intensity of rehabilitation inputs in the acute stage after stroke onset is essential to improve treatment and intervention outcomes.

An augmented exercise therapy time of at least 16 hours is known to improve functional recovery (activities of daily living [ADLs], instrumental ADLs, and walking speed) within the first 6 months after stroke[2]. Conversely, in early intervention, high-dose mobilization commencing within 24 hours of stroke did not promote favorable outcomes at 3 months in a Phase III, multicenter, randomized controlled trial[3]. In this study, the intervention group who underwent early and more frequent mobilization in addition to usual care did not influence the quality of life at 12 months[4]. Although the type of disease studied was not stroke, the goal directed early mobilization in the surgical intensive care unit, using a strict mobilization algorithm combined with facilitated inter-professional communication, shortened length of stay in the unit, and improved functional mobility at hospital discharge[5].

These findings indicate that the addition of rehabilitation services in an acute stroke setting is not necessarily efficient. This raises the clinical question: who is likely to benefit from early and more frequent rehabilitation? To answer the question above, this narrative review describes the medical rehabilitation needs and case complexity following a stroke. The objective was to lead the arrangement of an inpatient medical rehabilitation process for patients after stroke and innovative ideas to improve clinical outcomes.

Medical Rehabilitation Needs

Healthcare costs have recently increased because of increased treatment costs, increased care costs, and increasingly complex health problems that take longer to diagnose and treat[6]. In prior decades, case-mix measurement in medical rehabilitation was reported to determine the need for therapies and resources necessary for their care[7]. Case-mix[7] is an idea involving the complexity or types of patient conditions for classification. This patient classification refers to

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Table 1. Outline of a short checklist for general practitioners[11]

Domain for checking items	
	Underlying diseases
	Dysfunction and activity restriction
	Mental or emotional symptoms
	Risk of lifestyle disease
	Motivation/overcoming the illness
	Various therapies
	Working situation
	Inability to work
Physician's judgement	
	Rehabilitation is necessary and expected to be effective
	Rehabilitation is questionable (suspected of necessity)
	Rehabilitation is unnecessary

English translation is done by the author. The author gives a general meaning of the original German.

the determination of the appropriate payment system (e.g., episode length of stay and episode cost of daily services, including therapies). Patients with complex disabilities generally require more care and treatment, and greater hospital resources. Measurement is a method to consider patient characteristics in the determination of payment rates[7].

In Germany, the concept of medical rehabilitation needs was codified in the public healthcare system[8]. Raspe et al.[9] criticized the lack of a scientifically valid and operationally defined concept of "rehabilitation need." They focused on objectifying concepts derived from three keys: neediness, ability, and prognosis. Hansmeier et al.[10] pointed out that rehabilitation need cannot be directly measured and is a latent multidimensional and qualitative construct. Conversely, they introduced possible determinants of need, such as medical conditions, purposeful therapeutic approach, positive motivation, and active participation in therapies. To a certain degree, these determinants can be regarded as clues when observing the construct. For example, Deck et al.[11] used a short checklist for general practitioners to identify patients' potential need for medical rehabilitation. The domains for this objective assessment are listed in Table 1. They further conducted a subjective judgment of needs using a self-administered patient questionnaire. One of the interesting findings was that the agreement between physician and patient assessments was weak, and 13% of patients classified as having a subjective need for rehabilitation were questionable. Nevertheless, this checklist provides a clue for the measurable constructs.

Case Complexity in Neurological Rehabilitation

Rehabilitation needs have generally relied on physical dependency, as measured by functional independence. In neurological rehabilitation, including for patients after stroke, however, the actual supply of rehabilitation services depends on case-related characteristics such as comorbidities, cognitive impairment, behavioral disorders, and longer length of stay, rather than physical dependency alone. For efficient service provision, rehabilitation inputs should be matched as closely as possible to individual patient needs[12]. The following are some examples of measures used to capture case complexity (Table 2).

The Extended Rehabilitation Complexity Scale (RCS-E)

In the United Kingdom, Turner-Stokes et al.[13] developed the Rehabilitation Complexity Scale (RCS) as a measure of complexity in rehabilitation, considering basic care, specialist nursing, therapy, and medical intervention, the aim of which was to assist in justifying the resources used. The RCS captures the complexity of rehabilitation needs and/or interventions, which are applied in a timely manner and consider basic care, specialist nursing, therapy, and medical interventions[14]. The extended version of the RCS (RCS-E)[15] is a more sensitive tool for detecting patients with highly complex needs by adding the need for special equipment or facilities and the risk or need for supervision of patients who are ambulant but confused. The total score range of the latest version is 0–22[16]; a higher score reflects a higher level of complexity.

The Oxford Case Complexity Assessment Measure (OCCAM)

The OCCAM covers 27 items assessing 9 domains from the holistic, biopsychosocial model of illness, and healthcare fields[17]. Another feature of the OCCAM is the psychometrical possibility of predicting prolonged stays in the hospital and failure to return home, which indicates rehabilitation resource use and clinical outcome in the neurological rehabilitation setting. The total possible score range is 0–81, and the final score reflects the level of case complexity.

The patient categorization tool (PCAT)

The PCAT was initially developed as a checklist to identify patients with complex needs, and has since been validating methods of identifying patients with complex needs requiring specialist rehabilitation[12]. This tool comprises four domains (specialist medical/neuropsychiatric needs, clinical needs, additional needs, and expected duration of admission) with 18 items, each containing a level of need. The total possible score range is 16–50, and the final score reflects the level of complexity of the need for neurorehabilitation. The PCAT is scored once on admission (ideally by a consultant in rehabilitation medicine or deputy)[18]. Scaling properties such as unidimensionality and reliability have been satisfied for individual assessments of rehabilitation complexity[19].

Toward the Measurement of Rehabilitation Needs

The definitional core

The concept of rehabilitation needs was first introduced to German research by Raspe and Héon-Klin[8]. Wade[20]

Table 2. Contents of case complexity for assessing rehabilitation needs

RCS-E version 13	
Item	
Basic care and support needs	
Risk – cognitive/behavioral needs	
Skilled nursing needs	
Medical needs	
Therapy needs – discipline	
Intensity	
Equipment needs	
Total possible score range	0–22

OCCAM	
Category	Domain
Patient-centered item	Pathology
	Impairments
	Activities
Context-centered item	Social roles
	Physical context
	Social context
	Personal context
	Time
	Healthcare
Total possible score range	0–81

PCAT	
Category	Domain
Specialist medical/ neuropsychiatric needs	Medical/surgical needs
	Neuropsychiatric needs
	Intensity
Clinical needs	Physical needs
	Tracheostomy/ventilatory needs
	Swallowing/nutrition
	Communication
	Cognitive needs
	Behavioral needs
	Mood/emotion
	Complex disability management
	Social/discharge planning
	Family support
	Emotional load on staff
Additional needs	Vocational rehabilitation
	Medicolegal issues
	Specialist equipment/facilities
	Expected duration of admission
PCAT total score range	16–50

RCS-E, Extended Rehabilitation Complexity Scale; OCCAM, Oxford Case Complexity Assessment Measure; PCAT, patient categorization tool

subsequently stressed that this is the ability to benefit. Prior studies regarding case complexity have shown that RCS version 2 score is moderately correlated with the Barthel index (Spearman's rho −0.67, p <0.001)[14], functional independence measure (FIM) motor (−0.72, p <0.001), and FIM cognitive (−0.47, p <0.001) in a neurorehabilitation inpatient cohort[14]. Interestingly, the therapy score of RCS correlated less with the Barthel index and FIM motor (−0.26 and −0.26, respectively)[14]. The PCAT score was moderately correlated with the UK functional measure (Spearman's rho −0.56, p <0.0001) in inpatients with complex neurological disabilities[12]. Therefore, the scales of the complex need for rehabilitation do not capture the extent of disability using the Barthel index or FIM, which is commonly used to define it. Therefore, researchers must distinguish between complex needs and complex disabilities. Medical treatment is a priority in the acute stroke stage. During the rehabilitation period, patients often have problems such as multiple morbidities, behavioral disorders, lack of motivation, and low prospects for outcome. The need for rehabilitation under case complexity can be divided into two components. One is aimed at distinguishing the basic needs derived from primary dysfunctions due to stroke, while other individual needs are based on complex disabilities and contextual factors.

Measurement considerations

The construct of rehabilitation needs is defined as a latent multidimensional variable[10], and the related measurement tools should be psychometrically valid, reliable, responsible, and robust. To visualize a need construct and screen candidates with a higher need, the continuum from multiple items is preferably linear. Therefore, scoring should consist of a Likert scale. Subjective assessment of a patient's demands are sometimes not easily expressed because of advanced age, consciousness disorder, cognitive disorders, aphasia, etc. Therefore, a clinical expert is required to identify rehabilitation needs[12]. Therapists can judge a patient's needs temporarily during early contact after the start of rehabilitation provided they understand the biopsychosocial features of an acute patient. Therapists engage in regular interventions based on the common need for medical necessity. Measurement of rehabilitation needs should not be complicated. A simple and quick method to check items is therefore required.

Clinical Significance of Medical Rehabilitation Need

Enhancement in recovery after stroke

The need for rehabilitation services is difficult to determine[20], and assessing the complexity of rehabilitation needs is a challenge throughout the world[15].

Figure 1 shows the individual differences in potential needs regarding the benefit from rehabilitation inputs. In a neurological rehabilitation setting, healthcare services are

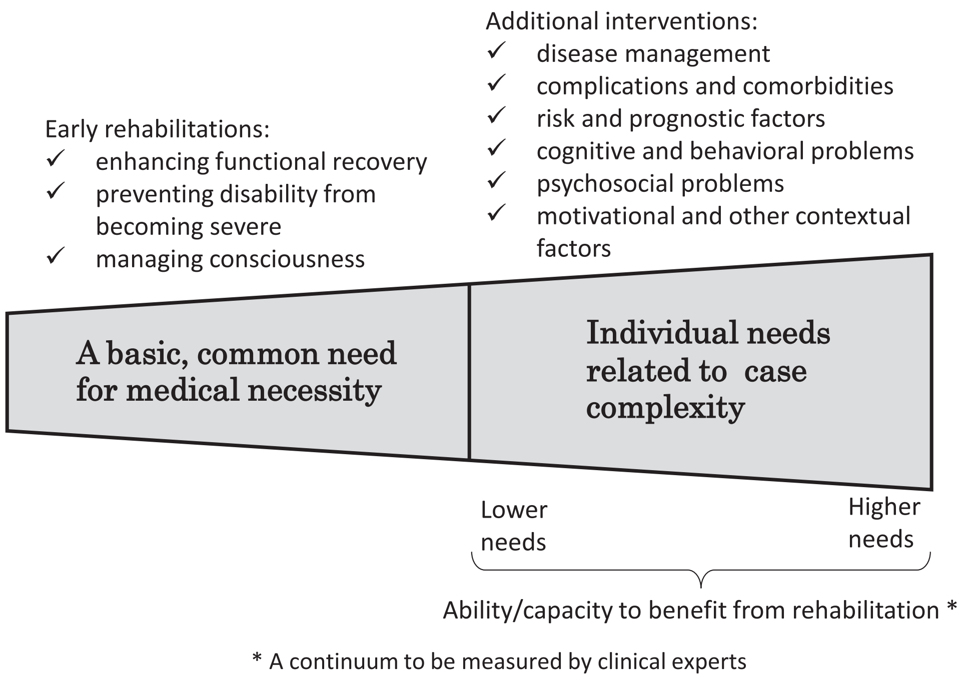

Fig. 1. Visible imaging to measure a latent concept of medical rehabilitation needs in the acute stage after a stroke

prescribed immediately after medical examination following hospitalization. Early rehabilitation for both common and basic needs must be provided based on medical necessity. Rehabilitation need complexity is based on multiple factors, including severity and prognosis, treatment difficulty, and the resources required. Under these difficult situations, most patients undertake therapeutic interventions aimed at enhancing functional recovery, preventing disability from becoming severe, and managing consciousness. Additional interventions are often provided with regard to disease management, complications and comorbidities, risk and prognostic factors, cognitive and behavioral problems, psychosocial problems, and motivational and other contextual factors. The difference in these aspects of need is not small between individuals. Early after stroke, additional intervention for patients with higher needs assumes the enhancement of effects on functional gains in a patient group; however, it is poorly discussed and lacks direct evidence of outcome improvements.

Efficient use of therapist resources

While rehabilitation needs always exist, the total number of needs change, whereas rehabilitation resources (i.e., the number of therapists, applicable time for therapy, available equipment and supplies, and organizational systems/rules) are limited. This raises an important clinical question: How can these resources be used most efficiently? In other words, efficient resource use (i.e., prioritized allocation of therapists' available time for patients in high need) may lead to additional improvements in ADLs independence in an inpatient group after stroke. To maximize clinical outcomes, it would be useful to consider a more advantageous supply of routine rehabilitation services utilizing limited organizational resources. Therefore, visualization of the case differences in need and the process of rehabilitation services can facilitate the control of some resource provisions. This can be used as an instructional material for the quality of healthcare services.

Challenging Issues for Efficient Practice of Stroke Rehabilitation

Identifying a patient with higher needs

Pooling of measurable items is required to identify patients with higher needs. These items must be related to the construct, that is, the ability or capacity to benefit from rehabilitation. Assuming that rehabilitation needs are close to the "positive expectation to reach the goal" or the "conditional situation requiring more assistance," the item contents by the Likert scale may be something like "forward-looking expectation in goal achievement," "less rejective and preclusive reasons to rehabilitation supply," and "educational needs of managing a disease or decreasing risks." The content validity of the items should be carefully confirmed. Patients with a complex need for medical rehabilitation may have lower levels of physical and cognitive independence and require higher recourses[12]. The item scores judged by therapists at baseline must have a positive correlation with the final functional status.

Hypothesis for further functional outcomes/extra functional gains

Many clinicians have recognized the importance of individual differences in patient conditions during the acute period after stroke. However, it is not clear whether consideration of individual differences in patient needs can lead to additional functional gains. Measurements may provide several important tips for the efficient practice of stroke rehabilitation. Quantitative capturing of a continuum (* in Figure 1) of the need construct will allow clinicians to recognize how well the routine services are provided. Clinicians are also accountable for arranging a more flexible method of rehabilitation supply, leading to the expansion of an efficient practice of medical rehabilitation. One possible hypothesis for this is that a better organizational resource arrangement regarding the amount of rehabilitation leads to enhanced functional gains in a patient group. Consideration of patient needs is also helpful for this arrangement. This may bring transparency to the rehabilitation supply process.

A clinical trial to verify these multiple hypotheses

Borschmann et al.[21] previously showed the necessity of identifying a clearer target in stroke recovery trials. First, to screen for those who could benefit from additional rehabilitation and who have relatively high needs, patients must be immediately assessed after admission and rated by clinical experts.

In an acute neurological care unit, rehabilitation resources are allocated based on stroke severity and/or specific treatment needs. Turner-Stokes et al.[12] stated that rehabilitation inputs should be matched as closely as possible to individual patient needs. A supervisor in the rehabilitation department should provide focused guidance for junior staff, to add interventions for high-need patients. Staffing at rehabilitation departments is limited by the national healthcare standards. The standard clinical pathway and intervention techniques in current hospital-based systems must be maintained practically and ethically. Therefore, we should arrange the control of therapy time in the form of an add-on or utilization of the spare time of staff each day.

Researchers must design a randomized controlled trial. Positive rehabilitation outcomes are generally defined by fewer days in the acute care unit and better functional mobility at discharge.

Clinicians' considerations are often not reflected in the maximization of staffing throughput efficiency. Issues aimed at maximizing clinical outcomes (i.e., better functional status of patients after rehabilitation) should be more active. The rational measurement of individual need complexity and purposeful service allocation (i.e., therapist resource utilization) will be key elements in achieving this aim.

Conclusions

This narrative review describes the need for medical rehabilitation and case complexity in stroke rehabilitation and proposes a method to more efficiently enhance recovery in the acute stage after stroke onset. Therapists may appropriately measure the concept of individual complexity around/beyond the basic and common needs for medical necessity and should identify acute patients who could benefit more from additional rehabilitation inputs. Application of this method could enhance the efficacy of healthcare services to manage therapists' allotted time to promote further recovery of acute stroke patients. We further propose that further research trials should be conducted to compare the effectiveness of the arrangement of rehabilitation service allocations based on needs assessment after stroke with the usual care pathway.

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Conflict of Interest: The author reports no conflicts of interest in this work.

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SCIENTIFIC RESEARCH ARTICLE

Predicting the Classification of Home Oxygen Therapy for Post-COVID-19 Rehabilitation Patients Using a Neural Network

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ABSTRACT. Objective: We evaluated the accuracy of a neural network to classify and predict the possibility of home oxygen therapy at the time of discharge from hospital based on patient information post-coronavirus disease (COVID-19) at admission. Methods: Patients who survived acute treatment with COVID-19 and were admitted to the Amagasaki Medical Co-operative Hospital during August 2020–December 2021 were included. However, only rehabilitation patients (n = 88) who were discharged after a rehabilitation period of at least 2 weeks and not via home or institution were included. The neural network model implemented in R for Windows (4.1.2) was trained using data on patient age, gender, and number of days between a positive polymerase chain reaction test and hospitalization, length of hospital stay, oxygen flow rate required at hospitalization, and ability to perform activities of daily living. The number of training trials was 100. We used the area under the curve (AUC), accuracy, sensitivity, and specificity as evaluation indicators for the classification model. Results: The model of states at rest had as AUC of 0.82, sensitivity of 75.0%, specificity of 88.9%, and model accuracy of 86.4%. The model of states on exertion had an ACU of 0.82, sensitivity of 83.3%, specificity of 81.3%, and model accuracy of 81.8%. Conclusion: The accuracy of this study's neural network model is comparable to that of previous studies recommended by Japanese Guidelines for the Physical Therapy and is expected to be used in clinical practice. In future, it could be used as a more accurate clinical support tool by increasing the sample size and applying cross-validation.

Key words: Machine learning, Neural network, COVID-19, Home oxygen therapy, Classification

(Phys Ther Res 25: 99–105, 2022)

The number of people infected with coronavirus disease (COVID-19) caused by severe acute respiratory syndrome coronavirus 2, reported to have been discovered in Wuhan, China, in 2019, was approximately 280 million worldwide at the end of December 2021[1]. The number of people infected in Japan was reported to be approximately 1.7 million as of January 2022[2]. With such a rapid increase in COVID-19 patients, the number of people infected with COVID-19 was expected to increase. This rapid increase in the number of COVID-19 patients has required rehabilitation professionals to provide respiratory rehabilitation for patients with unknown respiratory diseases in healthcare institutions. In March 2020, the Guidelines for acute physical therapy for patients with COVID-19 were published and recognized as the standard for acute rehabilitation of patients with unknown respiratory disease[3]. Several reports have been made on the indication criteria and efficacy of respiratory rehabilitation for patients with COVID-19[4–6]. Not only did critically ill patients lose motor and cardiopulmonary function during their treatment in acute hospitals[7], but further research reports have been needed on the effectiveness of respiratory rehabilitation for patients with COVID-19[5,6,8]. Therefore, predicting the prognosis of post-COVID-19 rehabilitation patients is one of the most challenging tasks for rehabilitation staff in clinical practice. In addition, several previous studies have reported on post-discharge home rehabilitation[9,10],

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and rehabilitation for post-COVID-19 patients may not be completed during the hospital stay. Sardesai et al. reviewed the protocol for home oxygen therapy[11]. These facts make it necessary for rehabilitation staff in clinical practice to predict not only the prognosis of post-COVID-19 patients but also whether they need home rehabilitation or home oxygen therapy after discharge.

In recent years, the medical application of artificial intelligence technology has been attracting attention. Several case studies were reported in which machine learning, a form of artificial intelligence, was used by physical therapists (PTs) and occupational therapists (OTs) in stroke rehabilitation[12,13]. Among machine learning, artificial neural networks have been applied in many fields because of their ability to handle data analysis easily and quickly[14]. Tang et al. proposed an artificial neural network algorithm that can be used for medical classification problems[13]. They reported the effectiveness of the proposed algorithm in classifying upper limb functions by artificial neural networks and stated that the results were highly correlated with the judgments of medical experts. We hypothesized that if machine learning could be applied to the rehabilitation of stable post-COVID-19 patients, it would be possible to predict whether they would require home oxygen therapy at discharge. Although there were several previous studies using artificial intelligence techniques to solve problems caused by the rapid spread of COVID-19[15,16], to the best of our knowledge, there were very few reports of the application of machine learning to assist PTs and OTs in the rehabilitation of post-COVID-19 patients.

The aim of this study was to test whether it was possible to use machine learning to predict the discharge status of post-COVID-19 patients who have survived acute treatment. For this purpose, a binary classification neural network model was constructed using patient data at the time of hospitalization as each input value, and the accuracy of the prediction results was evaluated. If it were possible to predict the future availability of home oxygen therapy based on information at the time of hospitalization, the rehabilitators of post-COVID-19 patients would be able to make the necessary preparations for the patient earlier. Earlier preparations could help to reduce the length of hospital stay for patients.

Methods

Participants

The participants of this study were 103 post-COVID-19 rehabilitation patients hospitalized in the Amagasaki Medical Co-operative Hospital (AMCH) in Japan between August 2020 and December 2021. The patients had been discharged from AMCH by the start of this study. Post-COVID-19 rehabilitation patients in this study are defined as patients who had been diagnosed with COVID-19 at AMCH or another hospital, had completed acute treatment, and had started rehabilitation at AMCH without being discharged to their home or an institution. However, patients whose rehabilitation period after acute treatment was within 2 weeks were excluded because discharge was confirmed at the start of rehabilitation in the following week, and they had already achieved the target condition. Furthermore, patients for whom no study information was provided were also excluded. As a result, 88 participants were finally selected for the study.

Table 1. Physical therapy implementation statistics

	Start (%)	End (%)
ROM exercise	68.2	76.1
Strength training	65.9	60.2
Get up and sit	30.7	19.3
Stand up and stand	30.7	13.6
Gait in parallel bars	12.5	6.8
Gait outside parallel bars	58.0	75.0
Balance control	6.8	6.8
Up and down stairs or steps	23.9	26.1
ADL training	9.1	10.2
Bicycle ergometer	5.7	18.2
Respiratory physiotherapy	18.2	15.9

ROM, range of motion; ADL, activities of daily living

Physical therapy implementation statistics

Based on electronic medical record information, the types of physical therapy given to 88 participants were investigated and are summarized in Table 1. The "start" was defined as the first week of rehabilitation after hospital admission, and the "end" was defined as the last week before hospital discharge. Activities of daily living (ADL) training included movements for excretion, movements in the bathroom, and standing and sitting movements on the floor. Respiratory physical therapy included respiratory instruction, respiratory assistance, assisting sputum discharge, thoracic softening, and respiratory muscle training.

Survey

The information (a)–(g) in the electronic medical records of the participants was studied. The study period was from December 5, 2021 to December 20, 2021. All "hospitalizations" and "discharges" mentioned in this paper were from AMCH.

(a) Age
(b) Gender
(c) Number of days from positive polymerase chain reaction (PCR) test to hospitalization
(d) Number of days between hospitalization and discharge
(e) Oxygen flow rate on hospitalization, at rest and during exertion
(f) Functional independence measure scores on hospitalization
(g) Presence of home oxygen therapy at discharge, at rest, and during exertion

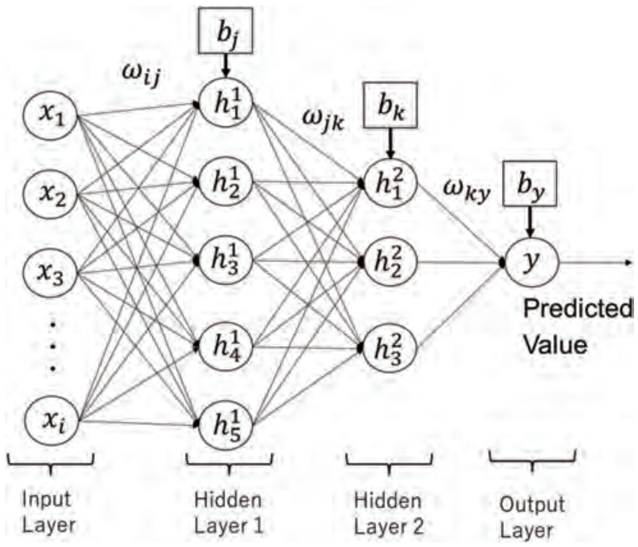

Fig. 1. The neural network model

x_i (i = 1, 2, 3, …, 7): input node. h_j^1 (j = 1, 2, 3, 4, 5), h_k^1 (k = 1, 2, 3): each intermediate node in the hidden layer. y: output node in the output layer. ω_{ij}, ω_{jk}, ω_{ky}: weights between each node of each layer. b_j, b_k, b_y: bias to each node of each layer

Machine learning model

In this study, we used the neural network model as our machine learning. The neural network was implemented based on R for Windows (ver. 4.1.2; R Core Team, 2021), and the "neuralnet" package was used. The neural network constructed in this study is represented in Figure 1. Henceforth, in this paper, "model" refers to this neural network model. Each input node x_i (i = 1,…, 7) in the Input Layer in Figure 1 is inputted with six features from survey items (a) to (f). In this case, i represents the number of input nodes. Hidden Layer is the two-layer structure with 5 and 3 nodes. In Figure 1, h_j^1 (j = 1,…, 5) represents each intermediate node of Hidden Layer 1 and h_k^2 (k = 1, 2, 3) represents each intermediate node of Hidden Layer 2. In this case, j is the number of nodes in Hidden Layer 1 and k is the number of nodes in Hidden Layer 2. In Figure 1, ω_{ij} represents each weight from the Input Layer to Hidden Layer 1, ω_{jk} represents each weight from Hidden Layer 1 to Hidden Layer 2, and ω_{ky} represents each weight from Hidden Layer 2 to Output Layer. b_j and b_k represent the bias of Hidden Layers 1 and 2, and b_y represents the bias of the output node. The last node y represents the output node of Output Layer. In this study, two prediction models were used to predict the state at rest and the state during exertion. For the classification of the prediction of continuation of home oxygen therapy in this study, the output values of y were rounded to the nearest whole number, with a result value of 1 meaning continuation of home oxygen therapy (CON: Continue) and 0 meaning finish of oxygen therapy (FIN: Finish). The learning algorithm for this model was the default, resilient back propagation, and the optimization algorithm was gradient descent[17]. We adopted the logistic (sigmoid) function as the activation function and the cross-entropy as the loss function. For the loss function, equation (1) is used, which is an adaptation of the equation reported by Günther et al. to our model[18].

$$E = -\sum_{l=1}^{L}\left(x_l \log(y_l) + (1-x_l)\log(1-y_l)\right) \tag{1}$$

where E is the value of the error, L is the number of subjects, and l is the number of each subject. x is the observed value obtained from the survey and y is the output value from the model.

Study procedure

The 88 participants were randomly numbered in a sufficiently large range of 1–1000 using the randbetween function in Microsoft Excel 2016 (Microsoft, Redmond, WA, USA). The randomly numbered participants were then rearranged in a descending order and again numbered in order from top to bottom with sample numbers 1–88. Then, following Yeh et al.[19], the top 75% of the sample numbers 1 to 66 were used as training data for the machine learning model and the bottom 25% of the sample numbers 67 to 88 were used as test data for performance evaluation. Among the survey items (a) to (f) of the training and test data, each datum except for (b), which was a binary variable, was normalized by the min–max normalization equation (2):

$$X' = \frac{x - \min(x)}{\max(x) - \min(x)} \tag{2}$$

where x is the training data before normalization and X' is the training data after normalization.

The data from (a) to (f) were used to train the model, using (g), which was one-hot encoded with "CON" set to "1" and "FIN" set to "0", as the teacher data. Each model was trained for 100 trials using the training data, and the model with the largest area under the curve (AUC) during the trials was selected. The performance of the selected model was evaluated by using items (a) to (f) of the test data as input values. The flow of this study is summarized in Figure 2.

Outcome measures

We trained two models, one at rest and one under exertion, with 100 trials each using the training data. After all trials, we selected the model with the largest AUC. We then defined the model of state at rest with the largest AUC as the ESO_2 model and the model of state on exertion with the largest AUC as the EWO_2 model. The output results of the models were used as predictions, and the observed and predicted values were tabulated in a cross-tabulation table to calculate the predicted probability (sensitivity) of CON, the predicted probability (specificity) of FIN, and the accuracy in the ESO_2 and EWO_2 models.

Ethics approval

The study was reviewed by the ethics committee of AMCH. As a result, it was decided that approval by the ethics committee was not required as the study was not a

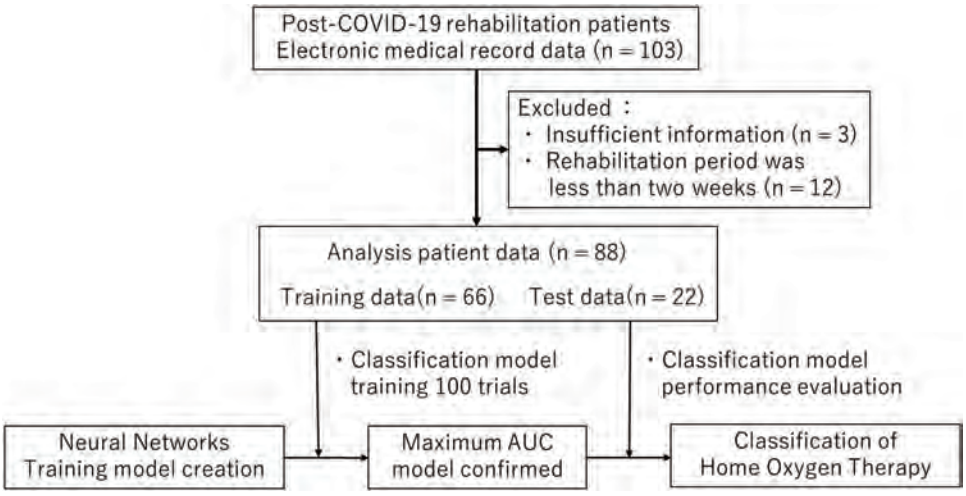

Fig. 2. Schematic diagram of subject data flow and machine learning through the study

Table 2. Summary of survey items

Survey items	Category	Average	SD
Age	–	75.22	11.62
Gender	Male	47 (53%)	
	Female	41 (47%)	
Number of days from positive PCR test to hospitalization (days)	–	8.73	55.32
Number of days from hospitalization to discharge (days)	–	44.25	35.47
Oxygen flow rate at hospitalization (L)	Rest	1.85	7.47
	Exert	2.23	7.51
FIM score at hospitalization (point)	–	76.70	29.50
Oxygen therapy at discharge:	Rest	15 (17%)	
Continue	Exert	27 (31%)	
Oxygen therapy at discharge:	Rest	73 (83%)	
Finish	Exert	61 (69%)	

SD, standard deviation; PCR, polymerase chain reaction; FIM, functional independence measure

clinical trial directly involving human subjects. In addition, the data for this study obtained from electronic medical record information was processed in such a way that personal information could not be identified. Therefore, consent and explanation to all patients for whom the data would be used were exempted based on the decision of the director of AMCH and the chief privacy officer.

Results

The summaries of the survey items (a)–(g) for the participants (n = 88) are shown in Table 2. Both the ESO_2 and EWO_2 models selected in the 100 trials using the training data had a maximum AUC = 0.82, Akaike's information criterion (AIC) = 134.01, and error = 0.006. Table 3 presents a summary of the observed values for CON and FIN for the test data and the predictions calculated from each of the two models. The ESO_2 model predicted 3 out of 4 CON and 16 out of 18 FIN, while the EWO_2 model predicted 5 out of 6 CON and 13 out of 16 FIN. Thus, the ESO_2 model had a sensitivity of 75.0%, a specificity of 88.9%, and a model accuracy of 86.4%. The EWO_2 model had a sensitivity of 83.3%, a specificity of 81.3%, and a model accuracy of 81.8%. The receiver operating characteristic curves of the ESO_2 and EWO_2 models are shown in Figures 3 and 4.

Discussion

Demeco et al. stated that COVID-19 survivors might suffer from severe sequelae and be bedridden in the intensive care unit for long periods[20]. We have seen in practice that the longer the patients stay in the hospital, the more difficult it is for the rehabilitation staff to predict the patient's condition at discharge. In this study, we investigated whether neural networks could be used to help predict the state of patients at discharge in post-COVID-19 patients.

The ESO_2 model selected in this study had a sensitivity of 75.0% and a specificity of 88.9%, while the EWO_2 model had a sensitivity and specificity of 81.3% and 83.3%, respectively. The first edition of the guidelines for physical

Table 3. Classification results in the use of home oxygen therapy

		Predicted		Total
		CON	FIN	
ESO_2 model	CON	3	1	4
Observed	FIN	2	16	18
EWO_2 model	CON	5	1	6
Observed	FIN	3	13	16

Unit: number of samples

CON, Continuation of oxygen therapy at discharge; FIN, Discontinuation of oxygen therapy at discharge

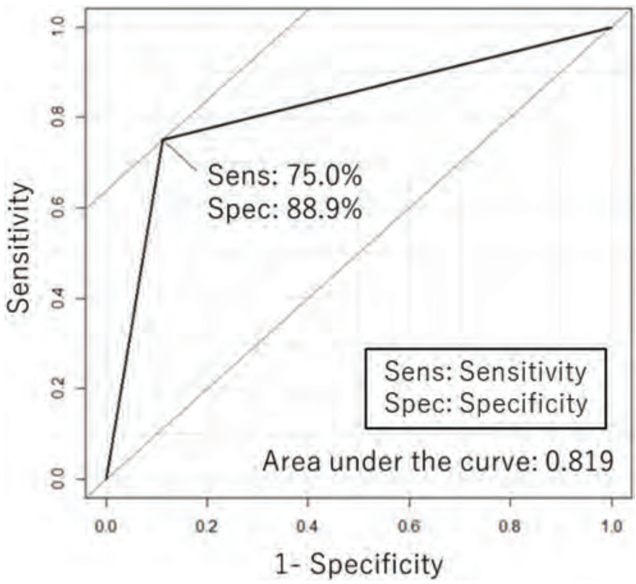

Fig. 3. ROC curve of the ESO_2 model

The classification performance of home oxygen therapy at rest at the time of discharge.

ROC, receiver operating characteristic

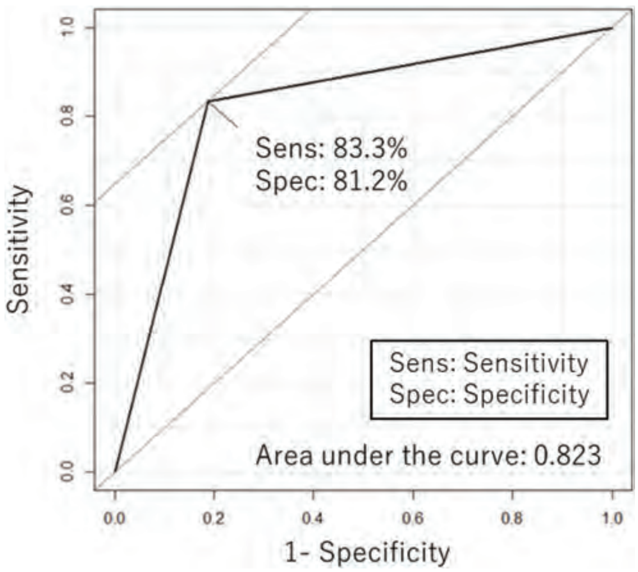

Fig. 4. ROC curve of the EWO_2 model

The classification performance of home oxygen therapy during exertion at the time of discharge.

ROC, receiver operating characteristic

therapy practice developed by the Japanese Physical Therapy Association[21] recommended the "geriatric depression scale" as a Grade A assessment tool with high reliability and validity; the sensitivity of this assessment tool was 0.78 and specificity was 0.85 when used in Parkinson's patients[22]. In addition, the "timed up and go test" was recommended as a Grade A assessment tool by the Japanese Guidelines for the Physical Therapy to classify elderly patients at a high risk of falling[21], and the cut-off value for this assessment tool was reported to be 87% for both sensitivity and specificity[23]. The sensitivity and specificity of the model selected in this study were comparable to those of the recommended Grade A assessment tool of the Japanese Guidelines for the Physical Therapy, and its classification performance was not necessarily poor. However, we don't claim the same reliability for these models as for the recommended Grade A of the guidelines. When referring to the model's accuracy, it is necessary to discuss the sample size.

The sample size that we were able to collect was small because the participants in this study were patients who had survived COVID-19 and were hospitalized at a single institution for rehabilitation. Previous studies reported that it was difficult to collect a sufficient sample size in studies where data were collected on human subjects[24]. It is known that there is a risk of overfitting to noise in the training data when small sample sizes are used in machine learning[25]. However, it cannot be said that the small sample size in this study reduced the model's prediction accuracy of new data. In a literature review of the prediction of brain injury diagnoses using machine learning, Arbabshirani et al. reported that many studies that reported high accuracy had sample sizes of less than 100 (median 88)[26]. In a previous study that surveyed several review articles, Varoquaux reported that the typical sample size was 100 when large datasets were inherently difficult to obtain and that the prediction accuracy of machine learning was higher with smaller sample sizes than with larger ones[27]. However, small sample sizes tended to increase the confidence intervals for prediction accuracy[27], so increasing the sample size was an ongoing issue in our model. The survey items (a)–(f) used as input variables for the model in this study were not research-specific items but instead common data that have been routinely measured in clinical practice. Therefore, the data set could be further expanded in the future. In addition, if we applied cross-validation to the predictive model, we could bring the model closer to the best accuracy from the same data and reduce the risk of deriving an inappropriate model[28]. However, since cross-validation was not applied in this study, it should be noted that there was a risk of overfitting due to biased data.

In a previous study, Lin et al.[29] predicted the ability to perform ADL in post-stroke patients using a machine learning-based method and stated that it was a practical tool in clinical practice based on the predictive accuracy of the results with AUC = 0.79. Makino et al. used logistic regression to predict the degree of progression of diabetic kidney disease[30]. They reported the mean AUC of 0.743 and the mean accuracy of 71%, which could support clinical decisions. Based on these previous studies, we believe that the accuracy of the model in this study has the potential to support predictions made by rehabilitation staff in clinical practice regarding home oxygen therapy in post-COVID-19 patients.

One of the limitations of this study was that comorbidities could not be included in the features. Although comorbidities are known as predictors of the prognosis of COVID-19, the date and classification of comorbidities could not be defined in this study due to the limited amount of information in the electronic medical records. This model was limited to patient information from a single facility. It was also necessary to collect patient information from multiple institutions to make the model more general.

Conclusion

This study evaluated the performance of a neural network model to classify and predict post-discharge home oxygen therapy with and without by inputting information at the time of hospitalization of post-COVID-19 patients into the neural network model. The model's classification accuracy was close to that of previous studies recommended in Japanese Guidelines for the Physical Therapy, and the results are expected to support rehabilitation staff in predicting prognosis regarding post-COVID-19 patients in clinical practice. In the future, we will work with more medical institutions to increase the sample size and apply cross-validation to improve the accuracy of the model further and use it as a more accurate support tool in the clinical setting.

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Conflict of Interest: The authors declare no conflicts of interest.

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PHYSICAL THERAPY RESEARCH

SCIENTIFIC RESEARCH ARTICLE

Sex-related Differences in Exercise Capacity Trends and Determinants after Cardiac Rehabilitation in Patients with Acute Myocardial Infarction

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ABSTRACT. Objective: This study aimed to investigate whether longitudinal changes in exercise capacity in patients with acute myocardial infarction (AMI) differ by sex and clarified what contributed to these differences. Methods: We retrospectively examined the differences in each variable between men and women in 156 patients with AMI (mean age: 65 ± 12 years; 82.0% male) who participated in a 3-month cardiac rehabilitation (CR) program and could be followed-up for exercise capacity 12-months after AMI onset. Sex-related differences in the change in peak oxygen uptake (peak VO_2) at baseline, 3-months, and 12-months after AMI were analyzed. Results: Male patients with AMI were younger and had higher body mass index and employment rate than women. The attendance of the CR program was higher in women (men vs. women; 10 [3–15] vs. 14 [11–24] sessions, p = 0.0002). Women showed a significant lower %change in peak VO_2 after 12 months (men vs. women; 7.8% [–0.49% to 14.6%] vs. 1.3% [–5.7% to 7.5%], p = 0.013). In multiple linear regression analysis, age (β = –0.76, 95% confidence interval [CI] = –1.0 to –0.50, p <0.0001) and female sex (β = –6.3, 95% CI = –9.1 to –3.5, p <0.0001) were negative independent predictors of change in peak VO_2 over 12 months, while CR attendance (β = 0.21, 95% CI = 0.0032–0.42, p = 0.047) and recommended exercise habit after the CR program (β = 2.1, 95% CI = 0.095–4.1, p = 0.040) were positive independent predictors of change in peak VO_2 over 12 months. Conclusion: In female patients, exercise capacity improved during the CR program but decreased to AMI onset levels after 12 months.

Key words: Acute myocardial infarction, Cardiac rehabilitation, Exercise capacity, Exercise habit, Sex difference

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Due to improved medical treatment and better control of cardiovascular risk factors, the mortality rate from acute myocardial infarction (AMI) has declined[1)]. Therefore, more patients require secondary prevention. Cardiac rehabilitation (CR) programs have been shown to improve exercise capacity and decrease hospital readmission and mortality rates in AMI patients[2,3)].

Due to patient education, physical activity increased after AMI onset but returned to pre-AMI level after several years[4)]. Furthermore, only 37%–45.5% of the cohort achieved guideline-directed secondary preventive goals of regular exercise at 1–2 years after AMI[5,6)].

There are sex differences in age and background factors that are related to AMI pathogenesis[7)]. Furthermore, in other countries, women had a lower adherence to CR programs[8)] and are less physically active than men during the first year after AMI onset[4)]. Therefore, to maintain the exercise capacity after CR programs, different strategies need to be employed

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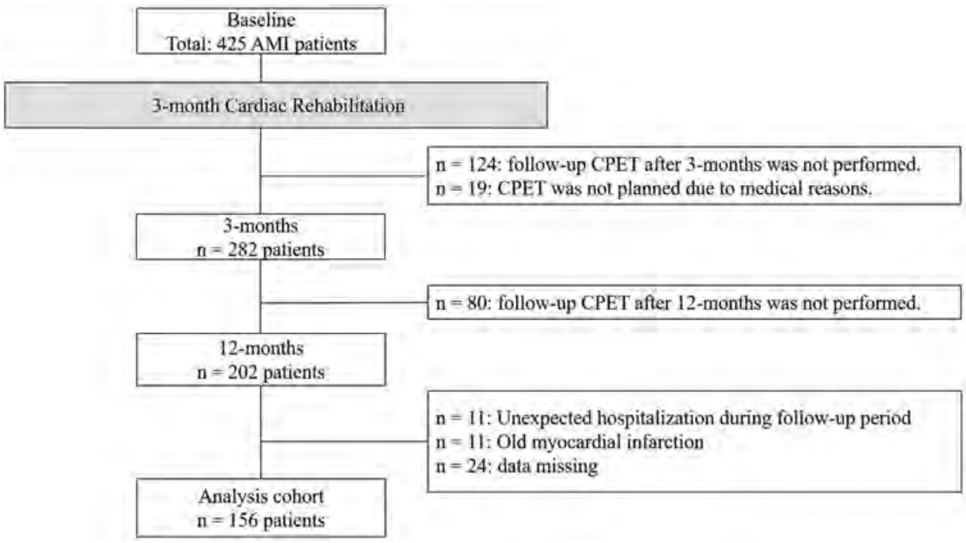

Fig. 1. Flow chart of patient selection

AMI, acute myocardial infarction; CPET, cardiopulmonary exercise test

for men and women. However, it is unclear whether patients enrolled in a CR program can maintain their exercise capacity for 12 months after AMI onset and whether there is a sex difference.

This study aimed to examine whether longitudinal changes in exercise capacity in AMI patients differ by sex and to clarify the factors that contribute to these differences.

Methods

Study design and population

A total of 425 AMI patients were hospitalized at the National Cerebral and Cardiovascular Center between December 2016 and March 2020. Of these, patients who completed the CR program and underwent assessments, including cardiopulmonary exercise test (CPET) at baseline and at the 3- and 12-month follow-ups, were screened retrospectively. Patients were excluded from the study if they were unexpectedly hospitalized during the follow-up period, had an old myocardial infarction (OMI), or had missing data. The study complied with the Declaration of Helsinki and was approved by the Institutional Ethics Committee of the National Cerebral and Cardiovascular Center (M26-015-7). As the need for the requirement of informed consent was waived by the ethics committee, the study was disclosed to patients via opt-outs.

The study design is outlined in Figure 1. Of the 425 AMI patients, 202 met the inclusion criteria. Of these, 46 patients were excluded from the analysis due to unexpected hospitalization (n = 11), OMI (n = 11), and missing data (n = 24). Thus, the final study cohort included 156 AMI patients.

Demographic characteristics and clinical variables of the patients

Demographic data and clinical variables were obtained from clinical records. Demographic characteristics of interest included age, sex, body mass index (BMI), employment status, presence of housemates, and smoking status. Comorbidities included hypertension, dyslipidemia, diabetes, orthopedics, cerebral vascular disease, and peripheral artery disease. Left ventricular ejection fraction (LVEF) was measured using the modified Simpson's method. Clinical variables of interest included the site of infarction, peak creatine kinase (CK) level, family history of cardiac disease, and number of CR attendances.

Cardiopulmonary exercise test

Symptom-limited CPET was performed using a cycle ergometer with respiratory gas exchange monitoring (AE-300S; Minato Medical Science, Osaka, Japan). The CPET consisted of an initial 2 minutes of rest, 1 minute of warm-up (0 W load), and full exercise using an individualized ramp protocol, with increments of 10–20 W/min until symptoms limited patient's performance. Expired gas analysis was performed throughout the testing on a breath-by-breath basis and minute ventilation oxygen uptake (VO_2), and carbon dioxide production data were obtained at 6-second intervals throughout the testing duration. Peak VO_2 was determined as the highest value of either the greatest VO_2 during exercise or the average VO_2 of the last three data points (18 seconds) before termination of exercise. The percentage of predicted peak VO_2 was calculated as peak VO_2 (mL/kg/min) divided by the predicted value using the following equation: $52.1–0.38 \times$ age (years) for men and $40.4–0.23 \times$ age (years) for women[9].

Laboratory analysis

Blood samples were collected to analyze the estimated glomerular filtration rate, hemoglobin, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides, and plasma B-type natriuretic peptide (BNP) levels, and hemoglobin A1c.

Table 1. Demographic and clinical characteristics of the study population

	All (N = 156)	Men (n = 128)	Women (n = 28)	*p*-value
Age (years)*	65 ± 12	63 ± 12	72 ± 8	0.0003
BMI (kg/m^2)†	23.6 (21.3–25.3)	24.0 (21.5–25.7)	21.5 (19.4–23.8)	0.0013
Employment status‡	91 (58)	83 (65)	8 (29)	0.0004
Housemate‡	136 (87)	114 (89)	22 (79)	0.21
Anterior infarction‡	80 (51)	68 (53)	12 (43)	0.40
Peak CK (IU/L)†	1967 (894–3670)	2253 (919–4140)	1343 (694–2104)	0.020
LVEF (%)†	53 (46–58)	52 (45–57)	55 (52–60)	0.0084
Hypertension‡	100 (64)	83 (65)	17 (60)	0.67
Dyslipidemia‡	126 (81)	104 (81)	22 (79)	0.79
Current smoking‡	58 (37)	53 (41)	5 (18)	0.029
Diabetes‡	54 (35)	45 (35)	9 (32)	0.83
Family history‡	47 (30)	38 (30)	9 (32)	0.82
Obesity (BMI ≥25)‡	48 (31)	45 (35)	3 (11)	0.012
Orthopedics‡	35 (22)	25 (20)	10 (36)	0.080
Cerebral vascular disease‡	11 (7)	7 (5)	4 (14)	0.11
Peripheral artery disease‡	3 (2)	2 (2)	1 (4)	0.45
Arterial arrhythmia‡	16 (10)	14 (11)	2 (7)	0.73
β-blocker use‡	121 (78)	99 (77)	22 (79)	1.00
ACE-I or ARB use‡	149 (96)	125 (98)	24 (86)	0.020
CCB use‡	18 (12)	14 (11)	4 (14)	0.71
Statin use‡	155 (99)	128 (100)	27 (96)	0.18
Depressive symptoms‡	12 (8)	9 (7)	3 (11)	0.45
eGFR (mL/min/1.73 m^2)†	65 (56–75)	65 (56–74)	65 (58–78)	0.51
Hemoglobin (g/dL)*	13.0 ± 1.4	13.3 ± 1.4	11.7 ± 0.8	<0.0001
LDL cholesterol (mg/dL)†	81 (64–103)	81 (63–102)	84 (66–107)	0.43
HDL cholesterol (mg/dL)†	37 (31–42)	36 (31–42)	42 (37–50)	0.0022
Triglycerides (mg/dL)†	108 (85–131)	108 (85–131)	99 (77–139)	0.84
HbA1c (%)†	5.9 (5.7–6.6)	5.9 (5.7–6.6)	6 (5.6–6.5)	0.97
BNP (pg/mL)†	79 (44–164)	77 (40–160)	92 (66–248)	0.11
Peak RER*	1.26 ± 0.11	1.27 ± 0.11	1.22 ± 0.10	0.050
Absolute peak VO_2 (mL/min)†	1307 (996–1679)	1447 (1146–1742)	896 (749–1023)	<0.0001
Peak VO_2/BW (mL/min/kg)†	20.1 (17.1–23.6)	20.7 (17.6–24.4)	17.6 (15.4–19.0)	0.0002
%predicted peak VO_2 (%)†	74.8 (65.4–86.6)	75.1 (65.4–87.6)	73.3 (65.4–83.2)	0.64

*Student's t-test; †Wilcoxon rank-sum test; ‡chi-squared test

Variables are expressed as mean ± standard deviation or median (interquartile range) or number of patients (%).

BMI, body mass index; CK, creatine kinase; LVEF, left ventricular ejection fraction; ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; CCB, calcium channel blocker; eGFR, estimated glomerular filtration rate; LDL, low-density lipoprotein; HDL, high-density lipoprotein; HbA1c, hemoglobin A1c; BNP, B-type natriuretic peptide; RER, respiratory exchange ratio; VO_2, oxygen uptake; BW, body weight

Depressive symptoms

Depressive symptoms were assessed using the Patient Health Questionnaire 9-item version (PHQ-9). The PHQ-9 is a well-validated questionnaire for patients with AMI[10,11]. Scores on each item range from 0 (not at all) to 3 (nearly every day). The score for each item was added to obtain the total score. The total scores ranged from 0 to 27, and a cut-off value of ≥10 was used to suggest major depressive symptoms[12].

Home exercise habits

To evaluate home exercise habits during and after the CR program, answers to the following two questions were obtained at the end of the CR program (3 months) and the follow-up (12 months): 1) "How many times a week did you continue the prescribed home exercise?" and 2) "How long did you exercise per session?" The home exercise duration was calculated by multiplying the number of exercises and the exercise time by the weekly exercise time. The patients

Table 2. CR attendance, exercise habit, and changes in exercise capacity during and after the CR program

	All (N = 156)	Men (n = 128)	Women (n = 28)	*p*-value
Number of CR attendance (times)[†]	11 (5–17)	10 (3–15)	14 (11–24)	0.0002
Exercise habit at 3 months[‡] (exercise time ≥150 min/week) (%)	72 (46)	59 (46)	13 (46)	1.00
Exercise habit at 12 months[‡] (exercise time ≥150 min/week) (%)	76 (49)	65 (51)	11 (39)	0.30
%Change in peak VO_2 during CR (%)[†]	5.8 (0.25 to 13.0)	6.3 (0.38 to 14.1)	4.4 (0.25 to 6.6)	0.18
%Change in peak VO_2 after CR (%)[†]	0.26 (–6.6 to 6.4)	0.69 (–6.3 to 6.8)	−1.4 (–7.5 to 3.2)	0.19
%Change in peak VO_2 throughout 1 year (%)[†]	7.1 (–1.9 to 13.8)	7.8 (–0.49 to 14.6)	1.3 (–5.7 to 7.5)	0.013

[†]Wilcoxon rank-sum test; [‡]chi-squared test

Variables are expressed as median (interquartile range) or number of patients (%).

CR, cardiac rehabilitation; VO_2, oxygen uptake

were categorized into two groups: recommended exercise habit (≥150 minutes of light- to moderate-intensity activity each week) and insufficient exercise habit (<150 minutes of light- to moderate-intensity activity each week)[13].

CR program

The 3-month CR program was started approximately 5 days after the AMI event and continued for 12 weeks, 1–3 times per week, according to the patients' convenience. The supervised exercise training consisted of aerobic and resistance exercises. Aerobic training consisted of walking and pedaling on a cycle ergometer, and resistance training consisted of two types of exercises: calf raises and half squats. The intensity of the exercise was determined individually at a workload corresponding to 40%–60% of heart rate reserve (HRR [HRR = peak HR – rest HR]) or anaerobic threshold level based on baseline CPET, or at level 12–13 ("somewhat hard") of the 6–20 scale perceived rating of exercise (original Borg scale)[14]. The initial exercise duration was 20 minutes and gradually increased to 40–60 minutes according to the patients' conditions. Patient education via one-on-one counseling was conducted by doctors and nurses for secondary prevention. Doctors prescribed the home exercise principles and the management status of the coronary risk factors at the beginning of the CR program, and nurses provided monthly counseling and correction methods for the coronary risk factors and lifestyle guidance.

Statistical analysis

The normality of continuous variables was evaluated using the Shapiro–Wilk test. Variables were presented as mean and standard deviation or median and interquartile range for continuous variables and numbers and percentages for categorical variables. For the difference in each variable between men and women, the Student's t-test or Wilcoxon rank-sum test was used for continuous variables as appropriate, whereas the Fisher's exact test was used for categorical variables. Analysis of variance was performed to examine the change in peak VO_2 at baseline, 3 months, and 12 months after AMI onset, and the Tukey–Kramer test was used for post-hoc analysis. Multiple regression analyses were performed between the change in peak VO_2 between baseline and 12 months after AMI onset and other variables of interest, including age, sex, BMI, employment status, presence of housemates, depressive symptoms, smoking status, diabetes, home exercise habit at 12 months, and peak VO_2 at baseline. As a sensitivity analysis, changes in peak VO_2 between baseline and 12 months after AMI onset and exercise habits at 12 months were examined in age-matched patients. Statistical significance was set at $p < 0.05$. All statistical analyses were performed using JMP for Macintosh (Version 14.2; SAS Institute, Cary, NC, USA).

Results

The baseline characteristics of the participants are shown in Table 1. The mean age of the participants was 65 ± 12 years, and 82% of the patients were men. Regarding demographic characteristics, men were younger (mean age, 63 ± 12 years vs. 72 ± 8 years, $p = 0.0003$), had higher BMI (24.0 [21.5–25.7] vs. 21.5 [19.4–23.8] kg/m^2, $p = 0.0013$), and had a higher rate of employment (65% vs. 29%, $p = 0.0004$) compared to women. Regarding clinical characteristics, the proportion of current smokers was higher among men (41% vs. 18%, $p = 0.029$). Compared to women, men had higher peak CK (2253 IU/L [919–4140 IU/L] vs. 1343 IU/L [694–2104 IU/L], $p = 0.020$), lower LVEF (52% [45%–57%] vs. 55% [52%–60%], $p = 0.0084$), higher hemoglobin level (13.3 ± 1.4 g/dL vs. 11.7 ± 0.8 g/dL, $p < 0.0001$), lower HDL cholesterol level (36 mg/dL [31–42 mg/dL] vs. 42 mg/dL [37–50 mg/dL], $p = 0.0022$), and a higher proportion receiving angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers (98% vs. 86%, $p = 0.020$).

Exercise habits and changes in peak VO_2 during and after the CR program are shown in Table 2. The number of CR attendances during the 3-month CR program was higher in women (14 [11–24] sessions vs. 10 [3–15] sessions, $p = 0.00020$). There was no sex difference in exercise habits that

Table 3. Time series of changes in blood sampling data and depressive symptoms throughout the 12 months

	All (N = 156)			Men (n = 128)			Women (n = 28)		
	Baseline	3 months	12 months	Baseline	3 months	12 months	Baseline	3 months	12 months
Depressive symptoms[‡]	12 (8)	6 (4)	9 (6)	9 (7)	5 (4)	6 (5)	3 (11)	1 (4)	3 (11)
eGFR (mL/min/ 1.73 m^2)[†]	65 (56–75)	64 (54–73)	64 (55–73)	65 (56–74)	64 (55–72)	64 (55–72)	66 (58–78)	65 (52–79)	64 (50–78)
Hemoglobin (g/dL)[#]	13.0 ± 1.4	13.6 ± 1.2	13.7 ± 1.3	13.2 ± 1.4	13.8 ± 1.2	13.9 ± 1.3	11.7 ± 0.7	12.7 ± 1.1	12.7 ± 1.1
LDL cholesterol (mg/dL)[†]	81 (64–103)	66 (55–79)*	63 (53–73)*	81 (63–102)	66 (54–79)*	63 (53–72)*	84 (66–107)	67 (58–82)*	63 (53–75)*
HDL cholesterol (mg/dL)[†]	37 (31–42)	47 (41–58)*	49 (42–58)*	36 (31–42)	46 (40–56)*	47 (41–57)*	42 (37–50)	54 (47–65)*	55 (51–70)*
Triglycerides (mg/dL)[†]	108 (85–131)	116 (77–154)	104 (79–157)	108 (85–131)	117 (79–157)	105 (79–167)	99 (77–139)	107 (63–140)	87 (72–123)
HbA1c (%)[†]	5.9 (5.7–6.6)	6 (5.8–6.4)	6.1 (5.8–6.4)	5.9 (5.7–6.6)	6 (5.8–6.4)	6 (5.8–6.3)	6.6 (5.6–6.5)	6.1 (5.8–6.7)	6.1 (5.8–6.8)
BNP (pg/mL)[†]	79 (44–164)	40 (24–81)*	34 (17–65)*	77 (40–161)	36 (21–69)*	32 (17–54)*	92 (67–248)	53 (26–91)*	56 (26–79)*

[#]Student's t-test; [†]Wilcoxon rank-sum test; [‡]chi-squared test

Variables are expressed as mean ± standard deviation or median (interquartile range) or number of patients (%).

*p <0.05 vs. baseline

eGFR, estimated glomerular filtration rate; LDL, low-density lipoprotein; HDL, high-density lipoprotein; HbA1c, hemoglobin A1c; BNP, B-type natriuretic peptide

met the requirement of >150 minutes of exercise per week both at 3 months and at 12 months. Although there was no sex difference in the % change in peak VO_2 during and after the CR program, women showed a significantly lower change in peak VO_2 throughout the 12 months after AMI onset (1.3% [–5.7% to 7.5%] vs. 7.8% [–0.49% to 14.6%], p = 0.013). The blood sampling results and PHQ-9 scores are shown in Table 3. Improvements in LDL cholesterol, HDL cholesterol, and BNP levels were maintained in both groups after 12 months.

The percentage trend of the predicted peak VO_2 is shown in Figure 2. In terms of the % predicted peak VO_2 adjusted for age, sex, and body weight, men reached 80% at 3 months and maintained this level after 12 months, whereas women reached 80% at 3 months, which decreased to <80% of the predicted peak VO_2 after 12 months (men: F = 6.3, p = 0.002; women: F = 1.36, p = 0.26).

In multiple linear regression analysis, age (β = –0.76, 95% confidence interval [CI] = –1.0 to –0.50, p <0.0001) and female sex (β = –6.3, 95% CI = –9.1 to –3.5, p <0.0001) were negative independent predictors of change in peak VO_2 over 12 months, while CR attendance (β = 0.21, 95% CI = 0.0032–0.42, p = 0.047) and recommended exercise habit after the CR program (β = 2.1, 95% CI = 0.095–4.1, p = 0.040) were positive independent predictors of change in peak VO_2 over 12 months after adjusting for baseline variables (adjusted R^2 = 0.27; Table 4).

Sensitivity analysis showed that the change in peak VO_2 between baseline and after 12 months in women was smaller (1.3% [–5.7% to 7.5%] vs. 10.5% [5.7%–16.3%], p = 0.0046) than in age-matched patients (28 women vs. 28 men). On the other hand, women had a lower percentage of recommended exercise habits after the CR program (39% vs. 71%, p = 0.031).

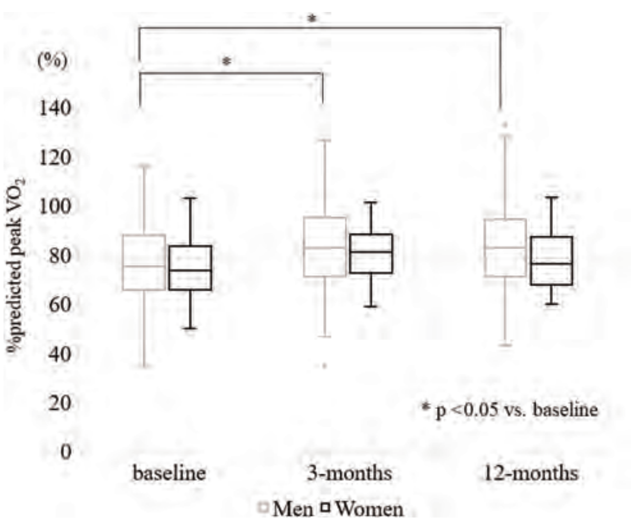

Fig. 2. Trends in the percentage of predicted peak VO_2 throughout 12 months

VO_2, oxygen uptake

Discussion

While the CR program improves exercise capacity in patients with AMI, it is unclear whether patients participating

Table 4. Multiple regression analysis of the correlation between change in peak VO_2 throughout the 12 months and baseline clinical parameters

	Standardized β	β	95% CI	*p*-value
Age	–0.67	–0.76	–1.0 to –0.50	<0.0001
Women	–0.37	–6.3	–9.1 to –3.5	<0.0001
BMI	0.032	0.11	–0.48 to 0.70	0.70
Employment status	0.059	0.78	–1.8 to 3.4	0.55
Presence of housemate	0.080	1.6	–1.16 to 4.3	0.26
Depressive symptoms	0.088	2.2	–1.2 to 5.5	0.21
Current smoking	–0.14	–1.9	–4.0 to 0.14	0.067
Diabetes	–0.13	–1.7	–3.7 to 0.24	0.085
Number of CR attendance	0.15	0.21	0.0032 to 0.42	0.047
Recommended exercise habit after CR	0.16	2.1	0.095 to 4.1	0.040
Baseline peak VO_2	–0.70	–0.022	–0.029 to –0.015	<0.0001

$R^2 = 0.32$, adjusted $R^2 = 0.27$

VO_2, oxygen uptake; β, the unstandardized coefficients of the independent variable; CI, confidence interval; BMI, body mass index; CR, cardiac rehabilitation; R^2, coefficient of determination

in the CR program can maintain their exercise capacity for 12 months after AMI onset. The present study demonstrated that peak VO_2 improved during the CR program and returned to its onset level after 12 months in women. Furthermore, female sex was determined to be a negative factor, and exercise habit after CR was determined to be a positive factor affecting peak VO_2 throughout the 12 months.

Here, home exercise habits after the completion of the CR program were positive factors for exercise capacity 12 months after AMI onset. According to several national clinical guidelines[15,16], the CR program improves exercise capacity in patients with coronary artery disease (CAD). Furthermore, the frequency of performing the CR program correlates with an improvement in exercise capacity[17]. This study showed that exercise habits after CR completion, in addition to CR participation, influenced changes in exercise capacity after CR completion. Although this study analyzed CR program completers, the number of patients who had established appropriate exercise habits after CR completion was low (76 patients, 49%). A previous study reported the influence of subjective factors on the reasons for CR non-participation[18]. Furthermore, a randomized controlled trial revealed that the addition of a behavioral medicine intervention in physiotherapy to a conventional CR program contributed to the maintenance of exercise capacity in patients with CAD[19]. Therefore, it is necessary to further examine strategies to instill exercise habits.

The present study revealed that changes in exercise capacity from the CR initiation to 12 months later differed by sex. In addition to sex, employment status is one of the factors related to a decrease in physical activity after AMI onset[4]. In this study, there were no sex differences in home exercise habits; however, the rate of employment was lower in women than in men. This finding might have resulted in a decrease in the amount of working time associated with physical activity after the CR program, which in turn might have decreased exercise capacity in women. Women are generally older at AMI onset[20], and they were also older in this study. Therefore, age may have an impact on the return of exercise capacity in women. On the other hand, sensitivity analysis showed that differences in exercise habits were observed in age-adjusted patients. This suggested that factors other than age might contribute to the reduced exercise capacity after CR in women, such as leisure time-associated physical activity. Leisure time-associated physical activity affected the long-term results of exercise training[21]. Therefore, the decrease in leisure time-associated physical activity might have contributed to the decrease in exercise capacity in women. To maintain or improve exercise capacity after the CR program, it may be necessary to consider sex differences to improve not only exercise habits but also leisure time-associated physical activity.

To our best knowledge, this is the first study to investigate the longitudinal changes in exercise capacity over 12 months and clarify sex differences in AMI patients. However, this study had some limitations. First, it consisted of CR participants and included only patients who were followed up until 12 months after AMI onset, which might have induced a selection bias. Second, this study was conducted at a single institute with a small sample size. Therefore, sex-specific sensitivity analyses could not be performed. Further studies on a larger scale are needed. Third, because all factors related to adherence, such as income and education, could not be investigated, factors related to sex differences may not have been adequately examined. Finally, since exercise habit is a subjective and insufficiently validated assessment, exercise habits and physical activity might not have been adequately distinguished. Future studies using validated questionnaires or objective indicators, such as the International Physical Activity Questionnaire[22] or accelerometers, are needed.

Conclusion

In conclusion, exercise capacity improved during the CR program and decreased to the onset level after 12 months in women with AMI. Thus, strategies to maintain exercise capacity after a CR program are particularly important for women.

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Conflict of Interest: The authors declare no conflicts of interest.

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PHYSICAL THERAPY RESEARCH

SCIENTIFIC RESEARCH ARTICLE

Relationship between Echo Intensity of Vastus Lateralis and Knee Extension Strength in Patients with Type 2 Diabetes Mellitus

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ABSTRACT. Objective: This study aimed to determine the association between echo intensity (EI) of vastus lateralis and knee extension strength (KES) in patients with type 2 diabetes mellitus (T2DM). Methods: This retrospective study included a total of 304 patients (189 males and 115 females) with T2DM who were hospitalized for treatment or care. EI and muscle thickness (MT) of the right vastus lateralis were assessed from transverse ultrasound images. Maximal isometric KES was evaluated using a dynamometer and normalized for body weight (%KES). Results: %KES was significantly positively correlated with MT and stages of change for exercise behavior, and significantly negatively correlated with age, T2DM duration, and EI. %KES was significantly higher in male than in female. %KES was significantly higher in non-diabetic peripheral neuropathy (DPN) than in DPN. Stepwise multiple regression analysis showed that sex, age, T2DM duration, EI, and stages of change for exercise behavior were significant determinants of %KES. Conclusion: The study results suggest that EI is associated with %KES in patients with T2DM.

Key words: Type 2 diabetes mellitus, Knee extensor strength, Echo intensity

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Muscle strength is lower in patients with type 2 diabetes mellitus (T2DM) than in healthy individuals[1,2]. In addition, the prevalence of sarcopenia and dynapenia is also higher in patients with T2DM than in healthy individuals[3]. Sarcopenia is age-related muscle loss and weakness[4,5]. Dynapenia is also age-related muscle strength impairment without reducing muscle mass[6]. Sarcopenia and dynapenia are geriatric syndromes and recognized as diabetic complications. Muscle weakness, a characteristic of sarcopenia and dynapenia, is associated not only with reduced motor functions but also with falls, frailty, and mortality. Furthermore, knee extension strength (KES) is associated with glucose metabolism and insulin resistance[7,8]. Muscle weakness in patients with T2DM is an important issue that should be improved by exercise therapy.

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Recently, it has been emphasized that muscle quantity including muscle cross-sectional area and muscle thickness (MT), and muscle quality indicated by intramuscular fibrous and adipose tissue are factors that affect muscle strength[9–12]. Excess energy is stored in adipose tissues, but lipids also accumulate in organs other than adipose tissues and are called ectopic lipids. Intramuscular lipids are ectopic fats that accumulate in skeletal muscles and not only cause abnormal glucose metabolism and insulin resistance[13,14] but also affect motor functions such as muscle strength and endurance[15,16]. Therefore, it is considered that an increase in intramuscular lipids deteriorates muscle quality.

Most of the subjects of the study investigating the relationship between KES and muscle quality are healthy elderly people, and there are few studies targeting patients with T2DM. Especially in patients with T2DM, intramuscular lipids increase compared to healthy subjects[17]. The main pathological conditions of T2DM are abnormal glucose metabolism and insulin resistance, and it is important to evaluate muscle quality. Nishihara et al. reported the deterioration of KES in men and women with diabetes compared to that in those without diabetes, but muscle quality deteriorated only in women with diabetes compared to those without diabetes[18]. However, the relationship between muscle quality and KES in patients with T2DM has not been fully clarified. Thus, this study aimed to investigate whether muscle quality is associated with muscle strength in patients with T2DM.

Methods

Participants

A total of 357 patients with T2DM who were hospitalized for treatment or care and underwent exercise guidance at our hospital between February 2015 and October 2016 were recruited to participate in the study. Out of the 357 patients whose motor function was evaluated by the first author, 53 patients with missing data were excluded. Thus, 304 patients (189 males and 115 females) were included in this study. All participants were independent of walking without amputation or blindness. This study was conducted in accordance with the Declaration of Helsinki and approved by the Kansai Electric Power Hospital Ethics Committee (approval number 27-81). This study was announced on our hospital homepage by opt-out.

Assessment of outcome

The relevant descriptive characteristics, including age, height, weight, T2DM duration, hemoglobin A1c (HbA1c), fasting blood glucose level, and fasting blood C-peptide level, were retrospectively extracted from the patients' medical records. Biochemical blood examination was performed on the day of admission, and ultrasonography and muscle strength measurement were performed within 3 days of admission. Body mass index (BMI) was calculated by dividing body weight (kg) by height (m) squared. C-peptide index (CPI), which indicates the insulin secretion capacity, was calculated by dividing the fasting C-peptide level (ng/mL) by the fasting blood glucose level (mg/dL) and multiplied by 100.

Diabetic peripheral neuropathy (DPN) was evaluated using the simple diagnosis criteria proposed by the Diabetic Neuropathy Study Group in Japan[19]. These criteria consist of a prerequisite condition and three neurological examination items. The prerequisite condition includes two items: (1) diagnosed as diabetes mellitus and (2) other neuropathies than DPN can be excluded. The criteria require any two or more of the following three items: (1) sensory symptoms considered to be due to DPN, (2) bilaterally decreased or absent Achilles tendon reflex, and (3) decreased vibratory sensation in bilateral medial malleoli.

Regular exercise was evaluated using the five stages of change for exercise behavior[20]. The precontemplation is the stage of "not engaging in regular exercise and lacking the intention to start exercising in the future." The contemplation is the stage of "having not started exercising yet but committed to taking action within 6 months." The preparation is the stage of "performing minimal exercises but not consistent." The action is the stage of "exercising consistently for less than 6 months." The maintenance is the stage of "exercising consistently for 6 months or more." Regular exercise was defined as exercising for more than 20 minutes per session and more than 2 days per week. Additionally, exercise was defined as intentional exercise for maintaining and improving physical fitness.

In this study, muscle quantity and quality were evaluated using MT and echo intensity (EI). Transverse ultrasound images of the right vastus lateralis were obtained using a B-mode ultrasound imaging device (Noblus; Hitachi, Tokyo, Japan) and a multifrequency linear transducer (10 MHz) (Fig. 1A). The participants were completely relaxed in a supine position with a knee extended. All measurements were conducted with the following settings: a frequency of 8 MHz and a gain of 58 dB. During imaging, the depth was allowed to change according to an individual's muscle size. The transducer was positioned perpendicular to the longitudinal axis of the vastus lateralis at the midpoint between the greater trochanter and lateral epicondyle of the femur[11,12]. The probe's inclination was adjusted so that the surface of the femur and lower fascia of vastus lateralis was clearly visible. A water gel was used to provide acoustic contact, and care was taken to avoid the excessive compression of the dermal surface by the probe. To minimize interobserver variation, all measurements of MT and EI were performed by the same examiner.

The MT of the vastus lateralis was measured using an electric caliper on frozen transverse images as the distance between the upper and lower fasciae of vastus lateralis above the femur (Fig. 1B). The EI was determined by computer-assisted 8-bit gray-scale analysis using the standard histogram function in Image-J (National Institutes of Health, Bethesda, MD, USA). Regions of interest were set in as much of the muscle as possible, excluding the surrounding fascia (Fig. 1C). When the transducer's pressure on the skin was minimized, both lateral ends of the ultrasound image were occasionally unclear. The unclear sections were excluded from the region of interest for EI measurements. The mean EI of the regions was expressed as the value between 0 (black) and 255 (white) (Fig. 1D). If EI is white, it is considered that muscle quality is deteriorated. An ultrasound image of a case with poor MT and EI is shown in Figure 2. An ultrasound image of vastus lateralis was obtained from eight healthy subjects to examine the reliability of our measurements. Then, intraclass correlation coefficients (ICC) (1.1) of MT and EI measurements was calculated using two images of vastus lateralis. ICC (1.1) values were 0.89 for MT and 0.98 for EI.

Maximal isometric KES was evaluated using a dynamometer (μ-TAS F-1; ANIMA, Tokyo, Japan). Measurements were performed in a seated position with the knee and hip flexed to 90°. The bed height was adjusted so that the soles did not touch the floor. The subject was instructed to

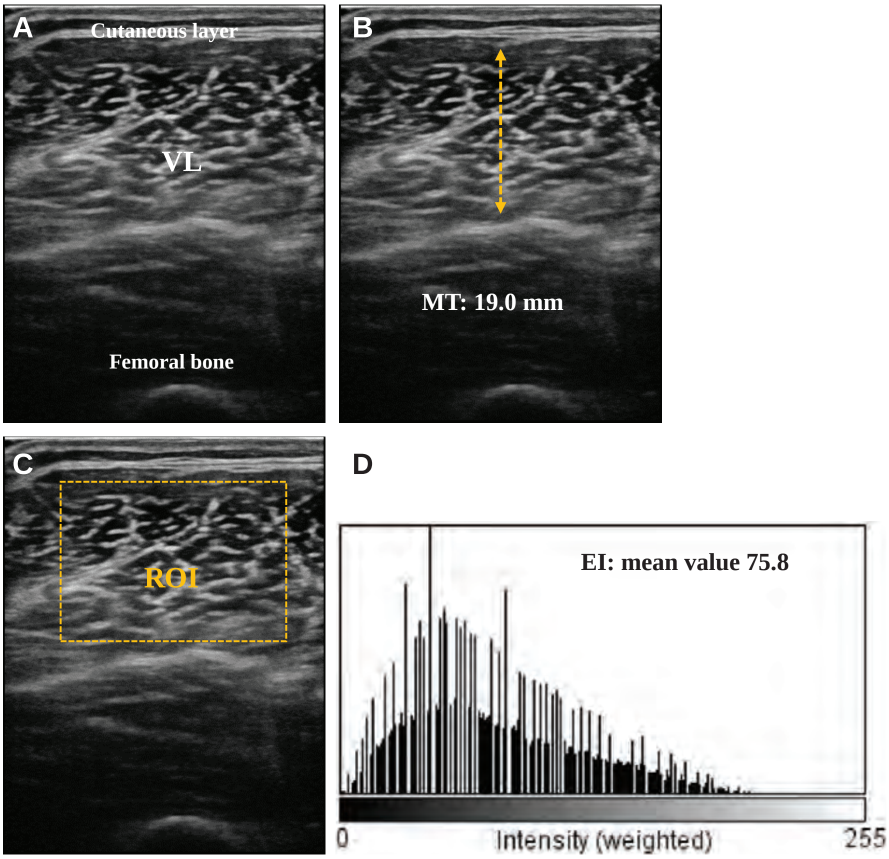

Fig. 1 Measurement of MT and EI of VL

(A) Ultrasound image of VL. (B) MT measurement. (C) ROI setting for EI measurement. (D) Histogram of gray-scale values

VL, vastus lateralis; MT, muscle thickness; ROI, region of interest; EI, echo intensity

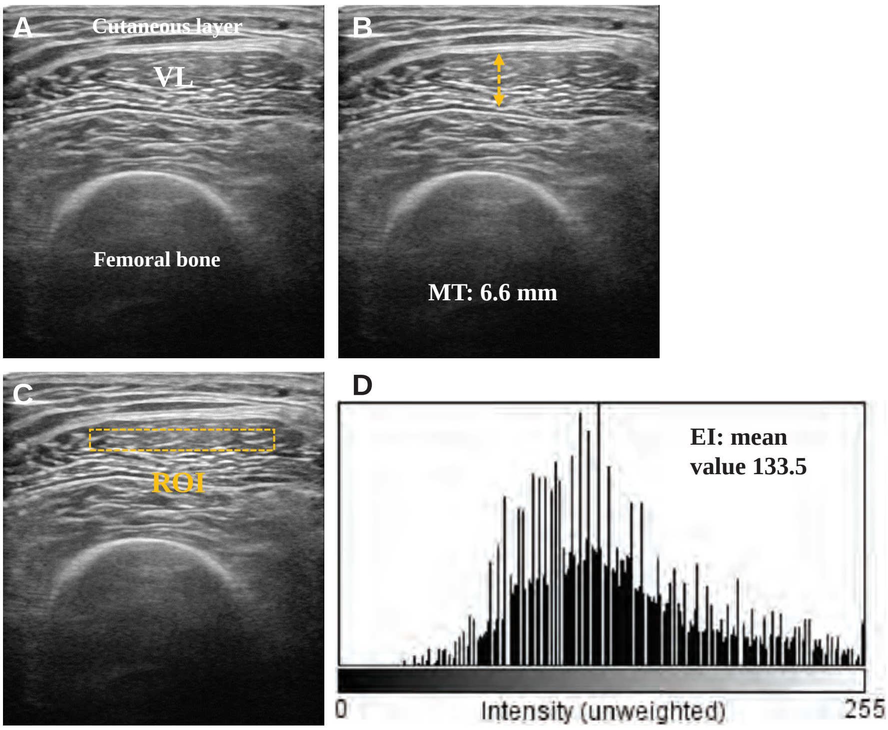

Fig. 2 Presentation of case with poor MT and EI

(A) Ultrasound image of VL. (B) MT measurement. (C) ROI setting for EI measurement. (D) Histogram of gray-scale values

VL, vastus lateralis; MT, muscle thickness; ROI, region of interest; EI, echo intensity hold the trunk vertically and fold both arms in front of the chest. The sensor was applied in front of the distal part of the lower leg and fixed using a belt. Muscle strength of the right lower limb was measured twice, and the higher value was used as KES. KES to body weight ratio (%KES) was calculated by dividing KES by body weight and multiplied by 100.

Statistical methods

The Shapiro–Wilk test was conducted to examine if each variable was normally distributed. Spearman's rank correlation coefficients were used to investigate factors related to %KES. The Mann–Whitney U test was used to compare %KES between the two groups by sex and DPN. Multiple regression analysis was conducted using a stepwise method. Sex was coded as 1 for male and 2 for female. DPN was coded as 0 for absent and 1 for existing. The stages of change for exercise behavior were coded as 1 for precontemplation, 2 for contemplation, 3 for preparation, 4 for action, and 5 for maintenance. Variables that were significantly associated with %KES were incorporated as predictive variables for multiple regression analysis of %KES. Statistical analyses were performed using IBM SPSS Statistics version 26 (IBM Japan, Tokyo, Japan). $P < 0.05$ was considered statistically significant.

Results

Table 1 shows the demographic data of patients with T2DM. The Shapiro–Wilk test determined that a normal distribution was not present for age, BMI, HbA1c, T2DM duration, fasting blood glucose, fasting blood C-peptide, CPI, MT, EI, and %KES ($P < 0.05$). Table 2 shows the correlation with %KES. %KES was significantly positively correlated with MT and stages of change for exercise behavior, and significantly negatively correlated with age, T2DM duration, and EI. %KES showed moderate correlations with EI; weak correlations with age, T2DM duration, and MT; and very weak correlations with stages of change for exercise behavior. Table 3 shows the results of comparison between the two groups by sex and DPN. %KES was significantly higher in male than in female. In addition, %KES was significantly higher in non-DPN than in DPN. Table 4 shows the results of multiple regression analysis with %KES as the dependent variable. Stepwise multiple regression analysis showed that sex, age, T2DM duration, EI, and stages of change for exercise behavior were significant determinants of %KES.

Discussion

This study investigated the relationship between EI of vastus lateralis and %KES in patients with T2DM, and suggested that muscle quality was associated with muscle strength.

EI reflects intramuscular fibrous and adipose tissue, so it is used to evaluate muscle quality[21–24]. Fukumoto et al. and Watanabe et al. reported that EI of the rectus femoris in healthy elderly persons was associated with KES[9,10]. Wilhelm et al. and Rech et al. reported that the EI of the rectus femoris, vastus lateralis, vastus intermedius, and vastus medialis in healthy elderly persons was associated with KES[11,12]. Although the subjects of this study were patients

Table 1. Participants' characteristics

Variables	Values
Sex	Male 189/Female 115
Age (year)	65 (55–72)
BMI (kg/m^2)	26 (23–28)
HbA1c (%)	9.0 (8.0–10.3)
T2DM duration (year)	11 (5–20)
Fasting blood glucose (mg/dL)	145 (119–176)
Fasting blood C-peptide (ng/mL)	1.65 (1.08–2.50)
CPI	1.13 (0.70–1.72)
DPN (%)	195 (64.1)
MT (mm)	17.2 (14.3–20.4)
EI (AU)	87.1 (77.0–97.8)
%KES (%)	48.4 (38.3–58.7)
Stages of change for exercise behavior	
Precontemplation (%)	1 (0.3)
Contemplation (%)	151 (49.7)
Preparation (%)	34 (11.2)
Action (%)	24 (7.9)
Maintenance (%)	94 (30.9)

Values are presented as median (interquartile range) or number (percentages).

BMI, body mass index; HbA1c, hemoglobin A1c; T2DM, type 2 diabetes mellitus; CPI, C-peptide index; DPN, diabetic peripheral neuropathy; MT, muscle thickness; EI, echo intensity; KES, knee extensor strength

Table 2. Simple linear regression analysis for %KES

Variables	r	P
Age	–0.38	<0.001
BMI	–0.09	0.11
HbA1c	0.02	0.69
T2DM duration	–0.29	<0.001
Fasting blood glucose	0.09	0.08
Fasting blood C-peptide	0.003	0.96
CPI	–0.04	0.46
MT	0.35	<0.001
EI	–0.50	<0.001
Stages of change for exercise behavior	0.18	0.001

KES, knee extensor strength; BMI, body mass index; HbA1c, hemoglobin A1c; T2DM, type 2 diabetes mellitus; CPI, C-peptide index; MT, muscle thickness; EI, echo intensity

Table 3. Comparison of %KES between the two groups

Variables	Male	Female	P	DPN	Non-DPN	P
%KES	54.2 (46.2–63.0)	38.7 (31.1–48.0)	<0.001	46.4 (37.0–56.4)	51.4 (43.6–62.5)	<0.001

Values are presented as median (interquartile range).

KES, knee extensor strength; DPN, diabetic peripheral neuropathy

Table 4. Multiple regression analysis for %KES

Variables	B	95% CI for B		β	P	VIF
		Lower	Upper			
Sex	–0.104	–0.134	–0.074	–0.337	<0.001	1.26
Age	–0.003	–0.004	–0.001	–0.191	<0.001	1.45
T2DM duration	–0.030	–0.004	–0.001	–0.186	<0.001	1.25
EI	–0.002	–0.003	–0.001	–0.239	<0.001	1.47
Stages of change for exercise behavior	0.020	0.010	0.029	0.175	<0.001	1.03

$R^2 = 0.44$, adjusted $R^2 = 0.43$

KES, knee extensor strength; B, unstandardized coefficients; CI, confidence interval; β, standardized coefficients; VIF, variance inflation factor; T2DM, type 2 diabetes mellitus; EI, echo intensity

with T2DM, a significant negative correlation was found between EI of vastus lateralis and %KES. MT has been used as an evaluation index of muscle strength in ultrasonography since muscle strength is proportional to muscle cross-sectional area. However, this study showed the usefulness of EI in evaluating factors that affect muscle strength in patients with T2DM.

In this study, MT was not selected, and EI was selected as a factor related to %KES in multiple regression analysis. In studies on healthy subjects, Young et al. and Watanabe et al. reported that EI was associated with intramuscular adipose tissue[23,24]. Pillen et al. reported that EI was strongly correlated with interstitial fibrous tissue, which was measured in biopsy samples[21]. Akima et al. reported that muscle cross-sectional area was the factor predicting the amount of intramuscular adipose tissue and MT was a factor affecting EI[25]. Therefore, these studies suggest that EI can be used as a comprehensive indicator of muscle composition, including intramuscular adipose tissue, fibrous connective tissue, and muscle mass, and may be more useful than MT in assessing muscle strength in patients with T2DM, as decreased skeletal muscle mass and increased intramuscular adipose tissue occur in these patients.

In this study, %KES was not significantly correlated with HbA1c, fasting blood glucose level, fasting C-peptide level, and CPI. In previous studies, it has been reported that KES decreased with the deterioration of HbA1c and fasting blood glucose levels and when HbA1c was 8.0% or 8.5% or more[2,26]. In this study, the median HbA1c was 9.0% and the fasting blood glucose level was high at 145 mg/dL, but HbA1c and fasting blood glucose level did not show a significant correlation with %KES. This study targeted patients who were hospitalized for treatment or care of T2DM and included patients with acute exacerbation of glucose metabolism. Therefore, it is possible that acute deterioration of HbA1c and fasting blood glucose did not affect the decrease in %KES. However, a significant negative correlation was found between the T2DM duration and %KES. Previous studies have reported that KES decreases when the diabetes duration is 6 years or 10 years or more[2,27]. This study included patients with long-term T2DM, with a median duration of 11 years, and chronic glucose metabolism disorders may be associated with decreased %KES.

In this study, there was a significant difference in %KES between the DPN group and the non-DPN group, but it was not extracted as a factor affecting %KES in multiple regression analysis. In the early onset of sensory neuropathy, paresthesia appears at the toes, and paresthesia ascends to the lower legs and thigh. Furthermore, motor neuropathy is usually inconspicuous clinically, but it has been reported that DPN reduces muscle strength in lower extremity muscle strength[28]. In this study, DPN was evaluated using the simple diagnosis criteria proposed by the Japanese Study Group on Diabetic Neuropathy[19]. Although these simple diagnosis criteria are highly valid and useful for daily medical care, evaluation by the nerve conduction test is required to confirm the diagnosis of DPN. The nerve conduction test did not confirm the diagnosis of DPN. These simple diagnosis criteria can determine whether the patients with T2DM suffer from DPN but cannot determine the DPN severity. If the DPN severity is low, DPN may affect the muscle strength of the ankle joint but may not affect the strength of the knee joint due to the difference in the length of the motor nerve. Therefore, DPN may not affect %KES as an independent factor.

In this study, the stages of change for exercise behavior were extracted as a factor affecting %KES. Kojima et al. reported that KES was significantly higher in the elderly group with higher physical activity than in the group with low physical activity[29]. The stages of change for exercise behavior evaluate the implementation status of exercises performed to maintain and improve physical fitness. This study suggested that the continuation of regular exercise is involved in increased %KES since the maintenance of the stages of change for exercise behavior corresponds to those who have continued regular exercise for 6 months or more.

There are some limitations to this study. First, the study participants are patients with T2DM who were hospitalized for treatment or care. Therefore, they have acute deterioration of glucose metabolism that may affect the relationship between glucose metabolism and %KES. Second, the participants were able to walk and were independent of daily living activities, but no detailed evaluation was made regarding locomotor disorders. Therefore, it cannot be ruled out that locomotor disorders may have affected %KES. Third, EI and KES were not examined for healthy subjects in this study, so the difference between healthy subjects and patients with T2DM could not be mentioned. Fourth, in examining the factors that affect KES, the method of measuring EI of the quadriceps femoris by ultrasonography is not unified. In this study, the vastus lateralis of quadriceps femoris was measured, and its relationship with KES was investigated. Rectus femoris is a bi-articular muscle involved in motor control and has a small amount of muscle mass. Vastus intermedius is deep and it is difficult for ultrasonic waves to reach it. Vastus medialis is affected by knee joint disease and is prone to muscle atrophy. Therefore, EI was not measured with these three muscles in this study. Further studies are needed to determine EI of quadriceps femoris in investigating the factor that affects KES.

Conclusion

This study showed that muscle quality in patients with T2DM, assessed based on the EI of skeletal muscle, was related to %KES in multiple regression analysis. This study suggests that EI may be useful for evaluating factors that affect muscle strength in patients with T2DM.

Conflict of Interest: The authors have no conflict of interest to disclose.

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PHYSICAL THERAPY RESEARCH

SCIENTIFIC RESEARCH ARTICLE

Social Network Moderates the Association between Frequency of Social Participation and Physical Function among Community-dwelling Older Adults

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ABSTRACT. Objective: Social participation is an essential component of active aging. Physical dysfunction is restriction of social participation, but it is inconclusive that improvement of physical function contributes to promote social participation. Therefore, understanding the other factor that moderates the association between physical dysfunction and social participation is important, and social network (i.e., ties with family and friends) may be a key factor. The aims of this study were to investigate the association between physical function and frequency of social participation, with social network as a moderator, and to examine the gender differences on the relationships. Methods: We conducted a cross-sectional study among 287 community-dwelling older adults. We asked how often they participated in social groups in a week to measure frequency of social participation. Physical function and social network were measured by using the modified version of Short Physical Performance Battery for community-dwelling older adults and the abbreviated Lubben Social Network Scale, respectively. To investigate the association, we performed a linear regression analysis. Results: After adjustment, a linear regression analysis showed interactions between physical function and social network on frequent social participation (β: –0.20, 95% confidence interval [CI]: –0.40 to –0.01). Furthermore, the same association was observed only in women (adjusted β: –0.33, 95% CI: –0.65 to –0.02). Conclusion: Our results suggested that social network moderates the association between physical function and social participation, and observed gender differences on the relationships. The findings of this study indicated the importance of multidimensional assessment and measures for improving social participation, not only physical function but also social network.
Key words: Social participation, Social network, Social support, Physical function

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Social participation is an essential component of successful aging; public interest in social participation has been increasing yearly[1,2)]. Social participation has positive effects on quality of life and decreases the risk of incidence of functional disability in older adults[3–5)]. A recent study reported that frequent social participation was significantly related to a reduced risk of disability and good self-reported health[6)]. Thus, social participation has an important role on preventing a condition of need for long-term care, and promoting social participation among older adults have become an area to explore through the perspective of preventive physical therapy.

Previous studies have consistently reported that physical dysfunction restricts social participation[7–11)]. Older people with physical dysfunction such as slow gait speed and muscle weakness are likely to restrict mobility, which likely restricts social participation[12)]. Thus, declining physical function is

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a barrier to frequent social participation. Recent meta-analysis suggested that primary care interventions using exercise and nutrition supplementation may reduce physical frailty[13,14], but it is inconclusive that improvement of physical function contributes to promote social participation[15]. Therefore, there may be factors that modify the relationship between physical function and social participation, and understanding these factors is important for maintaining frequent social participation. As an example of this factor, a previous qualitative study about interviews with frail community-dwelling older people suggested that social network is a key factor of social participation[16]. Social network is the measure of ties with family and friends, and promotes social participation[16]. The influence of social network, such as the support and encouragement from friends, plays an important role for participating in activities[17,18]. Previous studies reported that community social networks provide more opportunities for social participation and encourage residents to participate in activities[19]. In addition, a systematic review, investigating barriers and facilitators to social participation, suggested that the size of social network is one of the factors[20], and a longitudinal population-based study suggested that a large social network is associated with a high level of physical function[21]. Therefore, a large social network may weaken the association that physical dysfunction restricts frequent social participation. However, no study has investigated whether a social network moderates the association between physical function and frequency of social participation.

Furthermore, the form of social network differs between men and women. Previous studies suggested that women have a large network with lower density than men; they are likely to maintain connections to family, friends, and neighbors[22–24]. Therefore, women may get the benefit of social network on social participation more than men. Thus, the relationship that social network moderate the association between physical function and social participation may depend on sex.

The first aim of this study was to investigate the association between physical function and frequency of social participation, with social network as a moderator. The second one was to investigate whether the relationship that social network moderate the association between physical function and social participation depended on sex. We hypothesized that the association between physical function and frequency of social participation is weakened for older people with a large social network compared to those with social isolation, and the association may be observed in women than in men.

Methods

Subjects and settings

In this cross-sectional study, 315 community-dwelling older adults aged 65 years or older were recruited from community clubs using flyers. Data collection took place in Kobe city during the period from September to October 2019. The exclusion criterion was scored <24 on the Mini-Mental State Examination (n = 16). A total of 299 participants met all the criteria and were included in the study. The Research Ethics Committee of Kobe University Graduate School of Health Sciences approved the study (No. 625-2), and informed consent was obtained from all subjects prior to participation.

Measurements

Frequency of social participation

Based on previous studies, social participation was defined as participating in at least 1 group of six social groups, which were identified as follows: hobby groups, volunteer groups, senior citizen's club, sports club, political groups, and religious or church groups[3,6,25]. Participants were asked how often they participated in 6 social groups per week on average[26].

Physical function

Physical function was measured by using the modified version of Short Physical Performance Battery for community-dwelling older adults (SPPB-com)[27,28]. It consisted of 3 tests: walking speed, standing balance test, and chair stand test. The sum scores from all three tests were used for analysis, with scores ranging from 0 to 10[28].

Social network

Social network was measured by using the Japanese version of the abbreviated Lubben Social Network Scale (LSNS-6-J)[29,30]. The scale consisted of 6 items, which evaluated the size of a social network in kinship ties and nonkin ties. The test was scored on a Likert-scale that ranged from 1 to 5 for each question, with a maximum achievable score of 30. This scale could calculate subscale (family subscale and friend subscale) with a maximum score of 15. Social isolation was defined as a LSNS-6-J score <12, and social isolation on each subscale was defined as a score <6[29]. LSNS-6-J has been shown to have good reliability and validity for Japanese[30].

Demographic and confounding factors

Data on the following demographic and confounding factors were recorded: age, gender, years of education, people living together (yes or no), depressive symptoms, and self-reported comorbidities (hypertension, stroke, hyperglycemia, diabetes, cardiovascular disease, respiratory illness, cancer, hip osteoarthritis, knee osteoarthritis, osteoporosis, and spinal disk herniation). Depressive symptoms were measured using the Geriatric Depression Scale-15 (GDS-15)[31]. A GDS-15 score ≥6 was defined as a depressive symptom[32]. Number of comorbidities were calculated from self-reported comorbidities and categorized into three groups: none, one, and two or more.

Statistical analysis

To describe the demographic characteristics of participants, we calculated means (standard deviation) for age,

Table 1. Demographic characteristic of participants

Variables	All participants N = 289	Men n = 115	Women n = 174	*p* value
Age (years)	76.6 ± 5.5	77.0 ± 5.5	76.3 ± 5.6	0.285
Years of education (years)	12.6 ± 2.2	13.1 ± 2.7	12.2 ± 1.8	<0.01
Frequency of social participation (day)	2.6 ± 1.3	2.5 ± 1.4	2.7 ± 1.1	0.04
SPPB (points)	6.8 ± 2.2	6.7 ± 2.1	6.8 ± 2.2	0.75
Social isolation†	52 (18.0)	23 (20.0)	29 (16.7)	0.47
People living together				<0.01
No	69 (23.9)	6 (5.2)	63 (36.2)	
Yes	220 (76.1)	109 (94.8)	111 (63.8)	
Depressive symptoms	37 (12.8)	29 (25.2)	8 (4.6)	<0.01
Number of comorbidities				<0.01
None	77 (26.6)	17 (14.8)	60 (34.5)	
One	89 (30.8)	43 (37.4)	46 (26.4)	
Two or more	123 (42.6)	55 (47.8)	68 (39.1)	
Self-reported comorbidities				
Hypertension	143 (49.5)	62 (53.9)	81 (46.6)	0.22
Stroke	12 (4.2)	7 (6.1)	5 (2.9)	0.23
Hyperglycemia	84 (29.1)	42 (36.5)	42 (24.1)	0.02
Diabetes	40 (13.8)	20 (17.4)	20 (11.5)	0.16
Cardiovascular disease	30 (10.4)	15 (13.0)	15 (8.6)	0.23
Respiratory illness	27 (9.3)	10 (8.7)	17 (9.8)	0.76
Cancer	54 (18.7)	29 (25.2)	25 (14.4)	0.02
Hip osteoarthritis	7 (2.4)	2 (1.7)	5 (2.9)	0.71
Knee osteoarthritis	55 (19.0)	19 (16.5)	36 (20.7)	0.38
Osteoporosis	44 (15.2)	11 (9.6)	33 (19.0)	0.03
Spinal disk herniation	16 (5.5)	7 (6.1)	9 (5.2)	0.74

Data are expressed as mean (standard deviation) or n (%).

†Social isolation was defined as LSNS-6-J score <12.

SPPB, short physical performance battery; LSNS-6-J, Japanese version of the abbreviated Lubben Social Network Scale

years of education, the frequency of social participation, and physical function. Gender, social isolation, people living together, and the number of comorbidities were calculated as a percentage of the total number of people (%). Descriptive statistics of the gender differences were examined using chi-square tests for the categorical variables and t-tests for the continuous variables.

We conducted a linear regression analysis to investigate the interaction of physical function and social network on frequency of social participation. The dependent variable was frequency of social participation and the independent variables were physical function (SPPB-com score), social network (large social network or social isolation), and interaction term (physical function × social network). The following variables were adjusted as confounding variables: age, gender, year of education, people living together, depressive symptoms, and number of comorbidities. In addition, a sub-group analysis was performed to examine the relationship between physical function and frequency of social participation in each sub-group of the social network, and the interaction of social network groups was assessed. As a visual aid to interpret the interaction, simple regression lines between physical function and frequency of social participation were shown for each sub-group of social network.

These analyses were also performed for each sex because the form of social network differs between men and women. All confounding variables were selected based on previous studies[6,9,33]. Beta-values, 95% confidence interval (CI), and the adjusted determination coefficients (R^2) were calculated using linear regression analysis.

Statistical significance was set at p <0.05, and all analyses were conducted using R version 3.6.1 (R Core Team, 2019).

Results

Demographic characteristics of participants

Of 299 participants, older adults who had missing data in independent, dependent, and confounding variables were excluded (n = 12), and 287 older adults were included the analysis. Table 1 shows the characteristics of the participants.

Table 2. Association of social participation with the interaction of physical function and social network

	Unadjusted analysis			Adjusted analysis§		
	Beta	(95% CI)	Adjusted R²	Beta	(95% CI)	Adjusted R²
SPPB (points)	0.20*	(0.02 to 0.37)	0.20	0.19*	(0.02 to 0.37)	0.25
Social network†	2.00*	(0.70 to 3.31)		1.99*	(0.67 to 3.31)	
SPPB (points) × Social network	–0.21*	(–0.40 to –0.01)		–0.20*	(–0.40 to –0.01)	

§Adjusted for age, gender, years of education, people living together, depressive symptoms, and number of comorbidities

†Social network was divided into two groups: social isolation (Ref.) or decent social network.

*p <0.05

CI, confidence interval; SPPB, short physical performance battery

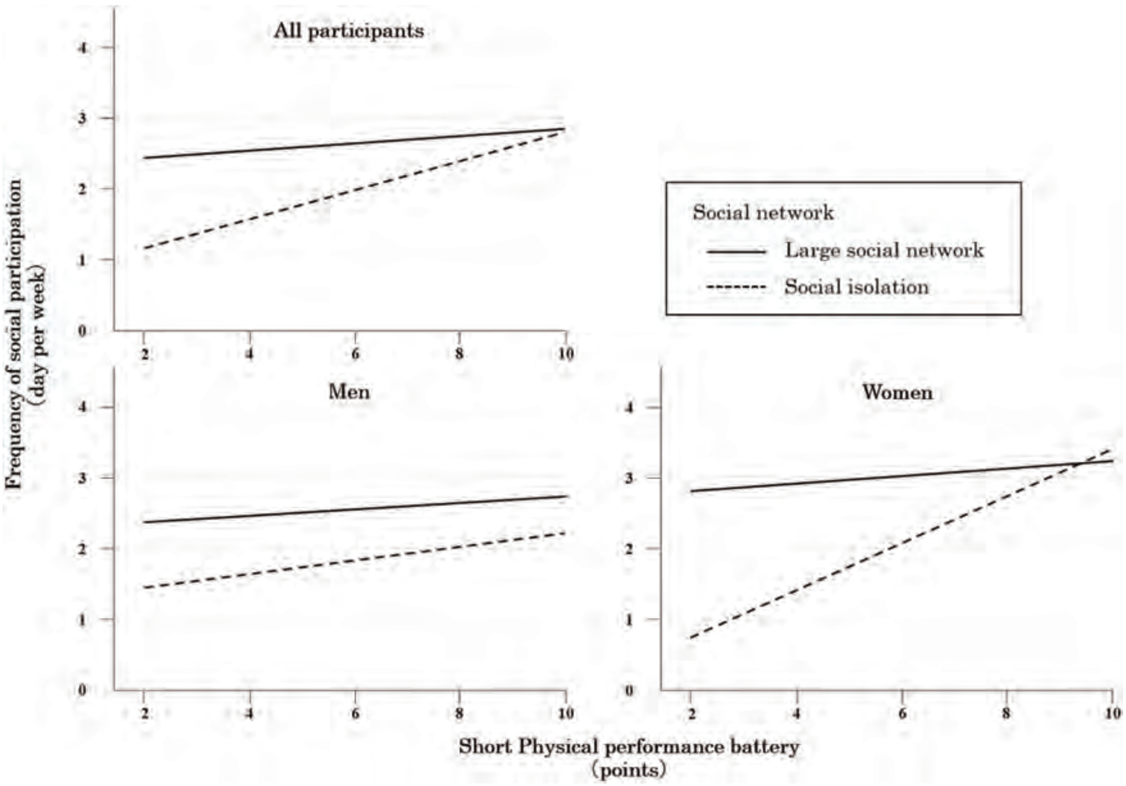

Fig. 1 Association between physical function and frequency of social participation with social network as a moderator

The subjects had a mean age of 76.6 ± 5.6 years and female were 60.2%. The mean number of days for social participation was 2.6 ± 1.3; the score for SPPB-com was 6.8 ± 2.2; 18.0% of the participants were in social isolation. The frequency of social participation was significantly higher in women than in men (p = 0.04). None of the subjects were older adults who had certification of long-term care need.

Association of social participation with the interaction of physical function and social network

Table 2 shows the results of the linear regression analysis. In the adjusted model, a higher level of physical function was associated with a higher frequency of social participation (adjusted beta: 0.19, 95% CI: 0.02–0.37), and a large social network was associated with a higher frequency of social participation (adjusted beta: 1.99, 95% CI: 0.67–3.31). Furthermore, the interaction of physical function and social network on frequency of social participation was observed (adjusted beta: –0.20, 95% CI: –0.40 to –0.01). Figure 1 shows the simple regression lines between physical function and frequency of social participation for each group of social network. The association between the physical function and frequency of social participation differed with the social network size.

Association of social participation with the interaction of physical function and social network: sex-stratified analysis

Table 3 shows the results of the stratified analysis. In adjusted analysis, the interaction of physical function and

Table 3. Association of social participation with the interaction of physical function and social network: stratified analysis

	Men (n = 115)			Women (n = 174)		
	Adjusted beta	(95% CI)	Adjusted R^2	Adjusted beta	(95% CI)	Adjusted R^2
SPPB (points)	0.06	(–0.12 to 0.30)	0.11	0.26*	(0.01 to 0.55)	0.45
Social network†	1.40	(–0.30 to 3.09)		3.07*	(0.89 to 5.25)	
SPPB (points) × Social network	–0.12	(–0.39 to 0.14)		–0.33*	(–0.65 to –0.02)	

Adjusted for age, years of education, people living together, depressive symptoms, and number of comorbidities

†Social network was divided into two groups: social isolation (Ref.) or decent social network.

*$p < 0.05$

CI, confidence interval; SPPB, short physical performance battery

social network on frequency of social participation was observed in women (adjusted beta: –0.33, 95% CI: –0.65 to –0.02), not in men (adjusted beta: –0.12, 95% CI: –0.39 to 0.14).

Sub-group analysis of social network

Supplementary Table 1 shows the results of linear regression analysis for each sub-group of social network. Even after adjustment, a significant association between physical function and the frequency of social participation was observed in each sub group of social network among all participants and women. Furthermore, the interaction of social network groups was significantly observed among all participants and women (all participants, *p* for interaction = 0.04; women, *p* for interaction = 0.01).

Discussion

The cross-sectional study investigated the association between physical function and the frequency of social participation, with social network as a moderator. Previous studies have shown the results that physical dysfunction was associated with the restriction of social participation[7–11]. As expected, this study showed that a lower level of physical function was associated with a low frequency of social participation. Furthermore, this study showed new findings that a large social network weakens the association that lower level of physical function restricts frequent social participation, and the same association showed only among women in sex-stratified analysis. About the relationship among physical function, social network, and social participation, a previous qualitative study mentioned that social network may be a key factor of social participation among frail older people[19]. However, no study has actually investigated whether social network moderates the association between physical function and frequency of social participation in community-dwelling older people, and examined the differences between men and women. Although social participation is an important component of active aging, it can easily be restricted by physical dysfunction. Therefore, clarifying the factors that it may enable to participate in social activity frequently even in those with physical dysfunction is important. Thus, our findings expanded on the findings of previous studies and provided the value of focusing on social network to promote social participation.

Our findings suggested that a social network moderates the association between physical function and frequency of social participation, suggesting the importance of social network on social participation among older people with declining physical function. This result was likely to be related to extensive support provided by a large social network. The reasons why physical dysfunction can restrict social participation includes the burden of mobility. It increases, especially among older people with physical dysfunction; as a result, they participate in social activity less frequently[9,34]. Therefore, it is difficult for older people with physical dysfunction to participate in social activity on their own, and they need physical and mental support. Previous studies have suggested that support from friends and neighbors facilitated social participation among frail older people[17], and the mental support such as encouragement from friends plays an important role in participating for activities[18,19]. Furthermore, the larger the social network, the more opportunities they have of receiving support from family, friends, and neighbors[35,36]. Thus, extensive support provided from a large social network may help older people to participate in social activity.

Moreover, the importance of social networks in social participation was suggested, especially among older women. We proposed the hypothesis that gender difference would depend on the size of our social network, because women have a larger social network than men[22–24]. However, no significant gender difference on the size of social network was observed. Other gender differences on social network include the types of people with whom older people connected. In previous studies, women are likely to maintain social network with friends and neighbors in the community, while men have continuous high density of network developed at midlife such as colleagues at work[37,38]. Social activity generally takes place in a community area, and participants are also residents of the community area. Therefore, women with more connections in the community are more likely to receive support when they participate in social activity. Moreover, previous studies suggested that women are more likely to ask for support and accept support from other people than men[39,40]. Men tend to choose administrative supports and avoid requesting their family and relatives for assistance[41]. Thus, gender differences on thought about support may also have an effect. However, this study has investigated the size of social network, not the types of people with whom older people connected and support. A previous study has also showed that types of social activities that have a positive impact on views of self-reported health differ by gender[6]. Further investigation is necessary to include the information about social support and types of social participation.

These days, community activities such as “kayoino-ba,” which is the measure for long-term care prevention among older adults by Japanese central and local governments, have been widely developed[42,43], and physical therapists are often involved as one of the community approaches to prevent a condition of need for long-term care. Our findings may help the community approach such as promoting social participation, suggesting the importance that physical therapists focus not only on physical function but also on social network.

Our study has some limitations. First, its cross-sectional design prevents the establishment of any causal associations. Therefore, a longitudinal study with a longer follow-up is required to uncover bidirectional associations. Second is selection bias of subjects. Participants were recruited from community clubs, and it may include many people who are already participating in a social activity. As can be seen from the high mean score for the SPPB-com score, our participants were also relatively healthy. Thus, the results of the present study should be interpreted with caution, so as not to underestimate the results. Further research including frail older people who are restricted social participation is required. Third, this study has no information about activities of daily living (ADL) that might affect social network and social participation. However, as the participants were relatively healthy, the effect of decline in ADL may be small. Fourth, considering the present study investigated the interaction of physical function and social network on frequency of social participation, there is also the possibility that physical function moderated the association between social network and social participation. To increase the certainty that social network is a moderator, further study is needed to identify the direction of the effect of social network and physical function on social participation.

Conclusion

In this cross-sectional study, social network moderates the association between physical function and frequency of social participation. The findings of this study indicated the importance of multidimensional assessment and measures for promoting social participation, not only physical function but also social network.

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Conflicts of interest: The authors declare no conflict of interest.

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Supplementary Material (Appendix)

All supplementary files are available online.

Supplementary Table 1. Associations between frequency of social participation and physical function: subgroup analysis of social network

PHYSICAL
THERAPY
RESEARCH

SCIENTIFIC RESEARCH ARTICLE

Effect of Electrical Muscle Stimulation on Vascular Endothelial Function during Prolonged Sitting

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ABSTRACT. Objective: While prolonged sedentary behaviors (SBs) increase cardiovascular disease (CVD) risk, interrupting prolonged sitting (PS) with frequent light exercise reduces arterial functional decline. Skeletal muscle electrical stimulation (EMS) enhances peripheral circulation through passive muscle contraction, suggesting that EMS reduces CVD risk by providing an alternative to active exercise for prolonged SBs. This study aimed to investigate the effects of EMS to skeletal muscles during PS on the endothelial function of the brachial artery (BA). Methods: Study participants included 12 healthy adult men who were subjected to 15 min of supine rest, followed by 1 h of PS only (control [CON] trial), or 20 min of EMS to the lower extremities at 50% of the maximum tolerance intensity during PS (EMS trial). Flow-mediated dilation (FMD) of the BA was measured before and 30 min after PS, and normalized FMD (nFMD) was calculated. Results: The nFMD of the CON trial significantly decreased 30 min after PS completion (6.21% ± 1.13%) compared with that before PS (7.26% ± 0.73%), and there was no significant change in the EMS trial before and after PS. The EMS trial showed a significant increase in the nFMD 30 min after PS completion (1.14 ± 0.77) compared with that before PS (0.84 ± 0.43). However, no significant difference was observed in the CON trials. Conclusion: Passive contraction of the lower extremity muscles by EMS increases BA nFMD, suggesting that prolonged sedentary lower extremity EMS use may reduce the risk of vascular endothelial dysfunction.

Key words: Electrical muscle stimulation, Endothelial function, Flow-mediated vasodilation, Prolonged sitting

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Most international physical activity guidelines recommend that adults engage in at least 150 minutes of moderate-intensity physical activity per week for health promotion and prevention of lifestyle-related diseases[1)]. Those who do not adhere to this recommendation are considered physically inactive, accounting for 27.5% of the population in other countries[2)]. Technological innovations and changes in the work environment, such as the mechanization of work, long hours of TV viewing or desk work, low-intensity physical activity, or sedentary behaviors (SBs), account for most of the waking hours in a day[3)].

The prevalence of such physical inactivity has been exacerbated by the recent increase in home-based work modules and restrictions on movement due to the COVID-19 pandemic[4)]. Studies on SB have shown that they are directly related to hypertension, obesity[5)], decreased blood flow to the lower extremities, decreased shear stress (mechanical stress on the vascular wall that reflects vascular endothelial function) resulting in reduced flow-mediated dilation (FMD)[6)], and an increased risk of atherosclerosis and cardiovascular disease (CVD)[7)]. Furthermore, since prolonged sitting (PS) increases the risk of total mortality, even when the recommended amount of physical activity is met[8)], it is urgent to promote the primary prevention of SB from the viewpoint of preventive and industrial rehabilitation.

FMD is an indicator of vascular endothelial function and an independent predictor of CVD[9)]. It has been reported that

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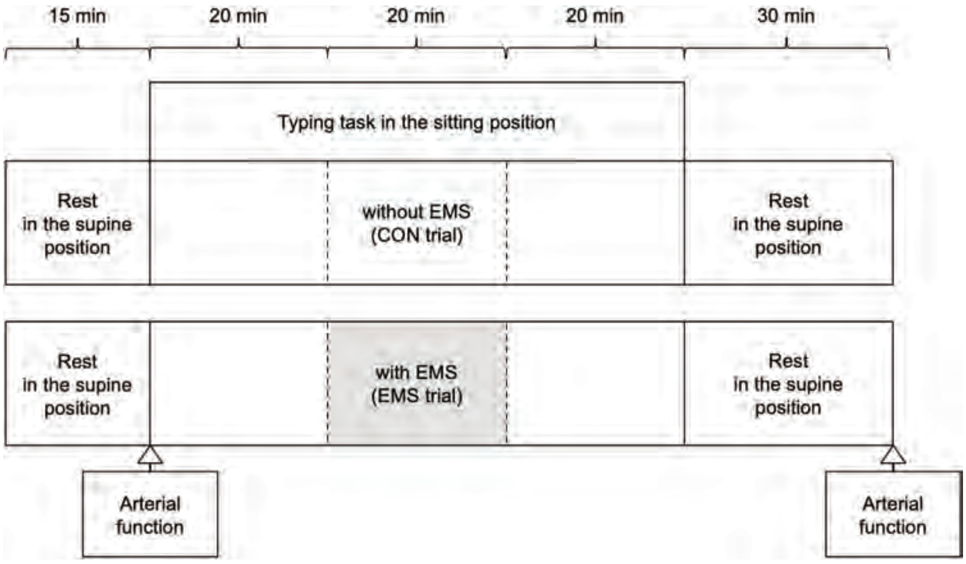

Fig. 1 Experimental protocol of test sessions

All subjects performed each test in random order.

Arterial function measurements: SBP, DBP, HR, Di, FV, and FMD

EMS, electrical muscle stimulation; CON, control; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; Di, vessel diameter; FV, blood flow velocity; FMD, flow-mediated dilation

vascular endothelial function is impaired by SB, hypertension, and obesity and can be improved by lifestyle modifications[9]. Endothelial dysfunction is one of the earliest pathological changes in the etiology of atherosclerosis and is associated with increased cardiovascular risk[10,11], a valid and noninvasive physiological indicator widely used as a research tool to quantify endothelial function[10]. Increased blood flow velocity due to exercise induces mechanical and shear stress in vascular endothelial cells. These cells release endothelium-dependent vasodilators such as nitric oxide (NO), which relaxes vascular smooth muscle, causing vessels to dilate[10]. The effects of SB on vascular function have been reported previously.

Prolonged SB negatively affects vascular function and the development of CVD; however, interrupting SB with frequent light physical activity has been shown to reduce the risk of CVD. In a previous study, while the endothelial function of the superficial femoral artery decreased after 3 h of SB, this functional decline was suppressed by intervals of physical activity during SB[12]. Additionally, two physical activity sessions during breaks in prolonged SB significantly reduced FMD of the popliteal artery compared with the condition without physical activity[13]. However, the physical activities conducted to interrupt PS in these previous studies were intermittent aerobic exercises primarily designed for the lower extremities, involving treadmills, bicycle ergometers, and similar equipment. Additionally, it is difficult for workers who are forced to sit for long periods, such as those working at desks, to incorporate these activities into their daily lives because of the problems in securing the time, places, and equipment to perform the exercises. In contrast, the use of other dynamic exercises, such as electrical stimulation, as an alternative to active exercises may lead to a decrease in vascular endothelial function risk.

Electrical muscle stimulation (EMS) of skeletal muscles has been reported to glucose metabolism and energy consumption[14,15] in transient and interventional studies. Similarly, EMS has been shown to activate endothelial nitric oxide synthase (eNOS), a vasodilator; induce endothelium-derived vasodilation; and increase blood flow[16]. Therefore, it is suggested that EMS during prolonged sedentary activities, as an alternative to active exercises, such as bicycle pedaling and jogging, can reduce the risk of decline in vascular endothelial function.

Therefore, this study aimed to investigate the assumption that EMS of the lower extremity can reduce the endothelial function of the brachial artery (BA) during PS.

Methods

Participants

The study participants were 12 healthy adult men (age: 21.6 ± 1.8 years, height: 173.7 ± 6.6 cm, weight: 67.4 ± 6.2 kg, body mass index: 22.3 ± 1.6 kg/m^2) who had never smoked or taken any regular medications. This study was approved by the Research Ethics Committee of the Department of Physical Therapy, Faculty of Health Science, Osaka Yukioka College of Health Science (#33-0005), Japan. Additionally, the participants were provided with an oral explanation of the content and purpose of the study, refusal, withdrawal, and interruption of participation, and the study was initiated with their consent.

Protocol

The protocol for each trial is shown in Figure 1. All participants were randomly assigned to either EMS of the skeletal muscle or the control (CON) trial, with a minimum

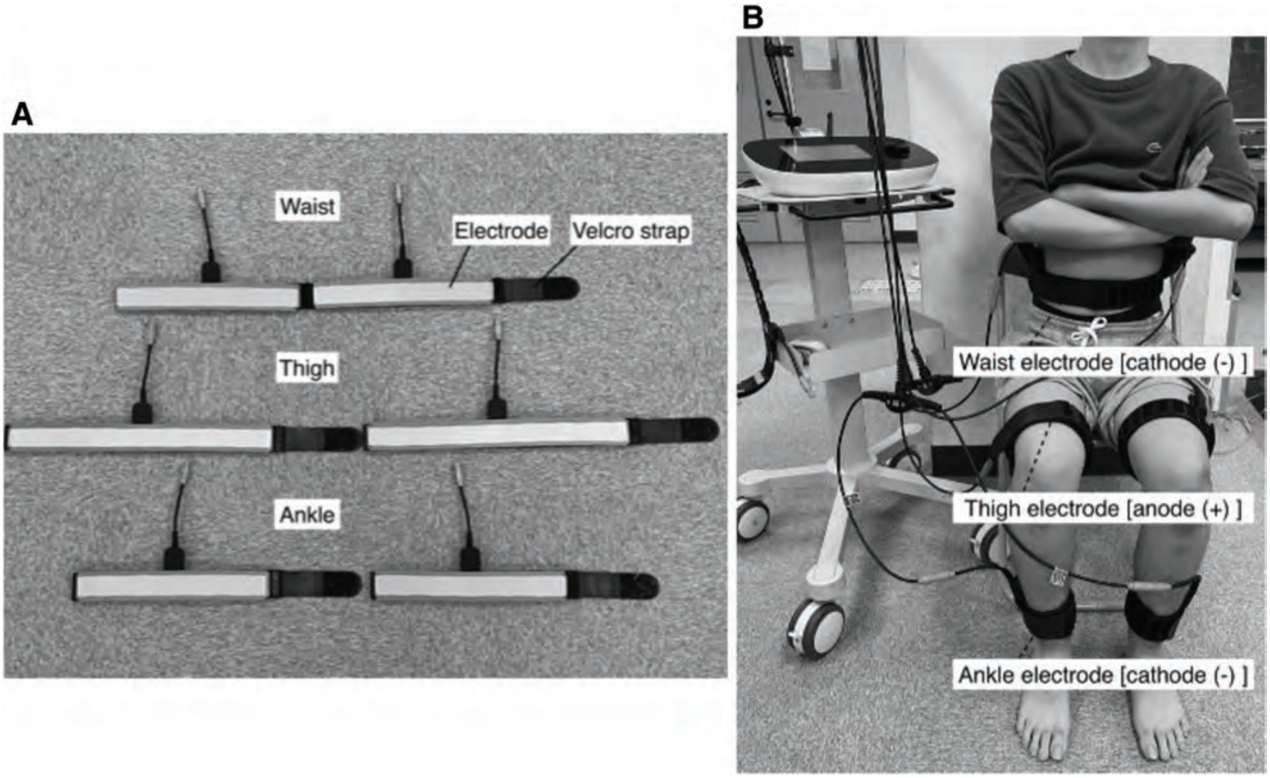

Fig. 2 (A) Belt and stimulation electrodes, and (B) belt electrodes (anode and cathode) were attached to the waist, bilateral distal parts of the thigh, and ankle with a strap.

interval of one week between the two trials. In the EMS trial, EMS was administered to the lower extremities in the seated position from 20 to 40 min after the start of the seated behavior, whereas in the CON trial, the seated behavior was continued without EMS. The electrode belts were placed at five locations: waist, bilateral thighs, and bilateral ankle joints. The maximum tolerance of all participants was measured before the stimulation intensity was set.

EMS

In the EMS trial, belt electrode-skeletal muscle electrical stimulation (G-TES; Homer Ion, Tokyo, Japan) was performed at a frequency of 4 Hz, pulse width of 250 μs[17], and exponentially increasing waves with a stimulation intensity of 50% of the maximum tolerance. EMS was applied to the calf and thigh muscles, including the quadriceps femoris, hamstrings, gastrocnemius, and hip adductor muscles using a stimulator. A frequency of 4 Hz was adopted because high-frequency EMS induces tonic contraction of skeletal muscles and induces muscle fatigue more easily than low-frequency EMS[18]. The value of 4 Hz was selected because this study aimed to promote peripheral circulation through aerobic exercises[19]. One silicon-rubber electrode band (5.3 × 93.3 cm) was wrapped around the lumbar region, two bands (5.3 × 69.6 cm) were wrapped around both distal parts of the thighs, and two bands (5.3 × 54.6 cm) were applied to both ankles (Fig. 2A and 2B). As the stimulation cycles of the bilateral thighs and lower legs were synchronized, the bilateral lower-extremity muscle groups were stimulated simultaneously. The stimulation was set to 50% of the maximum tolerance without causing discomfort (39–82 mA on the thighs, below 30 mA on the ankles).

Measurements

BA endothelial function

In this study, the endothelial function of the BA was assessed. The endothelial function of the BA is an indicator of systemic endothelial function[11], and FMD of the BA is highly significant because it is a predictor of CVD[20].

The participants were asked to rest in the supine position for at least 15 min to obtain resting arm systolic blood pressure (SBP) and diastolic blood pressure (DBP) using a standard sphygmomanometer on their left arm. An occlusion cuff was placed around the right forearm while two ECG leads were attached to the wrists to measure heart rate (HR). FMD was quantified by high-resolution ultrasonography (UNEXEF 38G; UNEX, Nagoya, Japan) to measure endothelial function. The BA was scanned longitudinally 5–10 cm proximal to the elbow joint. To occlude blood flow, the cuff was inflated 50 mmHg above the SBP for 5 min. Upon cuff deflation, the blood flow velocity and artery diameter were measured for an additional 3 min, and the change in BA diameter was immediately expressed as the percentage change relative to the vessel diameter before cuff inflation. FMD was calculated as the baseline value (Di_{base}) before the cuff was released to the peak value after cuff release (Di_{peak}). FMD was calculated using the following equation: FMD (%) $= \{(Di_{peak} - Di_{base})/Di_{base}\} \times 100$. A detailed description of the measurements is provided in a previous study[21].

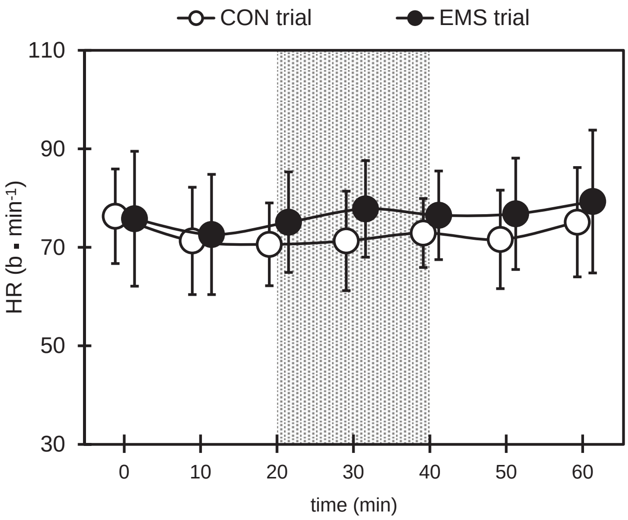

Fig. 3 Changes in HR during each trial

Gray areas represent EMS trials during electrical stimulation.

Values are presented as mean ± SD.

CON, control; EMS, electrical muscle stimulation; HR, heart rate; SD, standard deviation

All participants were instructed to limit alcohol consumption, caffeine intake, and strenuous exercise from the day before to the end of the experiment.

In this study, to compare FMD under different trials, we calculated the peak shear rate (PSR) from the vessel diameter and blood flow rate. The blood flow velocity was calculated from the color Doppler data and displayed as a waveform in real time. PSR was calculated as the difference in flow velocity between the hyperemic response (peak after cuff deflation: FV_{peak}) and baseline (FV_{base}) divided by the baseline BA diameter. Subsequently, normalized FMD (nFMD) was calculated using the following equation[22]:

$$PSR\ (s^{-1}) = (FV_{peak} - FV_{base})/Di_{base}$$

$$nFMD\ (a.u.) = FMD/PSR$$

All measurements were performed after 15 min of supine rest and 30 min after PS. The HR during PS was measured every 10 min using thoracic bipolar induction (POLAR H10; Polar, Tokyo, Japan).

Work efficiency

To examine the effect of EMS on work efficiency, the participants typed a specified novel on a personal computer (PC) for 60 min. The same novel was used for both trials, and different chapters were typed for each trial. The text and typing paper were set up as a 400-word manuscript, and the percentage of correct responses was calculated from the number of words typed and the number of words missed during the 60-min task.

Statistical analysis

The results of this study were analyzed for normality using the Shapiro–Wilk test to confirm the normal distribution of data. The measurements for each trial were compared using two-way ANOVA with repeated measures to test for the presence or absence of an interaction, and the Bonferroni test was performed for posterior analysis. All measurements are expressed as mean and standard deviation and were considered statistically significant at a significance level of <5%.

Results

HR during each trial

The changes in HR during the two trials are shown in Figure 3. No significant differences were observed between the two trials in all tests.

Work efficiency after each trial

The number of characters that could be typed in the novels in the EMS and CON trials was 1944.6 ± 467.1 in the EMS trial and 1962.8 ± 364.5 in the CON trial, with no significant differences between the trials. The percentage of correct responses was 96.4% in the EMS trial and 98.2% in the CON trial, with no significant differences between the trials.

BA function before and after each trial

The changes in SBP, DBP, HR, Di_{base}, Di_{peak}, FV_{base}, FV_{peak}, PSR, and FMD before and after each trial are shown in Table 1. In both trials, DBP showed a significant increase 30 min after PS compared to before PS ($p < 0.05$), and HR decreased significantly after each trial ($p < 0.01$). There was no significant main effect or interaction between SBP, Di_{base}, Di_{peak}, FV_{base}, FV_{peak}, and PSR before PS and 30 min after PS completion in both trials. There was a significant interaction for FMD ($F(1,11) = 5.258$, $p < 0.05$), and in the CON trial, there was a significant decrease 30 min after PS completion compared with that before PS ($p < 0.05$). The changes in nFMD before PS and 30 min after PS completion are shown in Figure 4 (0.84 ± 0.43 and 1.14 ± 0.77 in the EMS trial and 0.84 ± 0.43 and 0.74 ± 0.55 in the CON trial, respectively; $F(1,11) = 6.884$, $p < 0.05$). In the EMS trial, a significant increase was observed 30 min after PS completion compared with that before PS ($p < 0.05$).

Discussion

This study investigated the effects of EMS during PS on vascular endothelial function in healthy adult men. The results showed that the EMS trial with EMS to the lower extremities increased the nFMD of BA 30 minutes after the end of the trial compared to before PS. It was found that giving EMS during PS had a beneficial effect on nFMD.

Vranish et al.[23] reported that blood flow and shear stress in the lower extremities decreased within 10 min of the start of sitting, indicating that these are factors that induce a decrease in FMD in the lower extremities due to PS. In contrast, walking for 5 min during 3 h of SB suppressed the

Table 1. Characteristics of SBP, DBP, HR, Di, FV, PSR, and FMD before and after each trial

	EMS trial			CON trial			
	Pre	Post 30	Time effect within group p-value	Pre	Post 30	Time effect within-group p-value	Group × time interaction p-value
SBP (mmHg)	119.7 ± 6.5	117.2 ± 6.5	0.10	116.5 ± 6.8	115.3 ± 8.6	0.50	0.23
DBP (mmHg)	64.7 ± 3.4	67.6 ± 4.7	0.01**	65.7 ± 7.7	70.0 ± 7.7	0.01**	0.60
HR ($b \cdot min^{-1}$)	64.9 ± 8.8	59.5 ± 7.0	0.01**	64.7 ± 8.5	61.1 ± 7.5	0.01**	0.04*
Di_{base} (mm)	3.8 ± 0.3	3.8 ± 0.2	0.28	3.9 ± 0.3	3.9 ± 0.3	0.85	0.48
Di_{peak} (mm)	4.1 ± 0.3	4.1 ± 0.3	0.29	4.2 ± 0.3	4.1 ± 0.3	0.57	0.97
FV_{base} ($cm \cdot sec^{-1}$)	13.2 ± 5.8	11.8 ± 5.0	0.20	14.0 ± 8.5	9.9 ± 4.3	0.06	0.21
FV_{peak} ($cm \cdot sec^{-1}$)	52.4 ± 18.7	46.4 ± 20.7	0.08	50.3 ± 16.2	47.8 ± 14.8	0.61	0.43
PSR (s^{-1})	10.4 ± 4.4	9.3 ± 5.6	0.80	9.4 ± 2.8	9.8 ± 3.3	0.77	0.26
FMD (%)	7.2 ± 0.9	7.3 ± 1.1	0.17	7.3 ± 0.7	6.2 ± 1.1	0.04*	0.04*

*p <0.05, **p <0.01 vs. Pre

SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; Di_{base}, diameter baseline; Di_{peak}, diameter peak line; FV_{base}, flow volume base; FV_{peak}, flow-volume peak; PSR, peak shear rate; FMD, flow-mediated dilation; EMS, electrical muscle stimulation; CON, control

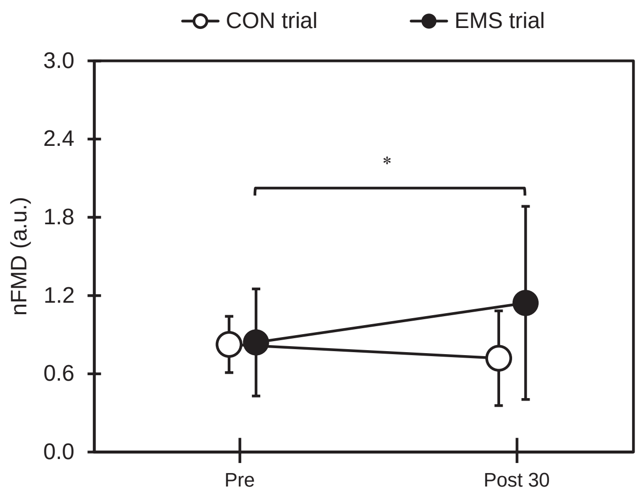

Fig. 4 Changes in nFMD before and after each trial

*Significantly different from Pre (p <0.05)

CON, control; EMS, electrical muscle stimulation; nFMD, normalized flow-mediated dilation

decline in FMD, indicating that aerobic exercise during SB suppresses the decline in vascular endothelial function[12]. Overall, these results indicate that physical activity during prolonged SB suppresses vascular endothelial dysfunction.

Most importantly, this study indicates that nFMD increased significantly in the EMS trial 30 min after PS completion compared to that before PS. This may be due to the increase in blood flow caused by the dynamic skeletal muscle contraction in response to EMS; vasodilation caused by the enhanced production of NO, lactate, and H^+; metabolic products of muscle contraction; and the inhibition of muscle sympathetic nerve activity (MSNA). The rhythmic rise and fall of intramuscular pressure due to skeletal muscle contraction increases blood flow[24]; increases shear stress, which is a mechanical stress on vascular endothelial cells; and promotes the production of NO, resulting in a vasodilator response. Previous studies have shown that eNOS is activated during EMS and exercise[16]. In addition, previous studies have shown that endothelium-derived vasodilatation occurs in patients with heart failure, causing an increase in the blood flow. Janssen et al.[25] reported that EMS to the lower extremity muscles at a frequency of 3 Hz and maximum tolerance intensity increased blood flow in the common femoral artery. In the present study, we used a low frequency of 4 Hz, which may have increased the blood flow in the lower extremities, as in a previous study. Furthermore, compared with voluntary exercise, EMS provides electrical stimulation to the entire lower extremity and produces muscle contraction; thus, blood flow can be expected to increase. EMS stimulation also releases substance P and calcitonin gene-related peptide from nociceptive C fibers; these substances have vasodilating effects and act on skin vasodilation[26]. Furthermore, a comparison of changes in skin blood flow under high-frequency stimulation (110 Hz) and low-frequency stimulation (4 Hz) revealed that low-frequency stimulation increases skin blood flow at stimulation sites[27]. Since these increases in cutaneous blood flow increase blood flow in conduit arteries, increased cutaneous blood flow is one possible mechanism for increasing FMD in conduit arteries. It is, therefore, a factor in the increased blood flow in the conduit arteries of the lower extremities, the site of EMS stimulation. In voluntary exercise, type I fibers are sequentially mobilized, whereas, in EMS, mobilization begins with type II fibers, which have a lower threshold, and the mode of mobilization is different[28]. Because of the different energy metabolism characteristics, metabolic vasodilators that inhibit sympathetic nerve activity such as lactate, H^+, and acidosis are easily produced in the lower limbs, which are active muscles. Kimura et al. have shown that EMS at an intensity that is not uncomfortable increases blood lactate concentration[29]. In the present study, the same effect may have occurred because of MSNA inhibition. Venous blood stasis induced by sitting posture causes an increase in MSNA[30], which dominates the vascular smooth muscle; an increase in blood pressure[31]; and a decrease in FMD[32]. However, in large muscles, such as the lower-extremity muscles, MSNA innervating the vascular smooth muscle is suppressed by a low-intensity bicycle pedaling exercise of approximately 50 W[33]. In addition, it has been shown that light-intensity activity and walking also suppress MSNA by inducing skeletal muscle contraction and promoting venous return[34]. These results suggest that the EMS trial in this study promoted venous return, suppressed blood flow congestion, and inhibited MSNA-induced vasoconstriction, whereas vasodilation was not inhibited.

On the other hand, FMD in the CON trial in the present study significantly decreased 30 min after PS completion compared with that before PS, and no significant change was observed in nFMD. In a previous study, a significant decrease in FMD was observed in the superficial femoral artery 1 h after PS initiation, whereas no significant change in FMD was observed in the BA[35]. In Thosar et al. study, upper-extremity activity during PS was not quantified because of the high degree of freedom of the upper extremities during PS, such as psychologically stress-free reading and PC use[35]. However, since the present study assumed desk work for workers, typing work using a PC was conducted during PS, suggesting that vasoconstriction was affected by prolonged mental tension and sympathetic hyperactivity. In the CON trial of the present study, the FV_{base} showed a decreasing trend 30 min after the end of sedentary activity compared with that before sedentary activity, suggesting that FMD decreased in the CON trial, whereas nFMD, which takes into account the blood flow velocity, did not show a significant change. In this study, all participants performed typing tasks using a PC with PS to assess work efficiency, but there were no significant differences between the two tests. Thus, the results suggest that the decrease in vascular function is suppressed without a decrease in work efficiency.

In summary, our results suggest that EMS to the lower extremities during sedentary work improves vascular endothelial function. Compared with other countries, workers in Japan, especially office workers, mainly work at desks and spend a lot of time in the sitting position[36]. In addition, the results of this study may provide basic data for comparing electrical stimulation tools that can be implemented during sedentary activities such as desk work.

This study has some limitations. Due to the transient nature of this study, the long-term impact of the intervention remains to be investigated. In the future, the effects of different intensities of EMS and the production of vasoactive substances, such as NO, could be examined, but this is unknown because biochemical tests have not been performed, nor have the effects of PS and EMS on the sympathetic nervous system. In addition, because the intensity of EMS stimulation is determined subjectively by the individual, there is a possibility that individual differences may occur in the amount of muscle contraction. Furthermore, factors such as exercise habits and age were predicted to cause differences in the vascular responses to the protocol used in this study. Future studies should consider differences in EMS intensity, duration, frequency, and amount of muscle contraction considering these factors.

Conclusion

These results suggest that the use of EMS as an alternative to aerobic exercises may reduce the risk of endothelial dysfunction when it is difficult to interrupt PS and exercises.

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Conflict of Interest: The authors declare no conflicts of interest.

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PHYSICAL THERAPY RESEARCH

SCIENTIFIC RESEARCH ARTICLE

Initiating Mobilization Is Not Associated with Symptomatic Cerebral Vasospasm in Patients with Aneurysmal Subarachnoid Hemorrhage: A Retrospective Multicenter Case-control Study

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ABSTRACT. Objective: The study aim was to investigate the association between initiating mobilization within 7 days after onset and symptomatic cerebral vasospasm (SCV) in patients with aneurysmal subarachnoid hemorrhage (aSAH). Methods: This was a retrospective multicenter case-control study in Japan. Patients with a diagnosis of aSAH who underwent physical therapy with/without occupational therapy were included and categorized into 2 groups according to the presence or absence of SCV. Initiating mobilization was defined as sitting on the bed edge (at least once, with/without assist, regardless of duration) within 7 days after aSAH onset. Cox proportional hazards regression analysis was performed to evaluate the association between initiating mobilization within 7 days after onset and SCV. Results: The analysis included 510 patients. Among all included patients, 57 (11.2%) patients had SCV. In the univariate Cox proportional hazards regression analysis, initiating of mobilization was not associated with SCV (hazard ratio [HR] = 0.78; 95% confidence interval [CI] = 0.45–1.32). In the multivariate analysis, only the modified Fisher scale was significantly associated with SCV (HR = 26.23; 95% CI = 1.21–571.0). Conclusion: Initiating mobilization within 7 days after aSAH onset was not associated with SCV in patients with aSAH.

Key words: Aneurysmal subarachnoid hemorrhage, Symptomatic cerebral vasospasm, Mobilization, Rehabilitation

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Aneurysmal subarachnoid hemorrhage (aSAH) is a serious disease. The proportion of aSAH is the lowest among all stroke types, ranging from 1% to 5%[1)]. However, the case fatality rate is as high as 25%–30%[1)]. Furthermore, several complications, such as rebleeding, symptomatic cerebral vasospasm (SCV), hydrocephalus, and seizures can occur[2)]. Therefore, treatment after aSAH is very complicated and difficult[2–4)]. Among the potential complications, SCV is strongly associated with poor functional outcome and mortality[5–7)]. SCV is observed in approximately 20%–30% of patients with aSAH[8–10)]. SCV may occur 4–14 days after onset[11,12)] and most frequently occurs approximately 7 days after onset[13,14)]. In this period, rehabilitation and mobilization require attention to SCV.

Various factors are known to be associated with increasing risk of SCV, such as age[8,9,15)], clinical grade[8,9,15)], thick subarachnoid hematoma[8,9,15,16)], and aneurysm location[13,16)]. However, the impact of mobilization during the early phase after aSAH on SCV is uncertain. Several clinical guidelines recommend early rehabilitation and mobilization after stroke, but protocols for rehabilitation and mobilization after aSAH are not mentioned[2,4,17,18)].

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Few studies have investigated the association between mobilization and SCV. A previous study suggested that early mobilization did not increase the incidence of SCV[19]. In contrast, another study found that early mobilization initiated 2–5 days after onset was caused by delayed cerebral ischemia[20]. Mobilization may increase intracranial pressure and decrease cerebral perfusion pressure, which may exacerbate cerebral vasospasm and delayed cerebral ischemia[21,22]. Cerebral blood flow autoregulation may be disrupted after aSAH[23]. Changes in head position due to mobilization may decrease cerebral blood flow, and there is a concern that this decrease in blood flow could induce SCV. However, in a previous study examining the effect of head-up on cerebral blood flow in patients with subarachnoid hemorrhage who had cerebral vasospasm, head-up did not decrease cerebral blood flow[24]. Data on the association between mobilization and SCV are limited. Furthermore, only single-center studies in small samples of patients have been conducted. To the best of our knowledge, no multicenter study has investigated the association between mobilization and SCV.

We hypothesized that initiating mobilization within 7 days after aSAH onset, a period when SCV often occurs, is not associated with SCV. If initiating mobilization after aSAH onset is not associated with SCV, this study may contribute to a strategy for promoting early mobilization in patients with aSAH. Therefore, we conducted a multicenter case-control study in Japan to investigate the association between initiating mobilization within 7 days after onset and SCV in patients with aSAH.

Methods

Study design

We conducted a retrospective multicenter case-control study in 5 hospitals in Japan (Naha City Hospital, Saitama Medical Center, Akita Cerebrospinal and Cardiovascular Center, Sapporo Shiroishi Memorial Hospital, and Yuuai Medical Center). This study was part of a project entitled Safety and Efficacy of Acute Rehabilitation in Subarachnoid Hemorrhage (the SEASAH study) and was approved by the ethics committee of Naha City Hospital (2021a11), Saitama Medical Center (2286), Akita Cerebrospinal and Cardiovascular Center (19-18), Sapporo Shiroishi Memorial Hospital (A01-2021), and Yuuai Medical Center (R01R045). The principles of the Declaration of Helsinki and the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines were followed. The requirement for informed consent was waived in all participating hospitals because this study only involved retrospective analysis of anonymous preexisting data.

Participants

The study included consecutive patients with a diagnosis of aSAH admitted to participating hospitals between April 2014 and March 2019, all of whom had undergone physical therapy with/without occupational therapy. The exclusion criteria were as follows: (1) patients who had died, (2) those without aneurysm treatment, (3) those with a recurrence of aSAH, (4) those who had undergone reoperation, (5) those who underwent aneurysm treatment >72 hours after the onset of aSAH, (6) those who were <20 years old, (7) those diagnosed with SCV before initiating mobilization, and (8) those for whom data were lacking. The included patients were divided into the SCV group (diagnosed) and the non-SCV group (no SCV present).

Outcome and clinical variables

Data were collected retrospectively through the electronic medical records of the participating hospitals by local study investigators. The primary outcome in this study was the incidence of SCV. The diagnosis of SCV was made by a neurosurgeon on the basis of the radiological examination and presence of delayed neurological worsening. The patient characteristics and clinical data included age, sex, history of hypertension and diabetes mellitus, the World Federation of Neurosurgical Societies (WFNS) grading system[25] and modified Fisher score (MFS)[26] on admission, aneurysm location, and treatment based on type, presence of SCV, days from aSAH onset to diagnosis of SCV, and initiating or not initiating mobilization within 7 days after aSAH onset. Age was dichotomized into <65 years (non-elderly patients) and ≥65 years (elderly patients). WFNS grade was dichotomized into 1–3 (mild–moderate condition) and 4–5 (severe condition). MFS was dichotomized into 1–2 (thin subarachnoid hematoma) and 3–4 (thick subarachnoid hematoma). Aneurysm location was dichotomized into anterior circulation (anterior cerebral artery, anterior communicating artery middle cerebral artery, internal carotid posterior communicating artery) and posterior circulation (posterior cerebral artery, posterior communication artery, vertebral-basilar artery). Type of aneurysm treatment was dichotomized into surgical and endovascular. Initiating mobilization was defined as sitting on the bed edge (at least once, with/without assist, regardless of duration) within 7 days after aSAH onset. Mobilization was initiated after aneurysm treatment and guided by a physical therapist or an occupational therapist. In participating hospitals, criteria and risk management of initiating mobilization depended on individually defined thresholds of vital sign and parameters, such as arterial blood pressure, intracranial pressure, heart rate, oxygenation, respiratory rate, body temperature, neurological symptoms, and subjective symptoms. These criteria and risk management were determined by a neurosurgeon and a therapist in the participating hospitals.

Statistical analysis

Categorical variables are presented as a number (%), and continuous variables are presented as a median with interquartile range. We performed the $\chi 2$ test or Fisher's exact test to compare categorical variables between the SCV group and non-SCV group, and we performed univariate

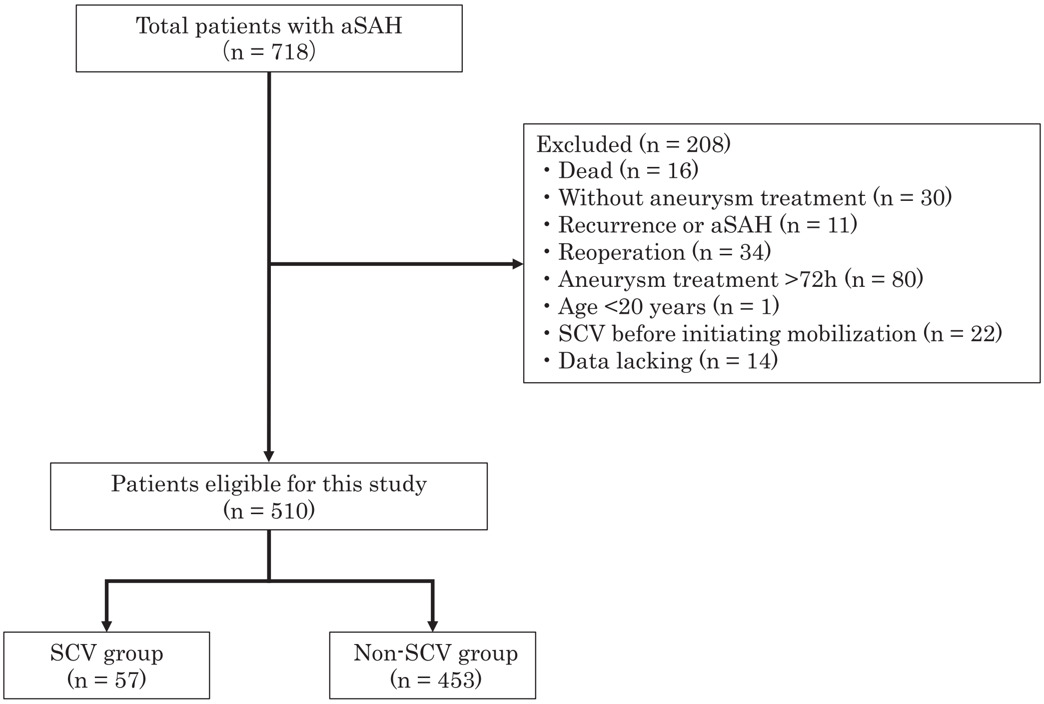

Fig. 1. Flowchart of the included patients

aSAH, aneurysmal subarachnoid hemorrhage; SCV, symptomatic cerebral vasospasm

and stepwise multivariate Cox proportional hazards regression analysis to estimate predictors of SCV. Multivariate Cox proportional hazards regression analysis was adjusted by age, history of hypertension and diabetes mellitus, WFNS grade, MFS, aneurysm location, and initiating or not initiating mobilization within 7 days after aSAH onset. These covariates, other than initiating mobilization, have been found to be associated with SCV in previous studies[8,9,13,15,16,27]. Cox proportional hazards regression analysis results were expressed as a hazard ratio (HR) with 95% confidence interval (CI). The difference in the incidence of SCV between with and without initiating mobilization was assessed by Kaplan–Meier curves and compared by performing the log-rank test. To assess the robustness of our findings, we performed three sensitivity analyses. We repeated the primary analysis (multivariate Cox proportional hazards regression analysis) after considering stricter definitions for mobilization and eligibility criteria. Mobilization was defined as initiating mobilization within 5 days after aSAH onset (Model 1) and within 9 days after aSAH onset (Model 2). Finally, we repeated the primary analysis after including only MFS 3 and 4 patients at high risk of SCV (Model 3).

To assess the characteristics of patients with mobilization initiated within 7 days and those with mobilization initiated after 7 days, we performed the $\chi 2$ test or Fisher's exact test and Mann–Whitney U-test to compare between the groups. Furthermore, we repeated the same analysis to compare values between the groups in only patients with SCV.

Values of $P < 0.05$ were considered to be indicative of statistical significance. All statistical analyses were performed using the SPSS statistical software (IBM SPSS Statistics for Windows, Version 22.0, Released 2013; IBM, Armonk, NY, USA).

Results

A total of 718 patients were screened, and 510 were included in the analysis. Figure 1 shows the flowchart of patient selection. Table 1 shows a comparison of the patients' clinical characteristics between the SCV group and the non-SCV group. The proportions of WFNS grades 4–5 and MFS 3–4 were significantly higher in the SCV group than in the non-SCV group (WFNS grades 4–5: 45.6% vs. 27.6%; P = 0.006. MFS 3–4: 100% vs. 83.0%; P = 0.016). The proportions of initiating mobilization within 7 days were not significantly different between the SCV and the non-SCV groups (38.6% vs. 45.5%; P = 0.397). There were no significant differences in age, sex, history of hypertension and diabetes mellitus, aneurysm location, and type of aneurysm treatment between the SCV and the non-SCV groups. Figure 2 shows the cumulative incidence curves for the different categories of with/without initiating mobilization within 7 days in the Kaplan–Meier analysis. There was no significant difference in the log-rank test between the patients with/without initiating mobilization (P = 0.344). Table 2 shows the Cox proportional hazards regression analysis results. The patients who initiated mobilization within 7 days had no significant association with SCV in the univariate analysis (HR = 0.78; 95% CI = 0.45–1.32; P = 0.348). In the multivariate analysis, only MSF was significantly associated with SCV (HR = 26.23; 95% CI = 1.21–571.0; P = 0.038). Initiating mobilization, age, hypertension,

Table 1. Comparison of the patients' characteristics between the SCV group and non-SCV group

	All patients (N = 510)	SCV group (n = 57)	Non-SCV group (n = 453)	P value
Age, (years) n (%)				0.261
<65	271 (53.1)	26 (45.6)	245 (54.1)	
≥65	239 (46.9)	31 (54.6)	208 (45.9)	
Sex, n (%)				0.757
Female	363 (71.2)	42 (73.7)	321 (70.9)	
Male	147 (28.8)	15 (26.3)	132 (29.1)	
Hypertension, n (%)				0.561
Yes	180 (35.3)	18 (31.6)	162 (35.8)	
No	330 (64.7)	39 (68.4)	291 (64.2)	
Diabetes mellitus, n (%)				0.223
Yes	22 (4.3)	4 (7.0)	18 (4.0)	
No	488 (95.7)	53 (93.0)	435 (96.0)	
WFNS grade, n (%)				0.006
1–3	359 (70.4)	31 (54.4)	328 (72.4)	
4–5	151 (29.6)	26 (45.6)	125 (27.6)	
MFS, n (%)				0.001
1–2	77 (15.1)	0 (0)	77 (17.0)	
3–4	433 (84.9)	57 (100)	376 (83.0)	
Aneurysm location, n (%)				0.090
Anterior circulation	447 (87.6)	54 (94.7)	393 (86.8)	
Posterior circulation	63 (12.4)	3 (5.3)	60 (13.2)	
Type of aneurysmal treatment, n (%)				0.670
Surgical	301 (59.0)	32 (56.1)	269 (59.4)	
Endovascular	209 (41.0)	25 (43.9)	184 (40.6)	
Initiating mobilization within 7 days, n (%)				0.397
Yes	228 (44.7)	22 (38.6)	206 (45.5)	
No	282 (55.3)	35 (61.4)	247 (54.5)	

The data are presented as number (%).

SCV, symptomatic cerebral vasospasm; WFNS, World Federation of Neurosurgical Societies; MFS, modified Fisher scale

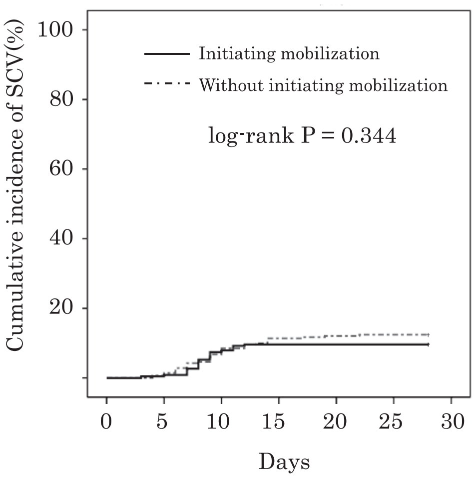

Fig. 2. Kaplan–Meier curves for cumulative incidence rate of SCV in patients with/without initiating mobilization within 7 days after onset

There was no significant difference in the cumulative incidence rates of SCV between the initiating mobilization group and without initiating mobilization group (log-rank P = 0.344).

SCV, symptomatic cerebral vasospasm

diabetes mellitus, WFNS grade, and aneurysm location were not significantly associated with SCV in the multivariate analysis. Furthermore, initiating mobilization was not associated with SCV in any of the sensitivity analyses (Table 3). MFS was only associated with SCV in models 1 and 2 (HR = 26.23; 95% CI = 1.21–571.0; P = 0.038) and in model 3 (HR = 2.38; 95% CI = 1.42–4.02; P = 0.001).

Table 4 shows a comparison of the characteristics of the patients with mobilization initiated within 7 days and those with mobilization initiated after 7 days. The incidence of SCV was 11.2% among all patients, 9.6% in the patients with mobilization initiated within 7 days, and 12.4% in the patients with mobilization initiated after 7 days. No significant difference was observed in the incidence of SCV. The proportions of no hypertension, WFNS grades 1–3, MFS 3–4, and endovascular treatment were significantly higher in patients with mobilization initiated within 7 days than in those with mobilization initiated after 7 days (no hypertension: 69.7% vs. 60.6%; P = 0.04. WFNS grades 1–3: 79.4% vs. 63.1%; P <0.001. MFS: 88.6% vs. 81.9%; P = 0.046.

Table 2. Cox proportional hazards regression analysis of factors associated with SCV

	Univariate analysis			Multivariate analysis		
	HR (95%CI)		P value	HR (95%CI)		P value
Age, (years) (ref: <65)	1.35	0.80–2.27	0.260			
Hypertension (ref: no)	0.84	0.48–1.46	0.531			
Diabetes mellitus (ref: no)	1.70	0.62–4.70	0.306			
Aneurysm location (ref: posterior)	2.65	0.83–8.48	0.100			
WFNS grade (ref: 1–3)	2.08	1.23–3.50	0.006			
MFS (ref: 1–2)	26.23	1.21–571.0	0.038	26.23	1.21–571.0	0.038
Initiating mobilization within 7 days (ref: no)	0.78	0.45–1.32	0.348			

SCV, symptomatic cerebral vasospasm; WFNS, World Federation of Neurosurgical Societies; MFS, modified Fisher scale; HR, hazard ratio; CI, confidence interval

Table 3. Sensitivity analysis

	Model 1			Model 2			Model 3		
	HR (95%CI)		P value	HR (95%CI)		P value	HR (95%CI)		P value
MFS (in Models 1 and 2; ref: 1–2)	26.23	1.21–571.0	0.038	26.23	1.21–571.0	0.038			
MFS (in Model 3; ref: 3)							2.38	1.42–4.02	0.001

Model 1: Mobilization was defined as initiating mobilization within 5 days after aSAH onset. Reference value was MFS 1–2.
Model 2: Mobilization was defined as initiating mobilization within 9 days after aSAH onset. Reference value was MFS 1–2.
Model 3: Only patients with MFS 3–4 were included. Reference value was MFS 3.

MFS, modified Fisher scale; HR, hazard ratio; CI, confidence interval; aSAH, aneurysmal subarachnoid hemorrhage

Endovascular treatment: 61.8% vs. 24.1%; P <0.001). Table 5 shows a comparison of the characteristics of the patients with mobilization initiated within 7 days and those with mobilization initiated after 7 days with SCV. The median days from aSAH onset to diagnosis of SCV was 9 days among all patients, 8 days in the patients with mobilization initiated within 7 days, and 9 days in the patients with mobilization initiated after 7 days. No significant difference was observed between the groups.

Discussion

To the best of our knowledge, this is the first multicenter study to investigate the association between initiating mobilization and the incidence of SCV in patients with aSAH. After adjustment for variables, we found that initiating mobilization within 7 days was not significantly associated with the incidence of SCV. This finding may contribute to developing a strategy for promoting early mobilization in patients with aSAH.

In this study, the proportion of all included patients who had SCV was 11.1%, which is less than the proportions previously reported (20%–30%)[8–10]. Our study included patients with aSAH who underwent physical therapy with/without occupational therapy, therefore, we did not screen patients with aSAH who did not undergo physical therapy with/without occupational therapy, which explains the difference in the proportions of patients with SCV between this study and previous studies cited above. However, another study that investigated the effect of rehabilitation reported that the incidence of SCV was 14% in the early rehabilitation group and 29% in the controls[19], which was similar to our results.

In a prospective interventional study, early mobilization did not increase SCV or worsen the frequency and severity of cerebral vasospasm[19]. In another study, mobilization with active exercise within 4 days reduced SCV in patients with aSAH[28]. This study found no association between initiating mobilization within 7 days after aSAH and SCV. This result was consistent with those of previous studies. Furthermore, we conducted sensitivity analysis to assess the robustness of our findings. The results of the three sensitivity analyses were similar to those of the primary analysis.

In patients with aSAH, cerebral autoregulation may be impaired, and mobilization may induce reduction of cerebral blood flow. In two previous studies, head-of-bed elevation (45°–90°) did not significantly affect cerebral blood flow[24,29]. Thick subarachnoid hematoma has been reported as a risk for SCV[8,9,15,16]. The head-shaking method with a subarachnoid hematoma draining effect has been reported to reduce SCV[30]. Since the head moves and the head position changes during mobilization, the effects of those head movements may be similar to the effect in the head-shaking method. In a laboratory study, mobilization with active exercise was not found to increase an injury marker (inducible nitric oxide synthase) in a rodent aSAH model[28]. Based on these mechanisms and

Table 4. Comparison of the characteristics of the patients with mobilization initiated within 7 days and those with mobilization initiated after 7 days

	All patients (N = 510)	Within 7 days group (n = 228)	After 7 days group (n = 282)	P value
Age, (years) n (%)				0.061
<65	271 (53.1)	132 (57.9)	139 (49.3)	
≥65	239 (46.9)	96 (42.1)	143 (50.7)	
Sex, n (%)				0.624
Female	363 (71.2)	165 (72.4)	198 (70.2)	
Male	147 (28.8)	63 (27.6)	84 (29.8)	
Hypertension, n (%)				0.04
Yes	180 (35.3)	69 (30.3)	111 (39.4)	
No	330 (64.7)	159 (69.7)	171 (60.6)	
Diabetes mellitus, n (%)				0.513
Yes	22 (4.3)	8 (3.5)	14 (5.0)	
No	488 (95.7)	220 (96.5)	268 (95.0)	
WFNS grade, n (%)				<0.001
1–3	359 (70.4)	181 (79.4)	178 (63.1)	
4–5	151 (29.6)	47 (20.6)	104 (36.9)	
MFS, n (%)				0.046
1–2	77 (15.1)	26 (11.4)	51 (18.1)	
3–4	433 (84.9)	202 (88.6)	231 (81.9)	
Aneurysm location, n (%)				0.344
Anterior circulation	447 (87.6)	196 (86.0)	251 (89.0)	
Posterior circulation	63 (12.4)	32 (14.0)	31 (11.0)	
Type of aneurysmal treatment, n (%)				<0.001
Surgical	301 (59.0)	87 (38.2)	214 (75.9)	
Endovascular	209 (41.0)	141 (61.8)	68 (24.1)	
SCV				0.397
Yes	57 (11.2)	22 (9.6)	35 (12.4)	
No	453 (88.8)	206 (90.4)	247 (87.6)	

The data are presented as number (%).

WFNS, World Federation of Neurosurgical Societies; MFS, modified Fisher scale; SCV, symptomatic cerebral vasospasm

evidence, our results suggest that initiating mobilization within 7 days after onset was not associated with SCV. In contrast, early mobilization initiated 2–5 days after onset was found to be the cause of cerebral vasospasm and delayed cerebral ischemia[20]. This previous study compared the early mobilization group (mobilization initiated 2–5 days after onset) with the non-early mobilization group (mobilization initiated after 12 days after onset), whereas this study compared the early mobilization group (mobilization initiated within 7 days after onset) with the non-early group (mobilization initiated after 7 days after onset). In the non-early group in both studies, the date of initiating mobilization differs by 5 days. Additionally, the subjects of previous study were in a mild-to-moderate condition, whereas the subjects of this study were in a mild-to-sever condition. These may be the reasons for the difference between the results of both studies.

Previous studies that investigated the characteristics of patients with subarachnoid hemorrhage who can mobilize in the acute phase are limited. Our study showed that the proportion of mild-to-moderate condition was higher in the group with mobilization initiated within 7 days, which is consistent with previous studies[22,31]. The proportion of endovascular treatment was also higher in this group. Endovascular treatment was less invasive than surgical treatment, which may have facilitated mobilization. The proportion of MFS 3–4, a risk factor for SCV[8,9,15,16], was higher in the group with mobilization initiated within 7 days. Nevertheless, SCV was not significantly increased in this group compared with the group with mobilization initiated after 7 days. This finding may support the main analysis of this study.

One of the strengths of our study is that it was conducted in multiple centers. The number of patients with aSAH was less than the number of those with cerebral infarctions or cerebral hemorrhages[1]. Because this was a multicenter study, it had the advantage of being able to investigate a larger patient sample. However, there were several study limitations that should be considered. First, this was a case-control study, which may have introduced selection

Table 5. Comparison of the characteristics of the patients with mobilization initiated within 7 days and those with mobilization initiated after 7 days in patient with SCV

	All patients (N = 57)	Within 7 days group (n = 22)	After 7 days group (n = 35)	P value
Age, (years) n (%)				0.785
<65	26 (45.6)	11 (50.0)	15 (42.9)	
≥65	31 (54.4)	11 (50.0)	20 (57.1)	
Sex, n (%)				1
Female	42 (73.7)	16 (72.7)	26 (74.3)	
Male	15 (26.3)	6 (27.3)	9 (25.7)	
Hypertension, n (%)				0.381
Yes	18 (31.6)	5 (22.7)	13 (37.1)	
No	39 (68.4)	17 (77.3)	22 (62.9)	
Diabetes mellitus, n (%)				0.635
Yes	4 (7)	2 (9.1)	2 (5.7)	
No	53 (93)	20 (90.9)	33 (94.3)	
WFNS grade, n (%)				0.111
1–3	31 (54.4)	15 (68.2)	16 (45.7)	
4–5	26 (45.6)	7 (31.8)	19 (54.3)	
MFS, n (%)				N/A
1–2	0 (0)	0 (0)	0 (0)	
3–4	57 (100)	22 (100)	35 (100)	
Aneurysm location, n (%)				1
Anterior circulation	54 (94.7)	21 (95.5)	33 (94.3)	
Posterior circulation	3 (5.3)	1 (4.5)	2 (5.7)	
Type of aneurysmal treatment, n (%)				0.1
Surgical	32 (56.1)	9 (40.9)	23 (65.7)	
Endovascular	25 (43.9)	13 (59.1)	12 (34.3)	
Days from aSAH onset to diagnosis of SCV, days	9 (7, 9)	8 (7.25, 9)	9 (7, 12)	0.262

The data are presented as number (%) or median (interquartile range).

SCV, symptomatic cerebral vasospasm; WFNS, World Federation of Neurosurgical Societies; MFS, modified Fisher scale; aSAH, aneurysmal subarachnoid hemorrhage; N/A, not applicable

bias. In this study, the neurosurgeons or physiatrists at the participating hospitals prescribed rehabilitation as needed; therefore, patients with asymptomatic or fatal conditions may not have been eligible for prescription. However, the patients in this study were those with a high need for rehabilitation, which was considered valid for this study. Second, this was a retrospective study, and although we could analyze the association between mobilization and SCV using multivariate analysis, we could not identify causal relationships as in a prospective study. Third, we controlled for measured confounding factors using multivariate Cox proportional hazards regression analysis. However, we were not able to control for unmeasured factors. Fourth, the influence of the race of the patients was not investigated. We only included Japanese patients. However, no evidence of an association between race and SCV was found in a previous review[32]. Fifth, the diagnosis of SCV was not unified as each hospital. At each facility, the diagnosis of SCV is made by neurosurgeons on the basis of the radiological examination and presence of delayed neurological worsening; therefore, it is considered reliable. However, in order to improve the accuracy of the diagnosis, it is necessary to unify the diagnostic criteria at each hospital in further studies. Sixth, although we investigated the impact of initiating mobilization on SCV, we could not collect detailed information about mobilization, such as the level, duration, frequency, and intensity of mobilization. In addition, we could not collect detailed information except for timing of initiating mobilization such as positioning, range of motion exercise, resistance exercise, and patient self-activity that may affect SCV. Furthermore, the decision to initiate mobilization was not made randomly, possibly leading to confounding by the indication used for each patient to initiate mobilization. Although mobilization was initiated as early as possible in each hospital, confounding was possible. Because of these limitations, the study results should be interpreted with caution because they lack information about the level, frequency, and duration of mobilization, which limits their generalizability. Thus, further study is needed to confirm the level, duration, frequency, and intensity of mobilization and their possible impact on SCV.

Conclusion

Our results showed that initiating mobilization within 7 days after aSAH onset was not associated with SCV. Although initiating mobilization may not increase SCV, further studies are needed to confirm the association between mobilization and SCV.

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PHYSICAL THERAPY RESEARCH

SCIENTIFIC RESEARCH ARTICLE

Prediction of Low-intensity Physical Activity in Stable Patients with Chronic Obstructive Pulmonary Disease

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ABSTRACT. Objective: To develop an equation of the predicted amount of low-intensity physical activity (LPA) by analyzing clinical parameters in patients with chronic obstructive pulmonary disease (COPD). Methods: In this cross-sectional study, we analyzed the assessments of clinical parameters evaluated every 6 months from the start of pulmonary rehabilitation in 53 outpatients with stable COPD (age 77 ± 6 yrs; 46 men; body mass index 21.8 ± 4.1 kg/m^2; forced expiratory volume in one second 63.0 ± 26.4% pred). An uniaxial accelerometer was used to measure the number of steps and the time spent in LPA of 1.8–2.3 metabolic equivalents during 14 consecutive days. We also evaluated body composition, respiratory function, skeletal muscle strength, inspiratory muscle strength, exercise capacity, and gait speed. Factors associated with the time spent in LPA were examined by multivariate regression analysis. Internal validity between the predicted amount of LPA obtained by the equation and the measured amount was examined by regression analysis. Results: Multivariate regression analysis revealed that gait speed ($\beta = 0.369$, $p = 0.007$) and maximum inspiratory mouth pressure (PI_{max}) ($\beta = 0.329$, $p = 0.016$) were significant influence factors on LPA ($R^2 = 0.354$, $p < 0.001$). The stepwise regression analysis showed a moderate correlation between the measured amount and predicted amount of LPA calculated by the regression equation ($r = 0.609$, $p < 0.001$; LPA = $31.909 \times$ gait speed + $0.202 \times PI_{max} - 20.553$). Conclusion: Gait speed and PI_{max} were extracted as influence factors on LPA, suggesting that the regression equation could predict the amount of LPA.

Key words: COPD, Low-intensity physical activity, Prediction equation

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Physical inactivity is the strongest predictor of hospitalizations and mortality in patients with chronic obstructive pulmonary disease (COPD)[1,2)]. Current COPD treatment guidelines state that it should be considered a high priority for future COPD therapies to ameliorate inactivity[3–5)]. Being more physically active is the ultimate goal in patients with COPD undergoing pulmonary rehabilitation (PR). In recent years, many studies have verified and reviewed the effects of interventions including PR on physical activity (PA)[6–9)]. A systematic review verified the effect of interventions using a pedometer as a feedback tool and confirmed a significant increase in PA[8–9)]; however, the number of studies analyzed was not large. Burge et al.[10)] reported a Cochrane review of interventions for promoting PA in 2020, which stated that improvement in PA had not been systematically demonstrated following any particular intervention, and that the optimal timing, components, duration, and models of interventions were unclear. Therefore, it is necessary to develop a PR program with a more concrete approach for PA improvement.

Goal setting is an effective key component in a health coaching program for successful behavior change[11)]. A pedometer is the most useful feedback tool as an intervention to improve PA[9)]. A reference number of steps per day has been reported in various studies on goal setting[12–14)], and a simple equation to calculate a recommended number of daily steps in patients with COPD has been developed[15)]. However, PA parameters that can be recommended other than daily steps remain unclear. Furthermore, daily steps

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using pedometers might be underestimated due to slow pace of walking in COPD patients[16,17]. Patients with severe COPD, especially those with limited walking ability, may need to set a target goal of low-intensity physical activity (LPA) with their allowable level instead of the number of steps. Even patients with mild to moderate COPD who have limited walking ability due to aging or are restricted by environmental factors like being admitted to hospitals or nursing homes also need to set this goal. Moreover, the predicted amount of LPA helps to suggest their individual recommended amount of PA in goal-setting interventions in PR. Since there is a report that the more severely ill the patients, the shorter their moderate-to-vigorous intensity physical activity (MVPA)[18], we hypothesize that factors (airflow obstruction, dyspnea, exercise capacity, etc.) that define the stage and severity of COPD patients primarily determine LPA.

The objectives of this study therefore were to develop a prediction equation of LPA using clinical parameters of COPD patients.

Methods

Subjects and study design

This study was a cross-sectional study. Of the 77 outpatients with COPD who were undergoing home-based PR with low-intensity exercise at Akita City Hospital, 53 patients with mild to very severe COPD were enrolled in the study, and their physical activities were measured between June 2012 and March 2021. The patient's flow diagram is shown in Figure 1. The prescriptions of medication for the patients included long-acting muscarinic antagonist or/and β_2 agonist, inhaled corticosteroid, and short-acting β_2 agonist as necessary. All patients were retired and met the following inclusion criteria: (1) diagnosis of COPD according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD)[19]; (2) being in a stable condition with no infection or exacerbation of COPD in the prior 3 months; (3) being able to walk unassisted and operate the device to measure PA; and (4) having no severe and/or unstable cardiac disease, orthopedic disease, or mental disorder that could impair physical activities in daily life. The detailed comorbidities in the patients are as follows: 4 osteoporosis, 5 diabetes, 12 chronic heart failure, 15 hypertension, 3 anemia, 8 hyperlipidemia, 1 chronic renal failure, 5 arthritis, and 8 spinal canal stenosis.

Study protocol

The assessment of PA in daily life, body composition, pulmonary function, skeletal muscle strength, inspiratory muscle strength, submaximal exercise capacity (six-minute walk distance [6MWD]), and gait speed was performed every 6 months from the initiation of PR by well-trained physical therapists who were independent of this study. We analyzed 88 assessments of clinical parameters in 53 participants from the initiation of PR to 3 years after. This study was approved by the medical ethical committee of Akita

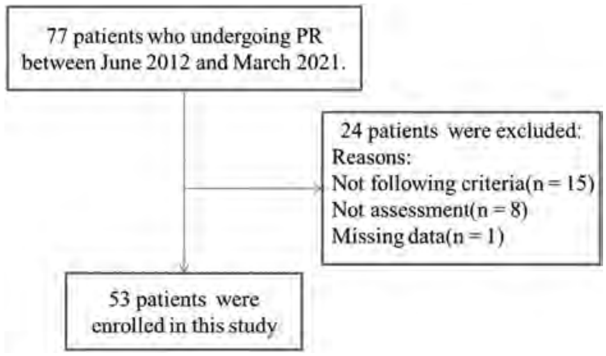

Fig. 1. Patient's flow diagram

City Hospital and Akita University School of Health Sciences (approval No. 658). Written consent was obtained after the objective and content of the study were orally explained to the participants. All participants were informed that their privacy would be sufficiently considered. All procedures were performed according to the research ethics guidelines of the Declaration of Helsinki[20].

Outcome measures

(1) Assessment of LPA in daily living

PA in daily life was assessed using a uniaxial accelerometer, Lifecorder GS (Suzuken, Aichi, Japan)[21], which is a small and lightweight activity monitor ($625 \times 465 \times 260$ mm^3, 40 g). The validity and reliability of this device have been proven[21,22]. This device categorizes the magnitude of movement (MM), which represents exercise intensity, every 4 seconds, into nine levels (MM 1 [minimal] to MM 9 [maximal]), which are subsequently converted to energy expenditure (kcal). MM levels were converted to approximate metabolic equivalents (METs) of activities. MM 1 was equivalent to slow walking (approximately 1.3 METs), while MM 9 was equivalent to fast running (approximately 9.1 METs). The participants were instructed to wear the device on their waist belts for 12 hours after waking up every day for 2 to 4 weeks. PA data were then collected and analyzed using dedicated software. We excluded participants from the analysis if the number of valid days of activity measurement was less than four or/and if they wore the device for 10 hours or less per day. Mean MM per day was calculated for each participant[23]. Since PA decreases during winter, the measurement was performed during seasons other than winter[24]. The time spent in LPA (MM 1–2; approximately 1.8–2.3 METs) and MVPA (MM 3–9; approximately 2.9–9.1 METs) was evaluated (min/day)[21].

(2) Other clinical measurements

Pulmonary function was assessed by forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), FEV_1/FVC, and FEV_1%pred[25] using a spirometer (FUDAC-77; Fukuda Denshi, Tokyo, Japan). Mouth pressure was measured as respiratory muscle strength using a respiratory dynamometer (Autospiro AS-507; MINATO Medical Science, Osaka, Japan) following American Thoracic Society

(ATS)/European Respiratory Society recommendations[26]. Body height was determined to the nearest 0.1 cm (HP-I; Fukui Doryoki, Kyoto, Japan) with subjects standing barefoot. Body weight was assessed with a beam scale to the nearest 0.1 kg (Omron, Kyoto, Japan) with subjects standing barefoot and in light clothing. Fat-free mass was estimated with single-frequency (50 kHz) bioelectrical impedance analysis (Omron). Resistance was measured with subjects in the supine position. Hand grip strength and quadriceps femoris muscle force (QF) were measured as skeletal muscle strength. Hand grip strength was measured twice using their preferred hand by using a Smedley-type hand dynamometer (Grip-D, T.K.K.5401; Takei Scientific Instruments, Niigata, Japan), and the higher value was recorded[27]. For QF, the maximum isometric extension and contraction were measured at 0°/sec 80° flexion using Hydro Musculator GT-160 (OG Giken, Okayama, Japan)[28]. For the measurements of exercise capacity, a 6-minute walk test (6MWT) was performed according to the ATS guidelines[29]. The patients were not encouraged during the 6MWT. Gait speed was measured as the time taken to walk 6 m at a normal pace without deceleration, according to the measurement recommendations by the Asian working group for sarcopenia 2019, and the average result of at least two trials was recorded for analysis[27]. Dyspnea was assessed using modified Medical Research Council (mMRC) dyspnea scale[30]. Disease-specific health-related quality of life was measured using the COPD Assessment Test[31]. The effect of comorbidities was assessed using Charlson comorbidity index (CCI)[32].

Statistical analysis

The sample size was calculated using G*Power ver 3.1.9.2 (Heinrich-Heine-Universität, Düsseldorf, Germany)[33]. Based on the determination coefficient of multiple regression analysis between the time spent in walking per day and 6MWD reported in our previous study[34], when we set the effect size to 0.35, alpha to 0.05 (two sided), beta to 0.05, and number of predictors to 11, the calculated total sample size was 83. Therefore, the minimum sample size was set at 83 participants. The data of the patients were entered and analyzed using IBM SPSS Statistics 21.0 (IBM, Armonk, NY, USA). Normality in data distribution was assessed using the Kolmogorov–Smirnov test with p values <0.05 considered significant. Univariate regression analysis was used to evaluate the association between the time spent in LPA and each clinical measurement. Multivariate regression analysis for the time spent in LPA was performed using each clinical measurements including age and FEV_1%pred as confounding factors. Stepwise regression was used to create a multivariate linear regression equation for the time spent in LPA. Linear regression analysis and residual analysis by the Kolmogorov–Smirnov test were performed to determine the validity of this equation. Moreover, Bland–Altman plots were used for comparisons between the measured and calculated amount of LPA to detect fixed and proportional bias.

Table 1. Patient's characteristics (n = 53)

Age, years	77 ± 6
Gender, M/F	46/7
BMI, kg/m^2	21.8 ± 4.1
FFM, kg	45.3 ± 8.9
FFMI, kg/m^2	16.2 ± 4.9
mMRC scale, 0/1/2/3/4	5/19/14/10/5
GOLD stage, I/II/III/IV	15/14/21/3
CCI	1.8 ± 2.0
FVC, L	2.9 ± 1.2
FEV_1, L	1.6 ± 0.8
FEV_1/FVC, %	63.0 ± 26.4
FEV_1, %pred	57.2 ± 19.1
Hand grip strength, kg	31.5 ± 8.2
QF, kg	38.1 ± 14.2
PI_{max}, cmH_2O	66.3 ± 27.5
6MWD, m	360.1 ± 155.9
Gait speed, m/s	1.0 ± 0.3
CAT, score	13.7 ± 9.2
LPA, min/day	25.4 ± 16.7
MVPA, min/day	16.0 ± 21.7
Steps/day	3570 ± 3212

mean ± SD.

BMI, body mass index; FFM, fat-free mass; FFMI, fat-free mass index; mMRC, modified Medical Research Council; GOLD, Global Initiative for Chronic Obstructive Lung Disease; CCI, Charlson comorbidity index; FVC, forced vital capacity; FEV_1, forced expiratory volume in one second; QF, quadriceps femoris muscle force; PI_{max}, maximum inspiratory mouth pressure; 6MWD, six-minute walk distance; CAT, chronic obstructive pulmonary disease assessment test; LPA, low-intensity physical activity; MVPA, moderate-to-vigorous intensity physical activity

Results

The mean age of the 53 patients was 77 ± 6 years, and the mean FEV_1%pred was 63.0 ± 26.4%. The patients' characteristics are presented in Table 1. The mean number of steps/day was 3570 ± 3212, and the time spent in LPA and MVPA was 25.4 ± 16.7 min/day and 16.0 ± 21.7 min/day, respectively. In all, 23, 16, 19, 20, and 10 assessments were performed at the initiation of PR, 6 months, and 1, 2, and 3 years after PR, respectively. A total of 16, 17, 10, and 2 patients performed the assessment 1, 2, 3, and 4 times, respectively (Appendix 1). All assessments were done at being in a stable condition with no infection or exacerbation of COPD in the prior 3 months.

Association between LPA and clinical measurements by regression analysis

The time spent in LPA was significantly correlated with age, mMRC scale, hand grip strength, QF, maximum inspiratory mouth pressure (PI_{max}), 6MWD, and gait speed by univariate regression analysis (Table 2 and Fig. 2). In multivariate

Table 2. Univariate and multivariate regression analysis of LPA

Variables	Univariate analysis			Multivariate analysis		
	B	95% CI	p-value	β	p-value	VIF
Age	–1.339	–2.014, –0.665	<0.001	–	–	–
BMI	0.371	–0.817, 1.560	0.536	0.091	0.428	1.007
FFMI	–0.374	–2.108, 1.361	0.669	0.021	0.864	1.028
mMRC	–0.6532	–10.135, –2.928	0.001	–0.292	0.014	1.271
CCI	–0.980	–2.825, 0.866	0.294	–0.066	0.541	1.027
FEV_1%pred	0.064	–0.103, 0.231	0.447	–	–	–
Hand grip	0.757	0.277, 1.237	0.002	0.216	0.063	1.136
QF	0.397	0.088, 0.706	0.012	0.207	0.063	1.065
PI_{max}	0.286	0.165, 0.407	<0.001	0.367	0.004	1.324
6MWD	0.055	0.027, 0.083	<0.001	0.359	0.006	1.404
Gait speed	41.351	24.939, 57.764	<0.001	0.392	0.001	1.286
CAT	–0.457	–0.936, 0.022	0.061	–0.160	0.141	1.041

Standardized partial regression coefficient (β) was adjusted for age and FEV_1%pred.

LPA, low-intensity physical activity; B, regression coefficient; CI, confidence interval; β, standardized partial regression coefficient; VIF, variance inflation factor; BMI, body mass index; FFMI, fat-free mass index; mMRC, modified Medical Research Council; CCI, Charlson comorbidity index; FEV_1, forced expiratory volume in one second; QF, quadriceps femoris muscle force; PI_{max}, maximum inspiratory mouth pressure; 6MWD, six-minute walk distance; CAT, chronic obstructive pulmonary disease assessment test

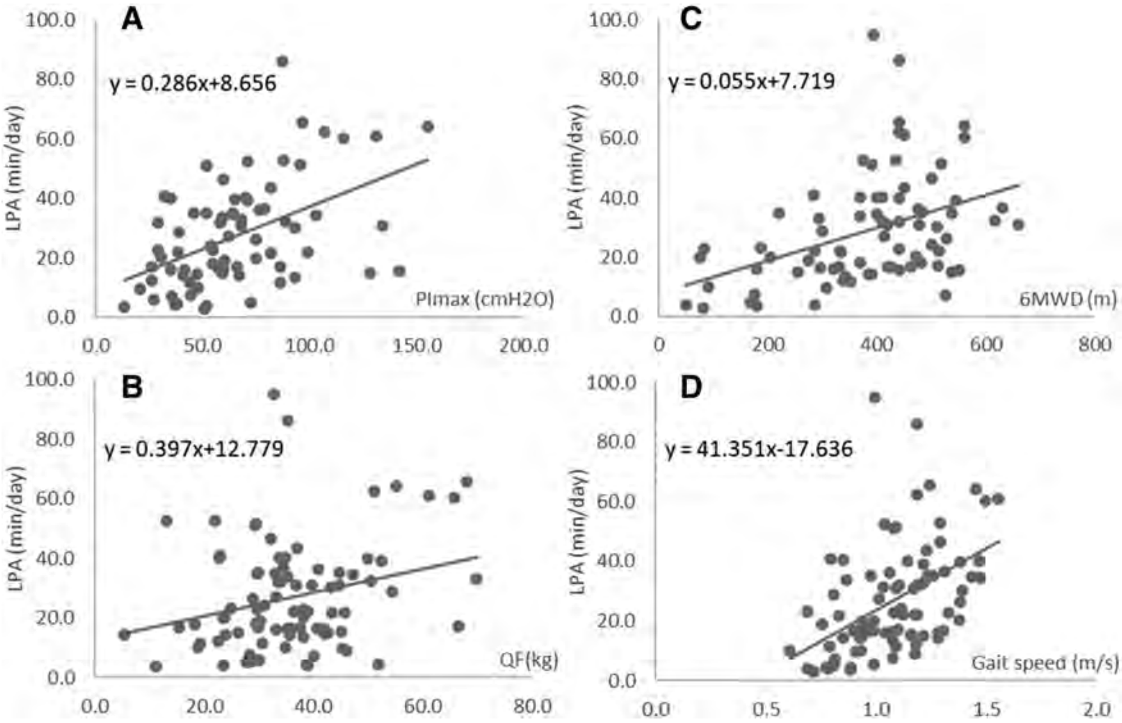

Fig. 2. Association between LPA and associated variables

(A) PI_{max}, (B) QF, (C) 6MWD, and (D) gait speed

LPA, low-intensity physical activity; PI_{max}, maximum inspiratory mouth pressure; QF, quadriceps femoris muscle force; 6MWD, six-minute walk distance

regression analysis using age and FEV_1%pred as confounding factors for PA, mMRC scale, PI_{max}, 6MWD, and gait speed were also correlated with the time spent in LPA (Table 2). When the stepwise regression was utilized with these factors, gait speed and PI_{max} were extracted as independent variables to create a linear regression equation of the time spent in LPA:

The time spent in LPA (min/day) = gait speed (m/s) × 31.9 + PI_{max} (cmH_2O) × 0.2 – 20.553

Validity of calculated LPA

A significant correlation was observed between the measured and calculated time spent in LPA by linear regression analysis ($R^2 = 0.362$, $p < 0.001$; Appendix 2A), and the validity of this linear regression equation was examined by residual analysis (D = 0.081, p = 0.200; Appendix 3). There was no fixed bias (mean of difference 95% confidence interval: −3.013 to 3.381, limit of agreement: −27.1 to 27.1) but there was proportional bias (r = 0.479, $p < 0.001$) by Bland–Altman plots (Appendix 2B).

Discussion

The presented data showed that the time spent in LPA was significantly correlated with age, mMRC scale, hand grip strength, QF, PI_{max}, 6MWD, and gait speed by univariate and multivariate regression analyses. PI_{max} and gait speed were utilized to create an equation for the time spent in LPA in patients with COPD using stepwise regression analysis (the time spent in LPA (min/day) = gait speed (m/s) × 31.9 + PI_{max} (cmH_2O) × 0.2 − 20.553). The validity of this equation was demonstrated by linear regression analysis and residual analysis. Using Bland–Altman plots, there was no fixed bias but there was proportional bias on the reliability of this equation.

A wide variety of factors are associated with or affect PA[34–36]. A systematic review by Gimeno-Santos et al.[35] reported that PA is influenced by age, gender, social factors, lifestyle, environment, as well as clinical and functional factors, such as dyspnea, exercise capacity, and disease severity. As for the influence of medications and comorbidities, bronchodilators had been prescribed to all subjects, and CCI was not a statistically significant factor for LPA as presented in our multivariate analysis; thus, it is concluded that they were not major confounding factors in this study. In addition, gait speed is reported to be correlated with PA measured by daily steps in previous studies[37,38]. Exercise intensity referred to daily activities that require standing such as housework and gardening, which might be associated with gait speed that reflects lower limb function rather than QF. Moreover, the activity monitor used in the present study is a uniaxial accelerometer and can detect movement related to walking, so that gait speed was extracted as a factor related to walking in the analysis. Exercise capacity such as 6MWD has been found to be associated with PA[34,35,39]. It is considered that gait speed that prescribes 6MWD indirectly affects PA and that the parameters of lower limb function more strongly affect the daily activities that require standing than the factors of exercise ability.

The equation created using stepwise regression analysis did not include mMRC scale. This may be because the COPD patients had lower intensity of daily physical activities in order to not cause dyspnea. COPD patients tend to perform daily activities more slowly than healthy individuals, to prevent dyspnea[16]. Those who have mild dyspnea can conduct more PA with relatively higher intensity like MVPA rather than LPA, while on the other hand severe dyspnea patients are not able to achieve even LPA in daily life. The time spent in LPA as a dependent variable is thus unlikely to be related to dyspnea as mMRC scale. Likewise, LPA is considered not necessarily dependent on the degree of airflow obstruction like FEV_1%pred, which was not a significant factor in the multivariate analysis. There have been reports that dynamic hyperinflation, which is a major factor causing dyspnea during exertion in patients with COPD, is associated with PA[36,40]. Inspiratory capacity (IC) that indicates the degree of dynamic hyperinflation has also been reported to affect daily steps[36]. Inspiratory muscle strength, which is measured as PI_{max}, contributes to IC and is associated with time spent in walking and standing in daily life[34]. Since inspiratory muscle training may increase the amount of PA by improving dynamic pulmonary hyperinflation with the improvement of PI_{max}[41], it is considered that PI_{max} was also extracted in the stepwise regression analysis as a factor of respiratory function. As a result, it is suggested that a new prediction equation of the time spent in LPA as PA other than daily steps using PI_{max} and gait speed may be generally utilized in various clinical practices.

The internal validity of the equation for the time spent in LPA in this study was confirmed by a significant correlation between the measured and calculated LPA by linear regression analysis and residual analysis. The multiple correlation coefficient of this equation ($R^2 = 0.349$), however, was insufficient for the calculation of predicted amount of LPA. This may have been resulted from various confounding factors related to PA in the patients with COPD[35]. In our study, there was no fixed bias but there was proportional bias between the measured and calculated time spent in LPA. This proportional bias suggests that the measured time spent in LPA tends to be slightly higher than the calculated time. Based on this result, the calculated time spent in LPA is considered to be the predicted amount of LPA and can be used as a minimum amount of PA for goal setting in COPD patients, especially in severe and very severe cases.

The prevalence of sarcopenia, which is associated with a high morbidity rate in elderly COPD patients[42], is reported to be higher in patients with severe COPD[43]. In patients with COPD and muscle wasting (fat-free mass index <16 kg/m^2 for male and <15 kg/m^2 for female), inflammatory markers increase with submaximal exercise[44]. Thus, it might be important to suggest not only the amount but also the intensity of PA in patients with sarcopenic COPD. Moreover, pedometers are known to have a reduced sensitivity when measuring steps during slow walking[17], which is commonly observed in COPD patients[16]. As a target indicator of PA, low-intensity activity time is more useful than the number of steps, especially for severe COPD patients.

There are several limitations to be addressed in this study. First, the number of accumulated data for analysis was 88 assessments from 53 participants, which might be influenced by case bias of each characteristic and assessment data from the patients who have been multi-evaluated. In addition, the 88 assessments were influenced from confounding factors over time including treatment management and the type of exercise therapy and must also be considered. On the other hand, it is also a single-center study, and although the results are limited, it is possible that the relationship between the LPA and other indicators correlated with LPA might be shown as one trend. We calculated the sample size based on our previous study that investigated the correlation between the time spent in walking and 6MWD because there are no reports to analyze the relationship between LPA and other factors. Thus, we set the effect size to 0.35 and attained the result by power calculation for the sample size. On account of this, a different number of subjects other than 83 might be required when using another set of data. Second, this study did not investigate the correlation of LPA with other factors, including gender, comorbidities, mental status, and environmental and social factors; therefore, it had proportional bias between the measured and calculated LPA obtained from the equation. The predicted equation in this study uses PI_{max}, which has not been easily obtainable in clinical practice so far, thus making the applicability limited. In addition, in a clinical setting, this predicted equation is limited to use for patients with COPD who have been assigned to a PR. Further study is required to create a more precise and suitable equation of LPA using other factors. Third, the predicted amount of LPA might be required in goal setting, especially for severe COPD patients, but we analyzed the data of the patients regardless of severity. The equation of the predicted amount of LPA should be created by analyzing data of COPD patients with all degrees of severity in a future study. Overall, this equation only indicates a reference value of LPA that might be associated with PI_{max} and gait speed.

Conclusion

In summary, the equation for the predicted amount of LPA was created using gait speed and PI_{max} in our present study. This equation could be useful for goal setting in patients with COPD. However, the precision and suitability of this equation create several limitations for application in all clinical settings. Further studies are needed to create a more precise equation in COPD patients with varying severity.

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Conflict of Interest: The authors have no conflicts of interest to declare.

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Supplementary Material (Appendices)

All supplementary files are available online.

Appendix 1. Flow diagram of the number of assessments in 53 patients

Appendix 2. The validity between the measured and calculated LPA

Appendix 3. Residual analysis between the measured and calculated LPA by the Kolmogorov–Smirnov test (D = 0.081, p = 0.200)

PHYSICAL
THERAPY
RESEARCH

BRIEF REPORT

Pain in Spinal Muscular Atrophy: A Questionnaire Study

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ABSTRACT. Objective: This study aimed to reveal the chronic pain prevalence in spinal muscular atrophy (SMA) patients and identify the clinical characteristics of these patients with chronic pain. The pain status was also investigated in SMA patients with chronic pain. Methods: This cross-sectional study was conducted between July 2018 and December 2018. SMA type II and type III patients in Japan were mailed a survey questionnaire. The survey items were chronic pain prevalence, clinical characteristics, and motor function. Patients with chronic pain also answered questions on various pain status parameters: pain intensity, frequency, duration, location using body map, and factors that exacerbated and relieved pain. Results: The questionnaire recovery rate was 61.1%. Sixty-four type II (mean age 17.3 ± 11.7 years) and 22 type III (mean age 44.9 ± 21.6 years) patients were eligible for inclusion. The prevalence of chronic pain in type II and III patients was 40.6% and 40.9%, respectively. Type II patients with chronic pain were more likely to report the inability to sit without manual support than those without pain ($p = 0.03$). Pain intensity in SMA patients was mild, but pain usually occurred daily, for prolonged durations, most often in the neck, back, and lower extremities. Sitting and high physical activity exacerbated pain the most. Conclusion: The percentage of patients with SMA with chronic pain was high, at above 40%. Moreover, the pain experienced by patients with SMA was low in intensity but frequent and most common in the lower extremities.

Key words: Spinal muscular atrophy, Neuromuscular disease, Pain, Questionnaire survey

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Spinal muscular atrophy (SMA) is a neurogenic muscular atrophy that arises because of spinal motor neuron degeneration, primarily in the anterior horn of the spinal cord[1)]. The morbidity rate for SMA is one per 6000–10,000 individuals[2,3)]. The symptoms of SMA are progressive and manifest as weakness of muscles in the trunk and proximal upper and lower limbs, respiratory distress, contractures, and scoliosis. SMA is classified into types I through III based on severity and age of onset[4)]. In SMA type I, motor function decreases rapidly from a few weeks after birth, with onset occurring up to 6 months postpartum. Sitting and stabilizing the head and neck are lifelong challenges due to issues with motor function, and use of mechanical ventilation is always necessary. The onset of SMA type II also occurs in infancy, at up to 18 months of age. Type II patients are able to achieve a sitting position, but it is difficult for them to stand or walk unaided. Onset of SMA type III occurs after 18 months of age. Patients are able to walk, but motor symptoms, such as a tendency to fall, appear gradually. Rehabilitation is essential for patients with SMA to maintain and improve motor function and activities of daily living (ADLs). One of the issues encountered by rehabilitation staff and SMA patients is pain.

Patients with slowly progressive neuromuscular disease (NMD), including SMA, commonly experience pain-related problems, increasing fatigue, and impaired ADLs[5–7)]. Previous studies have presented systematic reports on the pain status of patients with Duchenne muscular dystrophy (DMD)[8)] and amyotrophic lateral sclerosis[9)]. Conversely, as SMA is a rare genetic disease, there have been only few reports of large-scale investigations of pain status in SMA patients[10)]. Patients with NMD have significantly more persistent pain than the general population[5–9)], but the

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incidence and underlying characteristics of pain in SMA patients are not well understood.

Therefore, the primary study objective was to investigate the chronic pain prevalence and clinical characteristics of SMA type II and III patients with pain. The secondary objective was to survey the pain status of SMA patients with chronic pain. The previous study population included only few SMA patients. SMA type I patients were excluded from the subject pool due to the disease's severity, and SMA type II and III patients were analyzed independently because motor function differs depending on the type. Systematic surveys on the pain status of patients with SMA are useful to understand specific NMDs and for appropriate selection of therapeutic interventions and rehabilitation methods.

Methods

Study design and population

This cross-sectional questionnaire survey was conducted from July 2018 to December 2018. The participants were patients with SMA type II and III and their guardians. The survey method was approved by the SMA Family Association in Japan, and we sent questionnaires to Japanese SMA patients and their guardians. The SMA Family Association comprises patients with SMA types I, II, and III; their family members; and supporting healthcare staff and volunteers. The questionnaire used in this study was self-administered and sent via post, and the responses were collected using reply envelopes. If the patients were less than 18 years old, they were given the option to respond to the questionnaire with assistance from their guardians and to clearly indicate whether their guardians helped them. Patients with SMA type I were excluded because the severity of the disease caused difficulty in accurately assessing pain using questionnaires.

Questionnaire survey items and analysis

The questionnaire was designed by physical therapists, pediatricians, and rehabilitation doctors, referring to a previous study[10]. In addition, we asked two patients from the SMA Family Association in advance to confirm points that were difficult to understand and terminology when answering the questionnaire. The questionnaire survey items were designed to collect data of clinical characteristics and pain status. The clinical characteristics were sex; age; mechanical ventilation use; electric wheelchair use; presence of spinal fusion; history of tracheotomy, laryngotracheal separation, or gastrostomy; analgesic agents use; and motor function (walking, turning over/bottom shuffling, and sitting without manual support). For the pain status-related items, we first inquired about chronic pain (pain that persists for ≥3 months) in the muscle, bone, tendons, and skin or nerves. Pain caused by headaches or psychological pain was excluded from analysis[11]. To understand the clinical characteristic of SMA patients with pain, SMA type II and III were divided into two groups based on the presence or absence of chronic pain, and the clinical characteristic was compared between these two groups. Next, those who answered that they had chronic pain were asked about the pain status: pain intensity, frequency, duration, location, and factors that exacerbated and relieved pain.

Questions related to pain status

A numerical rating scale (NRS)[12,13] was used to determine pain intensity. The NRS evaluates pain intensity using an 11-point scale ranging from 0 to 10, wherein 0 indicates no pain and 10 indicates the maximum pain imaginable. The NRS was used to evaluate patients aged 5 years or older[14], while those younger than 5 years old were excluded from the analysis. A four-scale rating was presented to describe pain frequency—always present, several times a day, several times a week, and several times a month—while a five-scale rating was presented to describe the duration of continuous pain—not continuous, within 1 hour, 1–12 hours, 13–24 hours, and ≥2 days. The locations of pain were entered as painful locations on a body map[15]. Multiple answers were allowed if there were multiple locations of pain. These locations were classified into four groups based on the responses: neck/back, upper extremities, lower extremities, and others. The validity and reliability of the evaluation of painful locations using the body map have been confirmed in both children and adults[15]. The questionnaire had 13 items to determine which factors exacerbated or relieved pain. Previous studies of patients with NMDs, including those with DMD and SMA, were used as a reference to select the items[10].

Statistical methods

Chi-square test was used to compare sex; mechanical ventilation use; electric wheelchair use; presence of spinal fusion; history of tracheotomy, laryngotracheal separation, or gastrostomy; analgesic agents use; and motor function (walking, rolling over/bottom shuffling, and sitting without manual support). The unpaired t-test was used to compare the age differences between the two groups. All tests were performed using IBM SPSS Statistics for Windows, version 23 (IBM, Armonk, NY, USA). The level of significance was set at $p < 5\%$.

Ethics statement

This study was approved by the Ethics Committee of Tokyo Women's Medical University (approval number: 4462). A written explanation of the study was enclosed in the envelope used to send the questionnaire survey. Only individuals who gave their informed consent to participate were included in the study. In addition, the SMA Family Association ensured that personal information was protected and that the respondents could not be identified when the questionnaires were sent and collected.

Results

Demographic and clinical characteristics

The questionnaire was sent to 221 SMA patients and 135 responded, with a response rate of 61.1%. Among them,

Table 1. Demographic and clinical characteristics of spinal muscular atrophy type II and III patients and comparison of clinical characteristics between two groups of spinal muscular atrophy type II and III patients stratified based on the presence or absence of chronic pain

	Type II n = 64	Type II Pain (–) n = 38	Type II Pain (+) n = 26	p-value	Type III n = 22	Type III Pain (–) n = 13	Type III Pain (+) n = 9	p-value
Sex (male/female)	31/33	16/22	15/11	0.22	11/11	8/5	3/6	0.19
Age, years	17.3 ± 11.7	16.0 ± 9.3	19.3 ± 14.5	0.27	44.9 ± 21.6	42.6 ± 22.6	48.3 ± 21.0	0.56
Mechanical ventilation use, n	37 (57.8)	21 (55.3)	16 (61.5)	0.62	2 (9.1)	1 (7.7)	1 (11.1)	0.39
Electric wheelchair use, n	50 (78.1)	32 (84.2)	18 (69.2)	0.16	12 (54.5)	6 (46.2)	6 (66.7)	0.42
Presence of spinal fusion, n	14 (21.9)	8 (21.1)	6 (23.1)	0.89	0	0	0	–
History of tracheotomy, n	3 (4.7)	1 (2.6)	2 (7.7)	0.36	1 (4.5)	0	1 (11.1)	0.22
History of laryngotracheal separation, n	1 (1.6)	0	1 (3.8)	0.23	0	0	0	–
History of gastrostomy, n	7 (10.9)	2 (5.3)	5 (19.2)	0.09	0	0	0	–
Analgesic agents use, n	2 (3.1)	0	2 (7.7)	–	4 (18.2)	0	4 (44.4)	–
Motor function								
Walking, n	1 (1.6)	1 (2.6)	0	0.41	14 (63.6)	8 (61.5)	6 (66.7)	0.81
Rolling over or bottom shuffling, n	14 (21.9)	9 (23.7)	5 (19.2)	0.73	13 (59.1)	8 (61.5)	5 (55.6)	0.78
Sitting without manual support, n	25 (39.1)	19 (50.0)	6 (23.1)	0.03	13 (59.1)	8 (61.5)	5 (55.6)	0.78

Average ± standard deviation or n (%)

the type classification was 48 SMA type I patients, 64 SMA type II patients, 22 SMA type III patients, and 1 unknown. Table 1 shows the clinical characteristics and motor function of SMA type II and type III patients and comparison of the clinical characteristics of patients stratified into two groups based on the presence or absence of chronic pain. Spinal fusion was present in 14 type II patients (21.9%) but no type III patients. In terms of motor function, 1 type II patient (1.6%) and 14 type III patients (63.6%) could walk, 14 type II patients (21.9%) and 13 type III patients (59.1%) could roll over/bottom shuffle, and 25 type II patients (39.1%) and 13 type III patients (59.1%) could sit without manual support. In all, 26 type II patients (40.6%) and 9 type III patients (40.9%) reported chronic pain that persisted ≥3 months. SMA type II patients with chronic pain had limited ability to sit without manual support than those without chronic pain ($p = 0.03$). No other significant differences were observed between SMA type II and type III patients.

Pain status

We investigated the pain status of 26 SMA type II patients and 9 type III patients with chronic pain. The mean pain intensity, according to the NRS, was 3.3 ± 1.7 in type II patients and 3.6 ± 1.6 in type III patients. Pain frequencies ranging from "always present" to "several times a day" were considered to indicate high frequency, which was reported by 68.0% of the SMA type II patients and 62.5% of the type III patients. The duration of continuous pain was "within 1 hour" and "not continuous" in 36.0% and 28.0% of the SMA type II patients, respectively, accounting for two-thirds of the whole group. Long-term pain was detected in 62.5% of the SMA type III patients who responded "≥2 days." The location of pain was most commonly in the lower extremities in both SMA type II and III patients (65.4% and 44.4% of the patients, respectively). Other responses indicated pain in the neck/back and upper extremities (Table 2).

For both SMA type II and type III patients, "sitting" is the factor most commonly reported to exacerbate pain (Table 3). Further, "high physical activity" and "walking or attempting to walking" were reported to exacerbate pain in 27.8% and 11.1% of the SMA type III patients, respectively. The factor that was most commonly reported to relieve pain was "changing position" and "massage" for SMA type II patients and "resting" for SMA type III patients (Table 4).

Discussion

In this study, we describe the results of a questionnaire survey on pain administered to Japanese SMA type II and III patients and their families. Our results show that almost 40%

Table 2. Pain status in 26 spinal muscular atrophy type II patients and 9 type III patients with chronic pain

	Type II n = 26	Type III n = 9
Pain intensity	n = 23	n = 9
NRS	3.3 ± 1.7	3.6 ± 1.6
Pain frequency	n = 26	n = 9
Always present, n	8 (32.0)	4 (50.0)
Several times a day, n	9 (36.0)	1 (12.5)
Several times a week, n	4 (16.0)	0
Several times a month, n	4 (16.0)	3 (37.5)
Pain continued duration	n = 26	n = 9
Not continuous, n	7 (28.0)	2 (25.0)
Within 1 hour, n	9 (36.0)	0
1–12 hours, n	3 (12.0)	0
13–24 hours, n	3 (12.0)	1 (12.5)
≥2 days, n	3 (12.0)	5 (62.5)
Pain site	n = 26	n = 9
Neck/Back, n	11 (42.3)	3 (33.3)
Upper extremities, n	5 (19.2)	3 (33.3)
Lower extremities, n	17 (65.4)	4 (44.4)
Others, n	13 (50.0)	2 (22.2)

Average ± standard deviation or n (%)

NRS, numerical rating scale

Table 3. Factors exacerbating pain in 26 spinal muscular atrophy type II patients and 9 type III patients with chronic pain

	Type II n = 26	Type III n = 9
Sitting, n	19 (34.5)	6 (33.3)
High physical activity, n	9 (16.4)	5 (27.8)
Being lifted and transferred, n	4 (7.3)	2 (11.1)
Movement exercises, n	1 (1.8)	0
Muscle stretching, n	6 (10.9)	0
Standing or attempting to standing, n	0	0
Dressing, n	2 (3.6)	1 (5.6)
Walking or attempting to walking, n	1 (1.8)	2 (11.1)
Riding in car/on bus, n	1 (1.8)	1 (5.6)
Bathing or swimming, n	1 (1.8)	0
Wearing leg brace, n	1 (1.8)	0
Wearing spinal orthosis, n	2 (3.6)	1 (5.6)
Others, n	8 (14.5)	0

n (%)

Table 4. Factors relieving pain in 26 spinal muscular atrophy type II patients and 9 type III patients with chronic pain

	Type II n = 26	Type III n = 9
Resting, n	11 (17.5)	6 (35.3)
Changing position, n	19 (30.2)	4 (23.5)
Massage, n	12 (19.0)	1 (5.9)
Use of analgesics, n	3 (4.8)	3 (17.6)
Muscle stretching, n	6 (9.5)	1 (5.9)
Bathing or swimming, n	4 (6.3)	0
Relaxing, n	6 (9.5)	1 (5.9)
Movement exercises, n	0	0
Wearing leg brace, n	0	0
Standing or attempting to standing, n	0	0
TENS, n	0	0
Wearing spinal orthosis, n	0	0
Others, n	2 (3.2)	1 (5.9)

n (%)

TENS, transcutaneous electrical nerve stimulation

of the SMA type II and III patients experience chronic pain lasting at least 3 months. These findings are in agreement with those of previous reports that many patients with NMD have chronic pain[6,7]. In particular, Lager et al.[10] performed a pain survey of patients with NMD, including 17 SMA type II and III patients each, and reported frequent onset of low-intensity pain in the lower extremities and neck. However, the previous study included only few SMA patients[10]. To our best knowledge, this is the first study to survey the characteristics of chronic pain and pain status in SMA patients. We analyzed the survey results of 64 SMA type II patients and 22 type III patients who reported experiencing chronic pain. We observed that only 6 (23.1%) SMA type II patients with pain could sit without manual support, while 19 (50.0%) SMA II patients without pain were able to do the same (p = 0.03). Patients with NMDs and pain have lower motor function and fewer ADLs[16]. The highest functional attainment of SMA type II patients is usually sitting[17], and it is reasonable to assume that patients who experience difficulty sitting without manual support have a lower motor function.

Respondents to the questionnaire reported pain intensities ranging from mild to severe pain. An NRS score ranging from 1 to 3 is considered to represent mild pain, and scores ≥4 points are considered to represent pain that can restrict physical function[18]. The results of the NRS, which was used to evaluate SMA patients above 5 years old, suggest that chronic pain occurring in SMA is usually mild. However, the frequency of pain appears to be high for both SMA type II and III patients. Further, when the duration is continuous, SMA type II patients appear to experience short, intermittent periods of pain, whereas type III patients continuously experience chronic pain. Pain that is persistent and high in frequency can negatively affect patients' quality of life, despite low pain intensity[19]. For both SMA type II and type III patients, the most commonly reported location of pain was the lower extremities. It is presumed that the pain worsened due to decreased opportunities for muscle contraction in the lower extremities and deterioration of blood circulation[20].

The most commonly reported factors that exacerbated pain in SMA type II and type III patients were "sitting" and "high physical activity." This result was consistent with that reported for other NMDs. In contrast, the most commonly reported factors for pain relief were "changing position" and "massage" in SMA type II patients and "resting" in SMA type III patients. The pathophysiology of pain might be different between these SMA types II and III patients. Many SMA type II patients had low physical activity and experienced difficulty sitting straight without manual support. Low physical activity is likely to cause immobilization pain, which is a cause of pain and a risk factor for exacerbations[21,22].

The mechanism underlying the pathogenesis of pain is thought to be affected by the attenuation and disappearance of sensory stimulus input due to inactivity and joint contracture, which causes sensitization and plastic changes in the nervous system, including in the spinal cord and brain. It is believed that prolonged immobilization can cause changes in the nervous system, leading to chronic pain[23].

In addition, SMA type II patients include those who have undergone spinal fusion due to scoliosis. Spinal fusion improves sitting balance and endurance in the sitting position, but there is a risk of immobilization associated with spinal fusion[24,25]. On the other hand, many SMA type III patients had high physical activity. Patients with SMA have a weaker trunk than healthy controls, requiring excessive muscle contraction for various movements[26]. These patients have an increased risk of exercise-induced muscle injury and can easily experience fatigue from overwork, even when performing simple ADLs[27]. Therefore, it was considered that "changing position" and "massage" were effective for SMA type II patients, and that "resting" was effective for SMA type III patients.

This study had a few limitations. Pain reported by young SMA patients was based on their guardian's judgment and not direct observation. Previous studies have noted that guardians' judgments of pain tend to be valid, although parents may underestimate their child's pain[28,29]. Additionally, pain is frequently affected by physiological, psychological, and social factors; unfortunately, these were not investigated. Moreover, since the ages differ greatly between type II and type III, the effects of aging and contracture may differ. Finally, because the number of patients with chronic pain was small, it was not possible to analyze pain according to motor function for each type. In the future, it is necessary to increase the number of cases and verify the relationship between motor function and chronic pain.

Conclusion

In this study, the percentage of patients with SMA with chronic pain was high, at above 40%. Moreover, the pain experienced by patients with SMA was low in intensity but frequent and most common in the lower extremities. We believe our results can facilitate pain treatment for SMA patients in clinical practice and aid future studies to better evaluate the results of various therapeutic interventions.

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Conflict of Interest: The authors declare that there is no conflict of interest regarding the publication of this paper.

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PHYSICAL THERAPY RESEARCH

CASE REPORT

Early Pulmonary Rehabilitation with Neuromuscular Electrical Stimulation in a Patient with Acute Exacerbation of Rheumatoid Arthritis-associated Interstitial Lung Disease: A Case Report

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ABSTRACT. Introduction: Early implementation of neuromuscular electrical stimulation (NMES) has been reported to prevent muscle atrophy and physical functional decline in patients requiring mechanical ventilation. However, its effect in patients with acute exacerbation of interstitial lung disease (ILD) remains unclear. We herein report our experience using the NMES combined with mobilization in a patient with an acute exacerbation of rheumatoid arthritis-associated ILD (RA-ILD) requiring mechanical ventilation. Case Presentation: A 74-year-old man was admitted to the intensive care unit (ICU) and put on mechanical ventilation due to severe acute exacerbation of RA-ILD. Early mobilization and the NMES using a belt electrode skeletal muscle electrical stimulation system were started on day 7 of hospitalization (day 2 of ICU admission). The NMES duration was 20 min, performed once daily. The patient could perform mobility exercises on day 8 and could walk on day 16. We assessed his rectus femoris and quadriceps muscle thicknesses using ultrasound imaging, and found decreases of 4.5% and 8.4%, respectively, by day 14. On day 27, he could independently visit the lavatory, and the NMES was discontinued. He was instructed to start long-term oxygen therapy on day 49 and was discharged on day 63. His 6-minute walk distance was 308 m and his muscle thickness recovered to levels comparable to those at the initial evaluation at the time of discharge. Conclusion: Combining the NMES and mobilization started in the early phase and continued after ICU discharge was safe and effective in a patient with a severe acute exacerbation of RA-ILD.

Key words: Neuromuscular electrical stimulation, Skeletal muscle atrophy, Pulmonary rehabilitation, Acute exacerbation, Interstitial lung disease

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Both acute exacerbation of interstitial lung disease (ILD) and rheumatoid arthritis-associated ILD (RA-ILD) have poor prognoses[1,2)]. Regardless of patient survival, severe hypoxemia and dyspnea on exertion often cause prolonged physical inactivity, making it difficult to maintain physical functions and perform activities of daily living (ADL).

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The effectiveness of neuromuscular electrical stimulation (NMES) performed as part of a pulmonary rehabilitation program for chronic respiratory disease has been investigated[3–6)]. The NMES reportedly improves functional exercise capacity, quadriceps muscle mass, and strength in those with severe chronic obstructive pulmonary disease (Medical Research Council dyspnea score ≥4) and can even be used during acute exacerbation[4,5)]. However, in patients with ILD, the efficacy of the NMES has only been investigated in its stable phase[6)]. Although several reports of early implementation of the NMES in the intensive care unit (ICU) in critically ill patients have demonstrated improvements in muscle mass and strength[7,8)], recent systematic reviews concluded that these effects remain controversial[9,10)].

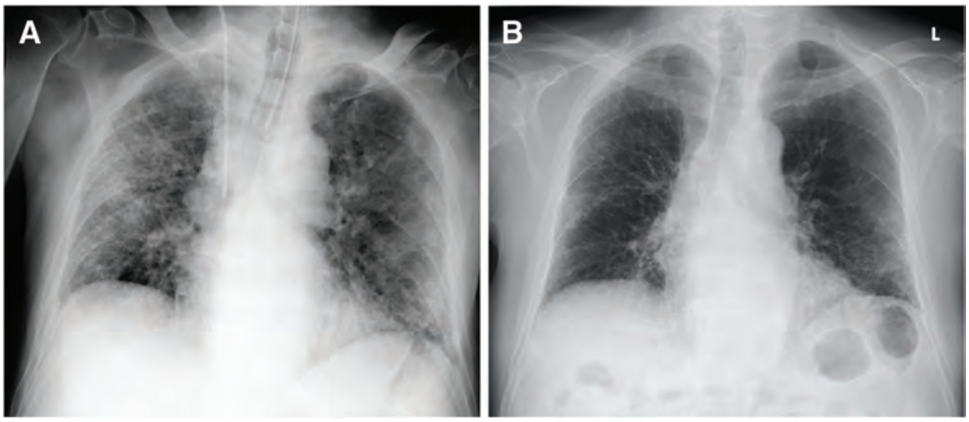

Fig. 1. Chest radiographs obtained at ICU admission (A) and hospital discharge (B)
ICU, intensive care unit

Table 1. Changes in laboratory parameters over the course of hospitalization

Variable	Unit	Day 2	Day 6	Day 27	Day 56
WBC	10^3/μL	15.9	20.7	13.6	11.7
Hb	g/dL	13.8	13.0	12.1	13.5
Alb	g/dL	2.6	2.1	2.3	2.8
CRP	mg/dL	18.5	12.84	0.84	0.16
KL-6	U/mL	1,171	–	1,086	1,060
SP-D	ng/mL	146	–	–	–

"–" indicates that the parameter was not measured on that day.

WBC, white blood cell; Hb, hemoglobin; Alb, albumin; CRP, C-reactive protein; KL-6, sialylated carbohydrate antigen KL-6; SP-D, pulmonary surfactant protein-D

Most studies included in these reviews have examined the effects of the NMES during ICU stay, although in some cases, the NMES might be useful for a longer period, including after ICU discharge. Patients with acute exacerbations of ILD may require mechanical ventilation in severe cases, and as mentioned above, inactivity is often prolonged after the critical phase due to severe dyspnea on exertion. To date, no studies have investigated the effectiveness of the NMES for such patients, although such patients may be highly suitable.

Herein, we report our experience of starting the NMES combined with mobilization in the early phase of severe acute exacerbation in a patient with RA-ILD. The patient required invasive mechanical ventilation and was expected to have prolonged exertional hypoxemia and dyspnea. Therefore, we considered applying early intervention to prevent muscle atrophy and weakness.

Case Presentation

A 74-year-old man (height: 171 cm, body mass index: 21.4 kg/m^2) with diabetes, hypertension, and RA treated with methotrexate, tacrolimus, and prednisolone was admitted to our hospital because of bacterial pneumonia and was started on antibiotics (tazobactam/piperacillin). On day 5 of hospitalization, chest radiographs revealed ground-glass opacities throughout the bilateral lung fields (Fig. 1A), and the patient experienced severe respiratory failure. Therefore, he was admitted to the ICU for mechanical ventilation initiation on day 6. The results of arterial blood gas analysis performed immediately after starting mechanical ventilation indicated a pH of 7.49, partial pressure of arterial oxygen (PaO_2) of 93 Torr, partial pressure of arterial carbon dioxide of 42 Torr, bicarbonate level of 30.5 mEq/L, and a ratio of PaO_2/fraction of inspired oxygen (FiO_2) of 116 (93/0.80). Steroid pulse therapy was administered for 3 days with subsequent tapering, and intravenous immunoglobulin was administered on day 5. The antibiotics prescribed (meropenem, levofloxacin, trimethoprim/sulfamethoxazole, and voriconazole) were changed according to the results of the inflammatory response and culture tests. Low-dose trimethoprim/sulfamethoxazole was continued as the maintenance therapy. The blood test results are presented in Table 1.

The clinical course, including medications, respiratory care, and mobilization level, is presented in Figure 2. Pulmonary rehabilitation involving mobilization and exercise therapy was started on day 7 (day 2 of ICU admission). Because of the patient's low level of consciousness, only passive exercise was performed initially. We expected that even after he was conscious and able to mobilize, exertion would lead to severe and prolonged hypoxemia and dyspnea. Thus, we considered it necessary to prevent muscle atrophy and weakness from the early phase. Therefore, we applied the NMES using a belt electrode skeletal muscle electrical stimulation system (G-TES; Homerion Laboratory, Tokyo, Japan). Belt electrodes were attached to the proximal thigh, above the knee and above the ankle on both sides. Muscles between the belt electrodes were stimulated, mainly the quadriceps femoris (QF), the hamstrings, the triceps surae, and the tibialis anterior. The NMES protocols used were the ones pre-set on the G-TES; these included the mild-disuse mode (frequency: 20 Hz, pulse width: 250 μs, duty cycle: 3 s stimulation and 2 s rest), which was used until day 9, and the disuse mode (frequency and pulse width: same as for the mild-disuse mode, duty cycle: 5 s stimulation and 2 s rest), which was used from day 10 onward. The

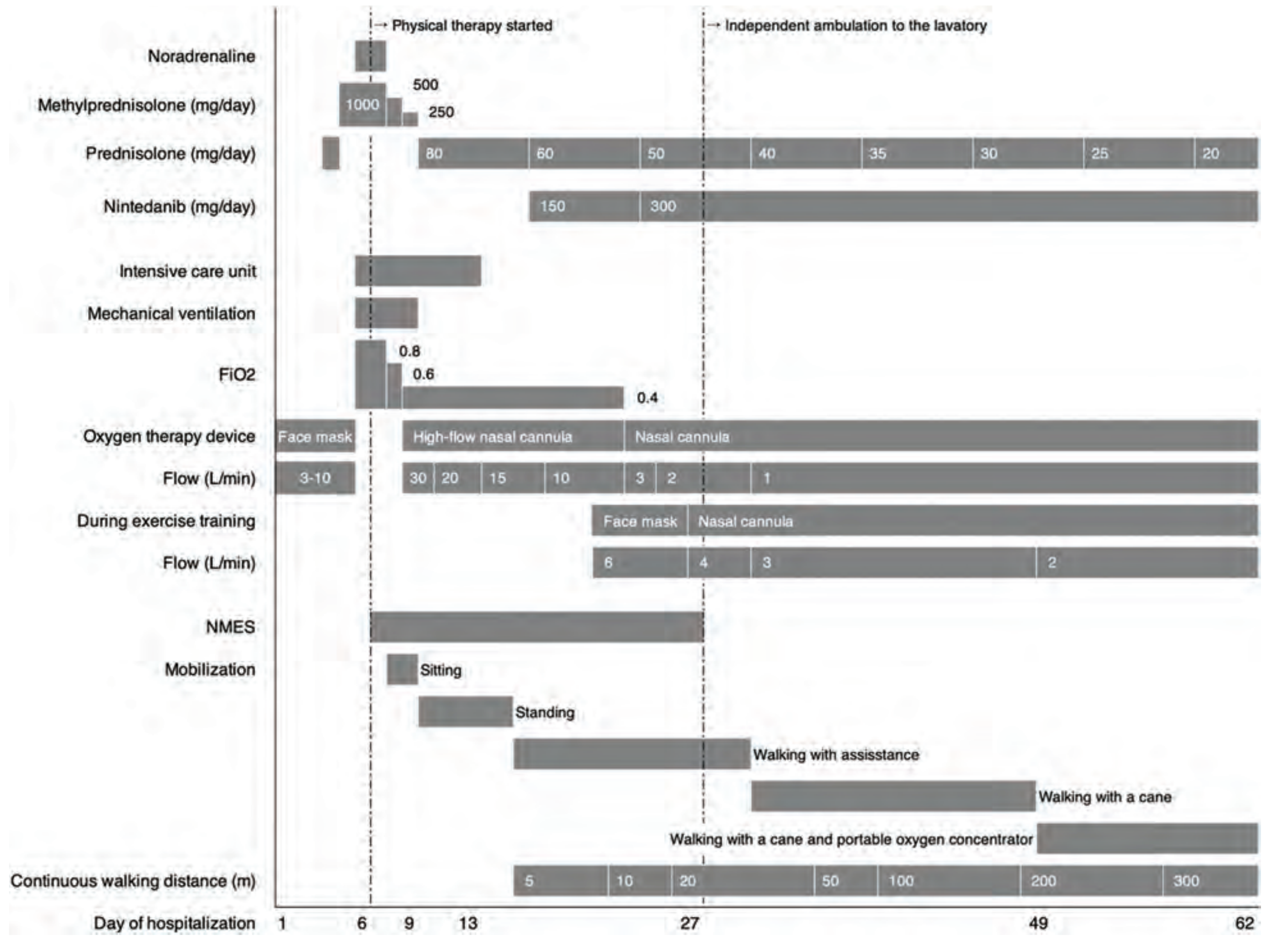

Fig. 2. The clinical course of the patient, including the medications, respiratory care, and pulmonary rehabilitation he received
FiO_2, fraction of inspired oxygen; NMES, neuromuscular electrical stimulation

stimulation intensity was adjusted to a level that would result in visible muscle contraction while not causing excessive pain. The stimulation duration was 20 min and performed once daily. Because the patient was conscious and his clinical status was stable, active exercises and mobilization were started on day 8. We assessed the grip strength of the dominant (right) hand using a digital dynamometer (Grip-D; Takei Scientific Instruments, Niigata, Japan) and global muscle strength using the Medical Research Council (MRC) sum score. The scores were 21.3 kgf and 58 points on day 8, respectively (Table 2). We also assessed the thickness of the rectus femoris (RF) and the QF (RF plus vastus intermedius) muscles on the right side (Fig. 3A). Muscle thickness was imaged with the patient in the supine position using B-mode ultrasonography with a 10-5 MHz linear transducer (iViz air; FUJIFILM, Tokyo, Japan) at the midpoint of the anterior superior iliac spine and the superior patellar border. At the initial evaluation (day 7), the patient's RF and QF thicknesses were 11.0 mm and 19.0 mm, respectively (Fig. 3B).

Oxygenation (PaO_2/FiO_2 ratio) gradually improved, and the patient was weaned from mechanical ventilation on day 9. The PaO_2/FiO_2 ratio immediately post-weaning was 205 (82/0.40). He was able to stand and walk on the spot at this point. The intravenous immunoglobulin was administered again on days 11–13. On day 13, he was discharged from the ICU, and the oxygen-conserving device was changed from a high-flow system to a low-flow system based on the oxygen demand. On day 14, his RF thickness was 4.5% lower and the QF thicknesses were 8.4% lower than those at the time of ICU admission (Fig. 3B). Walking with support was initiated on day 16. As the patient's condition improved, the oxygen flow rate during exercise was gradually tapered while ensuring that the percutaneous oxygen saturation (SpO_2) did not decrease by <85%. An anti-fibrotic drug (nintedanib) was prescribed on day 17, and the dose was increased on day 24. After 21 days (days 7–27) of the NMES, the patient could independently visit the lavatory, so the NMES was discontinued. No events necessitating the NMES discontinuation, such as excessive dyspnea or decreased oxygen saturation, or adverse events that could be attributed to the NMES, were observed. On day 39, he could walk with the aid of a cane for >100 m without stopping. He was instructed to start long-term oxygen therapy on day 49 and discharged to go home on day 63. The chest radiograph obtained at the time of discharge from the hospital is presented in Figure 1B.

No significant decline in handgrip strength or MRC sum score over the treatment course was observed (Table 2).

Table 2. Changes in physical function parameters over the course of hospitalization

Variable	Unit	Day 8	Day 27	Day 49	Day 62
Handgrip strength (dominant)	kgf	21.3	20.7	23.5	26.7
MRC sum-score		58	58	58	58
SPPB score		–	2	7	9
5STS	sec	–	Unable to perform	Unable to perform	31.8
Gait speed	m/s	–	–	0.90	1.03
6MWD	m	–	–	–	308

"–" indicates that the parameter was not measured on that day.

MRC, Medical Research Council; SPPB, Short Physical Performance Battery; 5STS, five-times sit-to-stand test; 6MWD, 6-minutes walking distance

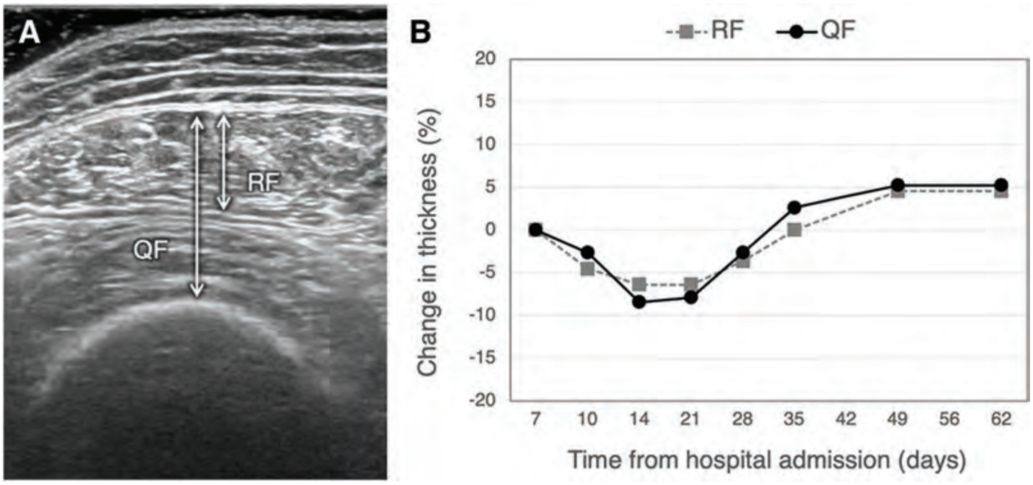

Fig. 3. (A) Ultrasonography image of the measurement of the RF and QF muscle thicknesses. (B) Percent change in the RF and QF muscle thicknesses

Solid lines indicate the change in RF muscle thickness, and dotted lines indicate the change in QF muscles thickness.

QF, quadriceps femoris; RF, rectus femoris

Until day 49, the patient used his upper extremities to support himself when rising from a 40 cm-high chair, although this was not required at the pre-discharge evaluation (day 62). The score of the Short Physical Performance Battery[11], which included the five-time sit-to-stand test and usual gait speed, was 9 points. The 6-minute walking distance at the predischarge evaluation was 308 m, with a minimum SpO_2 of 84% during the test as well as up to 3 min after completing the test, with an oxygen flow rate of 2 L/min via the nasal cannula. His RF and QF thicknesses did not decrease from the day 14 evaluation and had recovered to levels comparable to those at the initial evaluation on day 35 (Fig. 3B).

Discussion

The patient required mechanical ventilation due to severe acute exacerbation of RA-ILD. We provided pulmonary rehabilitation with the NMES, early mobilization, and exercise to him beginning in the early phase. The NMES was continued for 21 days until the patient could independently visit the lavatory. As a result, no significant muscle atrophy was observed in him during his ICU stay, and he regained function sufficiently to be able to walk independently. The patient was eventually discharged to go home after starting long-term oxygen therapy.

Early mobilization of critically ill patients requiring mechanical ventilation has been reported to promote recovery of muscle strength and physical function in some reviews and is widely performed as standard care[12,13]. However, patients with acute exacerbations of ILD, such as in the present case, frequently have worsening dyspnea and hypoxemia. These may promote inactivity and muscle atrophy, and inhibit the recovery of ADL. Therefore, we applied the NMES in combination with mobilization, which was started early, upon admission to the ICU. Several studies have reported that adding the NMES to early mobilization facilitated maintenance of muscle strength and mass more than early mobilization alone[7–9]. Global muscle strength was maintained throughout the course of the ICU stay in the present case. The RF and QF thicknesses had decreased by up to 4.5% and 8.4%, respectively, by the time of ICU discharge. A decrease in muscle mass during acute exacerbation of ILD has not yet been reported, while previous studies of critically ill patients have reported a decrease in muscle thickness of approximately 20% over 7 or 10 days[14]. In addition, a 15% cutoff value for the rate of decrease in the thicknesses of the RF and vastus intermedius for each muscle has been reported in critically ill patients with severe muscle weakness[15]. Therefore, we consider that both the RF and QF thicknesses were maintained relatively well in our patient despite the ICU stay of 8 days. It has been reported that loss of muscle mass is associated with poor prognosis in patients with ILD and that the presence of sarcopenia is associated with general well-being in the community-dwelling elderly[16,17]. Therefore, in patients with acute exacerbation of ILD, focusing on the maintenance of skeletal muscle mass and recovery of physical function is necessary from an early phase of exacerbation. Combining NMES and mobilization may help improve the abovementioned factors.

In the present case, severe muscle weakness corresponding to ICU-acquired weakness was avoided using early mobilization in combination with the NMES, early spontaneous awakening, and extubation. However, as expected, the patient's exertional hypoxemia and dyspnea were prolonged, and it took him 21 days to walk independently to complete daily activities. Older hospitalized patients often develop a hospitalization-associated disability, which has been reported to be associated with their physical activity level while in the hospital[18,19]. Therefore, in addition to mobilization and exercise, we continued the NMES until the patient was able to visit the lavatory independently to prevent physical function decline and the progression of muscle atrophy. Consequently, no significant decrease in muscle thickness was observed from ICU discharge to the time when the patient could independently visit the lavatory, while an increase in muscle thickness was observed thereafter. Therefore, we believe that we discontinued the NMES at the appropriate time. Most studies on the effects of the NMES plus mobilization in the ICU only administered it during ICU stay[9,10]; however, in clinical practice, many patients are not fully active at the time of ICU discharge, as in our case, and would benefit from continuing the NMES combined with mobilization. In contrast, a previous study comparing the NMES alone to a control in patients after ICU discharge showed no differences in muscle strength or physical functional status in the NMES group compared to the controls[20]. Therefore, it may be important to start the NMES in the early phase, in combination with mobilization and exercise, as in the present case. The optimal duration of the NMES combined with mobilization or active exercise remains unknown, although as in this case, discontinuing the NMES while increasing the number of ADL performed (e.g., visiting the lavatory independently) may help to prevent skeletal muscle atrophy and physical function decline. Although the effects of pulmonary rehabilitation in patients with ILD during the stable phase have been clarified[21], an appropriate program for the acute exacerbation phase has not yet been clearly defined. It may be beneficial to add the NMES to other pulmonary rehabilitation programs for patients with ILD requiring mechanical ventilation or whose daily activities are limited by severe dyspnea or hypoxemia.

In our patient, pulmonary rehabilitation was started on day 7 (day 2 of ICU admission). Therefore, the impact of the 6 days before rehabilitation on the patient's physical function and outcome is unknown. Moreover, current evidence of the feasibility of the NMES even in patients with stable ILD is insufficient[6]. Although no adverse events occurred in our patient, the feasibility of combining the NMES with conventionally prescribed mobilization and exercises for patients with acute exacerbation of ILD needs to be investigated in future studies.

Conclusion

We provided pulmonary rehabilitation with the NMES, early mobilization, and exercise to a patient with a severe acute exacerbation of RA-ILD who required mechanical ventilation. The NMES was initiated early and continued until the patient could independently visit the lavatory. Consequently, the patient's RF and QF muscle thicknesses were maintained, and he was discharged to go home.

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Consent for Publication: Written informed consent was obtained from the patient for the publication of this report and any accompanying images.

Conflict of Interest: The authors declare that there are no conflicts of interest associated with this manuscript.

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PHYSICAL
THERAPY
RESEARCH

CASE REPORT

Improvement in the Physical Function and Quality of Life through Exercise and Physical Activity Intervention Using a Smartphone after Allogeneic Hematopoietic Cell Transplantation: A Case Report

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ABSTRACT. Purpose: Physical activity (PA) interventions positively affect the physical function (PF) in patients with advanced cancer. However, patients must remain motivated during the intervention. We report a case wherein a smartphone application for PA intervention was useful in motivating the patient to improve adherence. Methods: A 40-year-old woman underwent an allogeneic hematopoietic cell transplantation (allo-HCT) for an advanced extranodal natural killer/T-cell lymphoma. On day 6, she developed the posterior reversible encephalopathy syndrome. She was managed in the intensive care unit for 3 days, and her PF declined markedly. We initiated a smartphone-based PA intervention from day 35. She was instructed to maintain a PA diary for self-monitoring of the daily steps and to set a new step-count goal every week. Results: The PA and PF improved within a short period thereafter. However, she developed severe acute graft-versus-host disease and was administered with high-dose systemic corticosteroids from day 49. The PA, PF, and quality of life (QOL) decreased again. The intervention was continued for 5 months with a high adherence. The PA, PF, and QOL improved gradually. She resumed independent activities of daily living and was discharged on day 202. Conclusion: Smartphone-based PA intervention may be effective against post-allo-HCT physical dysfunction.

Key words: Allogeneic hematopoietic stem cell transplantation, Exercise, Physical activity intervention, Physical function, Smartphone

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Extranodal natural killer/T-cell lymphoma (ENKL) is a rare lymphoma. Patients with advanced stage and relapsed/refractory ENKL have a dismal prognosis even after chemotherapy or chemoradiotherapy[1)]. Although allogeneic hematopoietic cell transplantation (allo-HCT) is an effective and curative treatment for advanced and relapsed/refractory ENKL, a portion of the patients develop severe complications (such as the graft-versus-host disease [GVHD]) after an allo-HCT[1)]. These complications limit the physical and psychological functions, which in turn decrease the quality of life (QOL)[2,3)]. Exercise has been identified as a strategy to mitigate these problems. However, in patients who develop severe complications or require intensive care, exercise alone is insufficient to recover the optimum physical function (PF)[2,3)]. Therefore, a new strategy is needed to improve the PF and QOL in patients who develop severe complications after an allo-HCT.

Previous studies have shown that physical inactivity is a major factor associated with a PF decline after an allo-HCT[4)]. In patients with colorectal cancer, physical activity (PA) interventions positively affect the PF and QOL[5)]. However, patients often experience difficulty in continuing the interventions due to a lack of motivation; a major reason is

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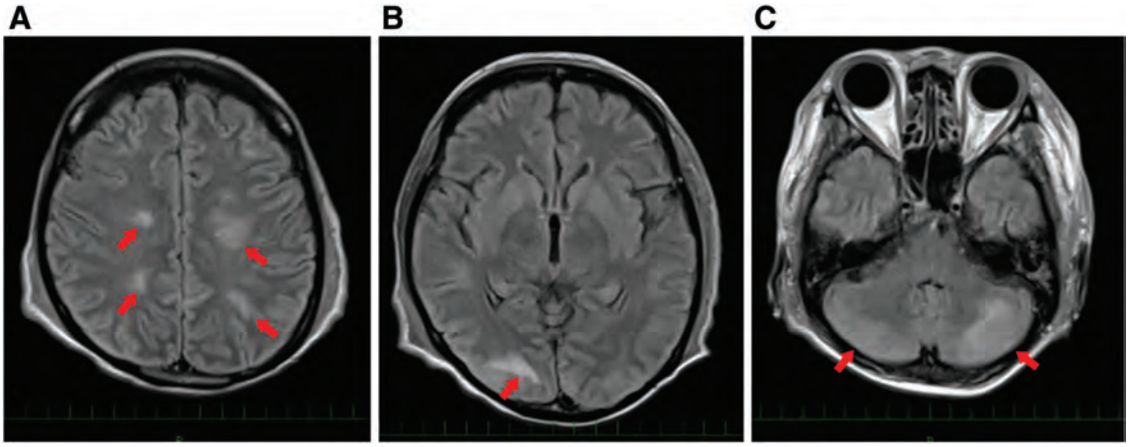

Fig. 1. Magnetic resonance imaging findings of PRES

Magnetic resonance imaging of the brain showed multiple areas of hyperintensity on T2-FLAIR in bilateral frontal and parietal lobes (A), right occipital lobe (B), and bilateral cerebellum (C). The arrows indicate lesions.

PRES, posterior reversible encephalopathy syndrome; FLAIR, fluid-attenuated inversion recovery

that they have to wear special devices, such as pedometers, to monitor the PA.

Although PA has been assessed mainly with pedometers in the past, a smartphone accelerometer application was developed recently, which is easy to use, validated for PA measurement[6)], and has higher adherence to interventions than pedometers[7)]. Furthermore, smartphone-based PA interventions can effectively improve self-efficacy[8)], leading to promoting PA[9,10)]. Although the smartphone accelerometer application has these advantages, there is no consensus on the best behavior change theory or model that should be used in smartphone-based interventions for PA promotion[11)]. In addition, reports of its implementation in patients after an allo-HCT are lacking. Herein, we report a case of a patient with ENKL who suffered from physical dysfunction due to severe complications after an allo-HCT, and improved following exercise and a smartphone-based PA intervention.

Case Presentation

A 40-year-old woman was referred to our hospital for a high fever and hepatosplenomegaly. She was diagnosed with an advanced ENKL (nasal type). A chemotherapy regimen comprising dexamethasone, methotrexate, ifosfamide, L-asparaginase, and etoposide was initiated; however, it was switched to another chemotherapy regimen comprising gemcitabine, carboplatin, and dexamethasone (GCD) due to disease progression. After three cycles of GCD, she achieved partial remission and underwent an allo-HCT. Before the allo-HCT, the PF was evaluated using the following: 1) 10-meter walk test (10MWT), 2) 30-second chair stand test (30CST), and 3) 6-minute walk distance (the total distance walked back and forth over a distance of 30 m repeatedly for 6 minutes). The QOL was also evaluated using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-C30. She was instructed to complete an exercise program before and after the allo-HCT to maintain her PF and QOL. The exercise program comprised specific resistance training and aerobic exercise[12)]. The resistance training consisted of one set of 20–30 flexion and extension exercises of the hip, knee, and elbow joints with 0–1.5-kg loads and two sets of 10 standing calf raises. The aerobic exercise consisted of walking, with 3–10 minutes of ergometer. The exercise intensity was set to "somewhat hard" and rated as "4" on the modified Borg scale. The exercise program was implemented for 20–40 minutes a day, five times a week. After a conditioning regimen of fludarabine and melphalan, she received a peripheral blood stem cell transplant from a human leukocyte antigen-matched sibling donor. GVHD prophylaxis consisted of tacrolimus and methotrexate. On day 6, she developed disturbance of consciousness and seizures. Brain magnetic resonance imaging revealed multiple hyperintense areas on T2-fluid-attenuated inversion recovery (Fig. 1); thus, she was diagnosed with the posterior reversible encephalopathy syndrome (PRES). She was intubated and transferred to the intensive care unit (ICU), wherein she received mechanical ventilation for three days. PRES was resolved after discontinuation of tacrolimus and initiation of methylprednisolone (2 mg/kg/day). She was extubated and returned to the HCT ward on day 9. She achieved neutrophil engraftment on day 11. Although she followed the exercise program routinely, except for on the day of the ICU admission, her PF markedly decreased on day 28 (Fig. 2); she was unable to perform the 30CST. Her QOL also decreased (Fig. 3). Furthermore, the daily average step count, calculated per week using a smartphone accelerometer application, was only 2765 steps; this is below the average Japanese middle-aged woman's step count of 7600 steps a day[13)]. Her exercise program was insufficient; therefore, PA intervention was included in the program[14)] from day 35. She was instructed to maintain a PA diary to self-monitor the daily steps. At each weekly evaluation, she

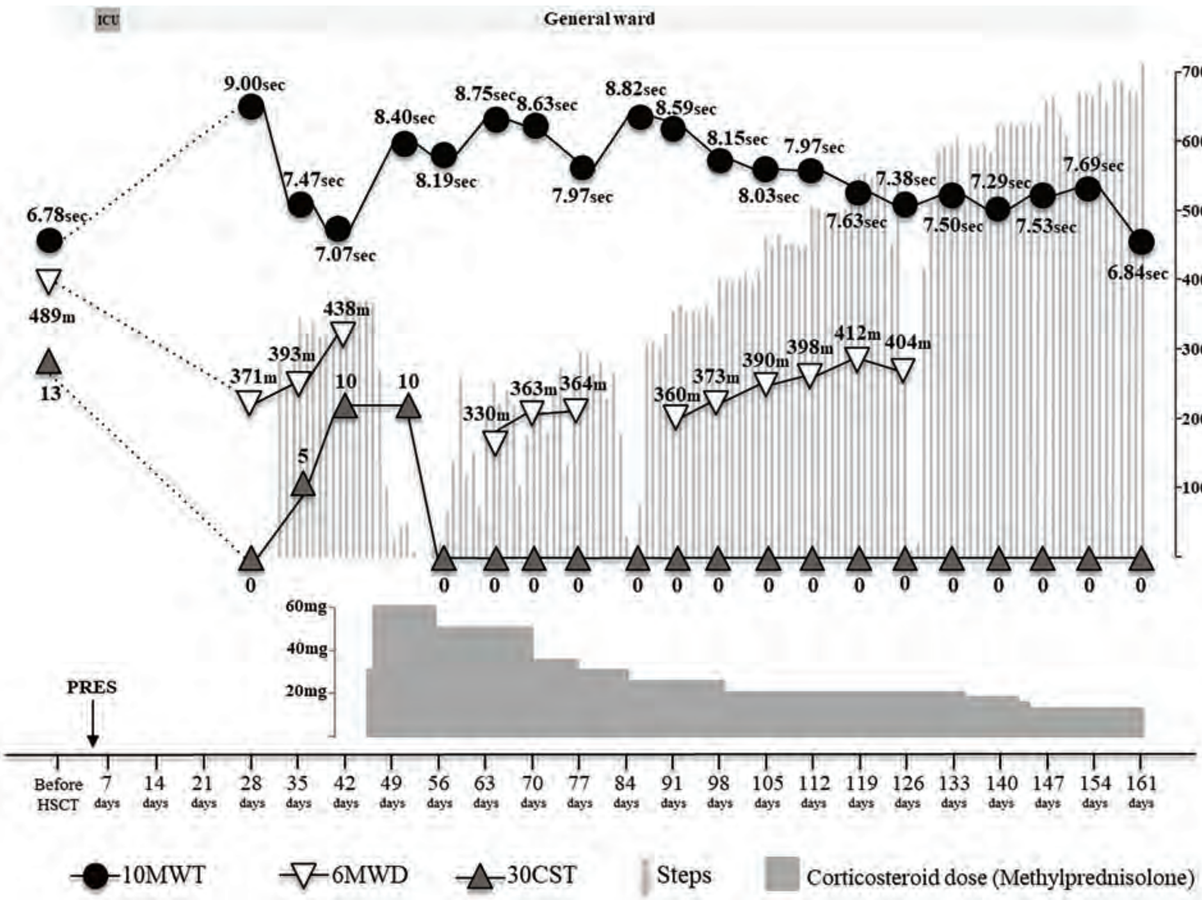

Fig. 2. Clinical course of PF and PA, and the dose of corticosteroid

A smartphone-based PA intervention was initiated from day 35, and the PA and PF improved within a short period. However, she developed severe acute GVHD and was administered with high-dose systemic corticosteroids from day 49. The PA and PF decreased again. The intervention was continued for 5 months with a high adherence. The PA and PF improved gradually.

PF, physical function; PA, physical activity; GVHD, graft-versus-host disease

was instructed to set a new step-count goal, which was calculated by adding 400 steps to the average step count of the most recent seven days[14]. After the introduction of the PA intervention, the PA (measured by steps) increased, and the PF and QOL improved within two weeks (Figs. 2 and 3).

The methylprednisolone dose was gradually tapered; however, she developed grade III acute GVHD with gastrointestinal involvement on day 49. Therefore, the methylprednisolone dose was increased to 2 mg/kg/day. Furthermore, antithymocyte globulin (1 mg/kg) was administered on day 52, and mesenchymal stromal cells were administered on day 56. The average steps at day 56 markedly decreased to 201 with worsening physical symptoms, such as fatigue, abdominal pain, diarrhea, and anorexia, due to severe GVHD (Fig. 4). On day 63, her PF and QOL also decreased. During systemic steroid therapy for GVHD and while tapering the steroids, the exercise program and PA intervention were continued with high adherence (exercise program adherence: 96.2%, PA intervention adherence: 100%). By day 161, her average step count gradually improved to 6755, the 10MWT time improved to 6.84 seconds (Fig. 2), the global QOL score improved to 75.0 (Fig. 3), and she resumed independent activities of daily living. She was discharged on day 202, although she was still unable to perform the 30CST.

Discussion

Physical dysfunction is often observed in patients after an allo-HCT[4]. The effectiveness of exercise for such physical dysfunction has been established[12], and all patients who receive an allo-HCT at our hospital are instructed to participate in an exercise program composed of resistance training and aerobic exercise[12]. In the present case, despite exercising, her PF markedly decreased on day 28 after developing PRES.

In previous studies, physical inactivity was the main factor for the decline in the PF after an HCT[4]. In fact, our patient's step count at day 28 was lower than that of Japanese women of the same age[13], suggesting physical inactivity. Recent studies have reported that PA intervention improved the daily step count[9,10]. Furthermore, it also has positive effects on PF, symptoms, and QOL[15]. Therefore, we focused on PA and proceeded with a new approach of adding a PA intervention to the exercise program in accordance with a previous study[14].

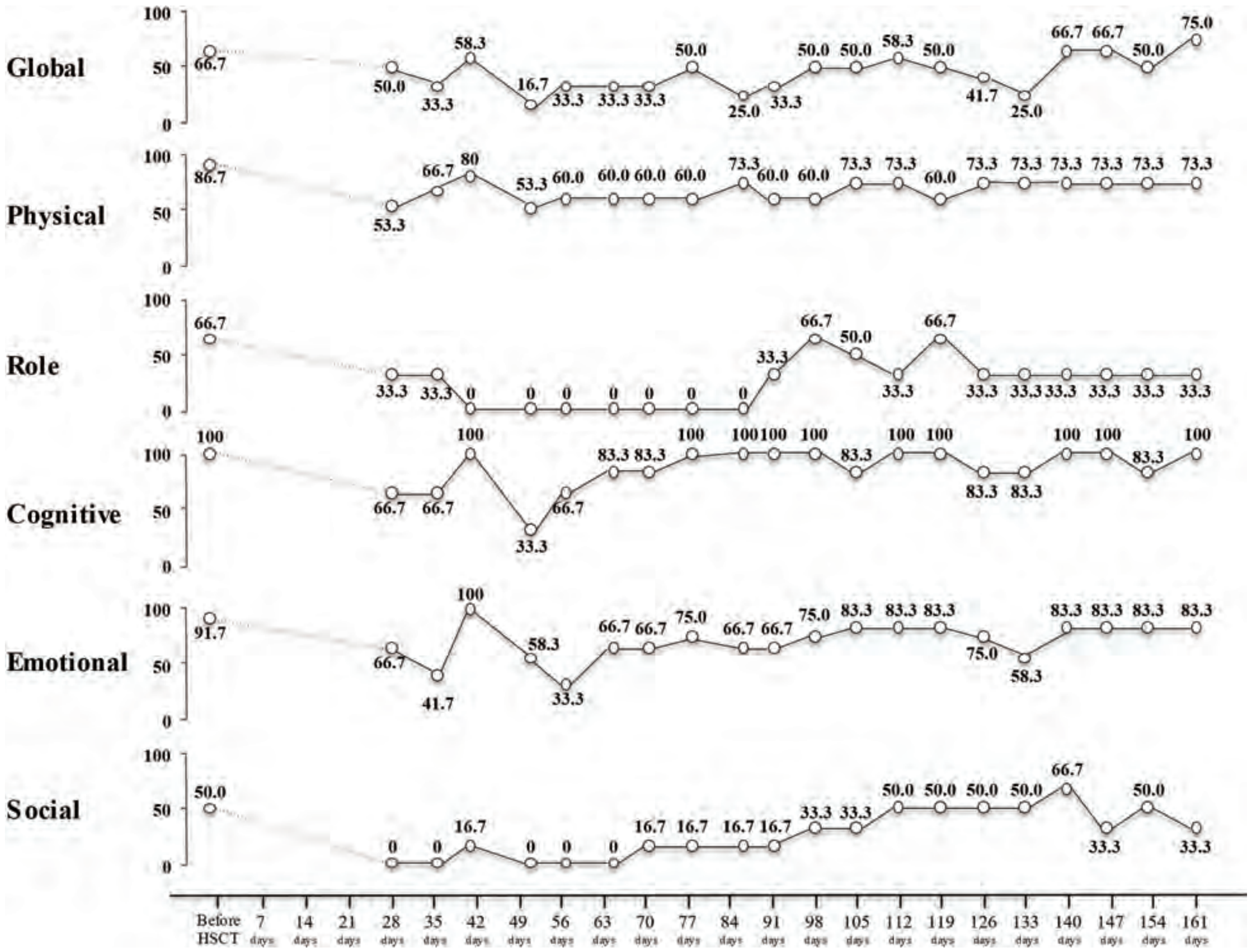

Fig. 3. Clinical course of QOL

A smartphone-based PA intervention was initiated from day 35, and QOL also improved within a short period. However, QOL declined with the onset of GVHD, which then improved after 5 months of highly adherent PA intervention.

QOL, quality of life; PA, physical activity; GVHD, graft-versus-host disease

Although the effectiveness of PA intervention has been reported, there are problems with motivation and adherence. To address these, in this case, a smartphone was used instead of a pedometer to measure the step count[7]. In addition, since self-monitoring is important to increase the adherence to the program, we instructed the patient to monitor the number of daily steps herself through a PA diary. We also instructed her to set a new step-count goal every week based on the diary. After the introduction of the PA intervention, the PA (measured by steps) increased and PF improved, as seen in previous studies[9,10]. Although the benefits of PA interventions have been reported to be achieved mainly after 4–8 weeks or longer[16], her PF and QOL improved within just 2 weeks. There are several reasons for this rapid improvement. First, the use of a smartphone to measure the step count was a factor that increased adherence and allowed us to monitor the daily steps accurately without a lapse. Second, the PA intervention used in this case was a multi-component intervention. In a previous study on PA intervention, it was reported that a multi-component intervention appears to more effective than a stand-alone application intervention[17]. The patient was instructed to measure her steps, keep a PA diary, and set a new step-count goal every week. Self-monitoring of daily steps helped make aware of her daily PA, which motivated her to become more physically active and achieve the new weekly goals[18]. These strategies that were aimed to facilitate a behavioral change and to increase adherence to the program led to successful improvement in the PA and PF.

After approximately 5 months of the exercise program and PA intervention, her average steps, gait velocity, and QOL improved considerably. However, her 30CST scores, which reflect the muscle strength of the lower extremities, did not improve. A previous study revealed that a high dose of corticosteroids was correlated with a decrease in the knee extensor muscle strength after a hematopoietic stem cell transplantation[19]. Furthermore, the GVHD and corticosteroid usage were the independent risk factors for a delayed recovery of the muscle strength[3]. The effect of exercise and our PA intervention was insufficient to recover the decline in the muscle strength of the lower extremities due to high-dose steroid therapy for severe GVHD. In previous studies, moderate exercise therapy, similar to our approach, has been recommended for steroid myopathy[20]. However, this

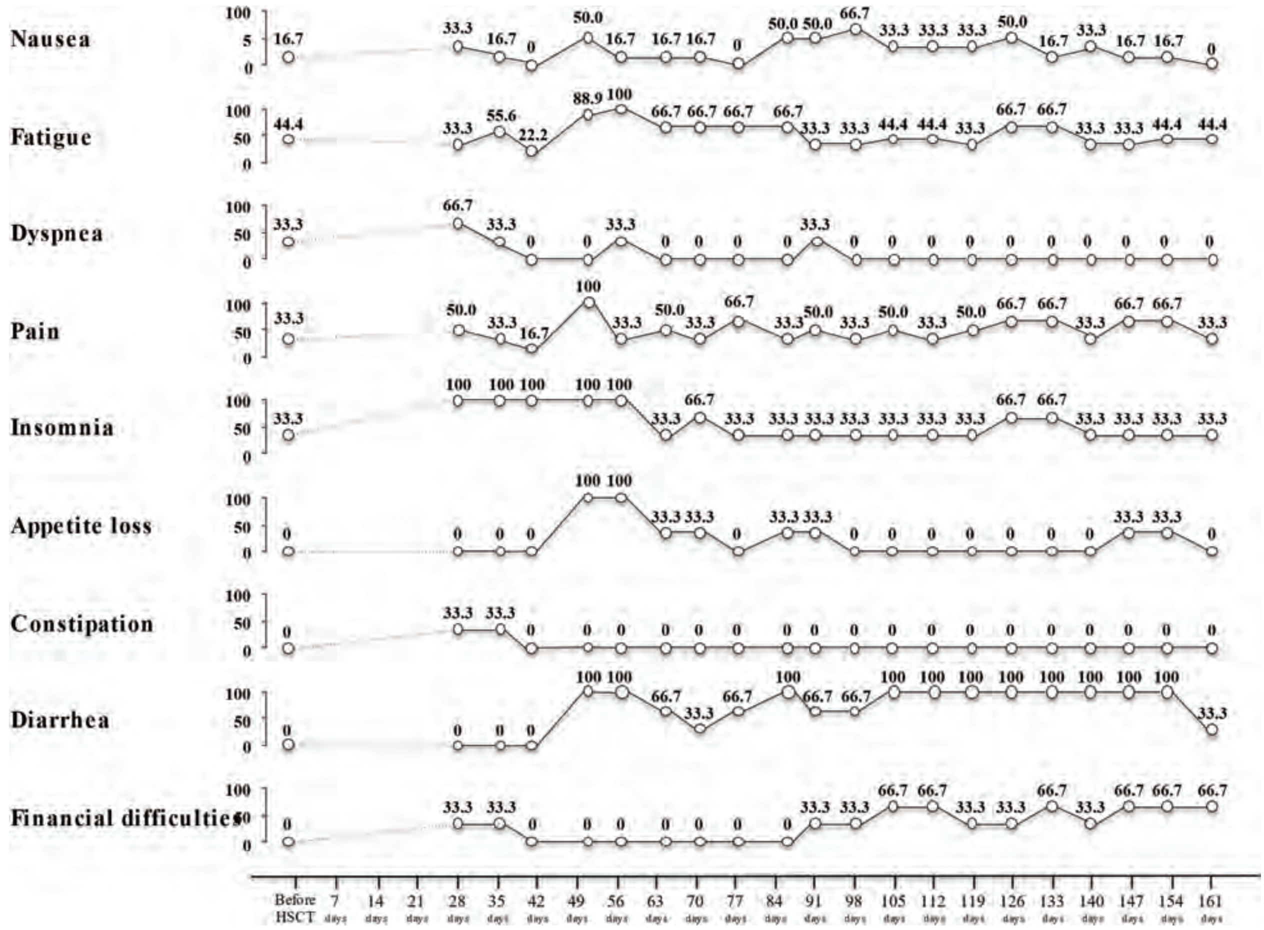

Fig. 4. Clinical course of symptoms

A smartphone-based PA intervention was initiated from day 35, and the patient's symptoms showed an overall improvement within a short period. However, some of her physical symptoms, such as fatigue, abdominal pain, diarrhea, and anorexia, worsened due to severe GVHD. After 5 months of adherence to PA intervention, her physical symptoms also showed improvement.

PA, physical activity; GVHD, graft-versus-host disease

approach may be insufficient in patients receiving high-dose and long-term steroid therapy, such as ours.

This case report has several limitations. First, factors other than PA intervention, such as an improvement of the GVHD, might have affected improvements in the PF and QOL. Second, we did not evaluate the daily steps before day 28. Third, only smartphone usage was examined, and a comparison of its outcomes with those of pedometer usage was not possible.

Conclusion

This case suggests that PA intervention using a smartphone may be an effective strategy in patients with physical dysfunction due to severe complications after an allo-HCT. The intervention used in this case can be applied to any patient, at any given time and place, as long as the patient has a smartphone. Further studies with a large number of patients are needed.

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Informed Consent: Patient's written informed consent was obtained for publication of this case report.

Conflict of Interest: The authors declare that they have no conflict of interest.

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Physical Therapy Japan Vol.48 (2021) ABSTRACTS

The Japanese Physical Therapy Association publishes the "Journal of the Japanese Physical Therapy Association", the most recent Japanese volume (Physical Therapy Japan) being number 48, which includes 69 articles. Each year 6 issues are published.
For the past 25 years, the English volume of "The Journal of the Japanese Physical Therapy Association" has been published once a year. The journal has changed its name to "Physical Therapy Research" and the publishing organization was changed to Japanese Society of Physical Therapy in 2016. The Society published the journal twice per year from 2017, and three times per year from 2021.
To further acquaint our English volume readers with the articles published in the Japanese volume, the English abstracts of the present Japanese volume will be included in the English volume published this year.

Vol. 48, No. 1 (pp 1-8)

The Utility of a Simplified Measurement for Leg Press Strength using a pull-type hand-held dynamometer in Community-dwelling Older Adults

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Objective: This study aimed to confirm the utility of a simplified measurement for leg press strength using a pull-type hand-held dynamometer (referred to as pull-type HHD).
Methods: The participants were 108 older people men and women. Measurements with pull-type HDD were performed for leg press strength, knee extension strength (referred to as KE) and knee flexion strength (referred to as KF). Leg press strength measurements were performed in two settings with a knee flexion angle of 60° and 30° (referred to as LP60 and 30). Indicators of mobility were the presence or absence of locomotive syndrome (referred to as locomo), and the maximum and the comfortable walking speeds. Intra-rater reliability of each muscle strength was verified using an intraclass correlation coefficient, ICC (1,1) and a Bland-Altman analysis. Correlations of each muscle strength with the locomo, and each gait speeds were verified by a multivariate analysis.
Results: For all measurements, the ICC (1,1) values were 0.92 or larger and fixed error was observed in each muscle strength. Significant factors were extracted: LP60 for the locomo, LP60, KE and KF for the maximum gait speed, and KE for the comfortable gait speed.
Conclusion: LP60 measurement by pull-type HHD is useful as a method to reflect locomo and maximum walking speed.

Key Words: Leg press strength, Knee extension strength, Older adult, Walking speed, Locomotive syndrome

Vol. 48, No. 1 (pp 9-18)

Effect of Body Function and Recognition for Body Function on the Movement Strategy of Older Adults in an Obstacle Avoidance Task

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Purpose: In recent years, the effect of visual function and recognition for body function on the movement of elder subjects has been investigated. The purpose of this study was to clarify the effect of body function and the recognition for body function on the movement strategy in an obstacle avoidance task designed for older adults.
Methods: Twenty older adults and 12 young adults participated in this study. They were told to walk along a 5-m pass and go through the gap with various width. The movement was recorded using a 3D motion capture system and the duration of gaze was measured using an eye mark recorder. Older participants were categorized based on physical assessment findings:, Low risk (LR) group and High risk (HR) group. To identify the level of recognition for body function, older participants were asked to assess whether they could go through the gap without rotating the body. According to the answer, these participants were further categorized as, correct and incorrect.
Results: Our findings showed that, in the LR and HR groups, the stride length reduced while passing through narrow gaps (gap width < body width), and the angle of rotation was greater in the HR group than in the LR group.
Conclusion: The results suggest that body function and body recognition influenced the kinematic changes and obstacle gaze time in obstacle avoidance movements performed by older adults.

Key Words: Body function, Body recognition, 3D motion analysis, Gaze duration

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An Investigative Study on the Experiential Learning Process of Physical Therapists (PT) and the Development of Support Methods: Experiences that Promoted the Development of Highly Skilled PTs, the Knowledge Gained, and Lessons Learned from those Experiences

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Objective: The purpose of this study was to use the experiential learning process theory to identify specific experiences that promote the development of highly skilled physical therapists (PTs) and to determine the particular knowledge gained from those experiences. This information will then be used to suggest experiential learning support methods for PTs.
Method: The subjects of this study were 3 highly skilled PTs. Qualitative research methods and the Matsuo experiential learning framework were utilized.
Results: At the beginning of their careers, accomplished PTs developed their “attitudes regarding topics such as interpersonal relationships, society, and lifestyle” from their hands-on experience of promoting social participation in patients with disabilities. From the beginning to the middle of their careers, their “unpredictable, negative experiences” exposed them to topics such as the “harsh reality of the field of medicine.” They also obtained a better understanding of “the effectiveness of using fundamental physical therapy techniques to improve the condition of critically ill patients.” Finally, from the middle to the end of the careers, their “experience supporting trainees and newcomers” “reinforced their knowledge and skills after self-reflection.” Additionally, they gained more knowledge about topics such as “communication” from their “experience of conducting interventions with a multidisciplinary team of health care professionals.”
Conclusion: We consider that highlighting the experiences that promote the success of highly skilled PTs, and allowing less skilled PTs to gain that experience, can help support their experiential learning.

Key Words: Physical therapist, Experiential learning, Investigative study

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Associations among Respiratory Function and Muscle Strength, Locomotive Function, and Cognitive Function in Japanese Community-dwelling Elderly Individuals

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Objective: The aim of this study was to cross-sectionally investigate the associations among respiratory function and muscle strength, locomotive function, cognitive function, and body composition in Japanese community-dwelling elderly individuals.
Method: The participants in this study were 347 Japanese community-dwelling elderly individuals aged 65 years or older. All the participants could independently perform activities of daily living. Individuals who had any respiratory disease or heart disease were excluded from this study. For the assessment of respiratory function, the forced vital capacity (FVC) and forced expiratory volume in 1.0 second (FEV1.0) were measured. For muscle strength and locomotive function, the grip strength, leg muscle strength, chair stand test, timed up and go test (TUGT), and comfortably paced and maximum-paced 5-meter walking times were assessed. The trail-making test part A (TMT-A) was assessed for cognitive function. Moreover, the skeletal muscle index and fat mass per body weight were measured for the index of body composition. The associations among respiratory function and muscle strength, locomotive function, cognitive function, and body composition were analyzed using multiple regression analysis adjusted for the following confounding factors: age, sex, height, weight, and smoking status.
Result: As the results of multiple regression analysis, accounting for the effect of confounding factors, the FVC was significantly associated with grip strength, TUGT, and TMT-A results. Similarly, the FEV1.0 was significantly associated with grip strength and TMT-A results.
Conclusion: It was suggested that respiratory function is comprehensively associated with muscle strength, locomotive function, and cognitive function in Japanese community-dwelling elderly individuals.

Key Words: Community-dwelling elderly individuals, Respiratory function, Physical function, Cognitive function, Body composition

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Factors that Influence the Ability to Put on Socks Three Weeks after Surgery in Patients with Total Hip Arthroplasty: A Study using a Decision Tree Analysis

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Objective: The goal of this study was to identify the factors that affect a patient's ability to put on socks three weeks after total hip arthroplasty surgery.

Methods: One hundred fifteen patients with total hip arthroplasty using the posterior approach were enrolled in this study. We investigated gender, age, range of motion (hip flexion, extension, adduction, abduction, and external rotation; knee flexion; thoracic spine flexion; and lumbar spine flexion), and the ability to put on socks in hip-abduction-in-flexion positions. The range of motion was used as the independent variable in a decision tree analysis with the ability to put on socks three weeks after surgery as the dependent variable.

Results: Decision tree analysis revealed that the range of motion (ROM) of hip flexion and external rotation, and thoracic spine flexion were factors affecting the ability to put on socks. In addition, it was found that patients with total hip arthroplasty are more likely to put on socks if hip external rotation ROM and thoracic spine ROM are good even if hip flexion ROM is poor.

Conclusions: Improvement of hip flexion and external rotation ROM, and thoracic spine flexion ROM are important for a patient's ability to put on socks in the early postoperative period following total hip arthroplasty.

Key Words: Total hip arthroplasty, Putting on socks, Range of Motion, Decision tree analysis

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Factors Predicting Basic Mobility at Discharge with Acute Cerebral Infarction Patients: A Prospective Multicenter Cohort Study

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Purpose: The purpose of this study was to investigate the predictors of basic mobility for acute cerebral infarction (CI) patients at discharge.
Methods: The participants were 259 patients with acute CI registered at 5 hospitals. Patients were evaluated medical characteristics, neurological impairments, balance disorders, and activity of daily living (ADL). Basic mobility which is a dependent variable used the revised version of the ability for basic movement scale (ABMS-II) Multiple regression analysis was used to identify independent variables related to basic mobility.
Results: In multiple regression analysis, National Institutes of Health Stroke Scale, scale for contraversive pushing, consciousness disorder, recurrence of CI, presence of hemorrhagic infarction, and pre-modified Rankin Scale were identified as predictors of dependent variable.
Conclusions: It was suggested that these indice may predict basic mobility in acute phase and may considered useful to effective programs of physical therapy.

Key Words: A prospective multicenter cohort study, Cerebral infarction, Acute, Basic mobility

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(pp 55-62)

Physical and Mental Factors Underlying Home-based Life Space of Disabled Elderly at Home

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Objective: This study aimed to investigate physical and mental factors associated with home-based life space in disabled elderly at home.
Methods: In the present study, 61 elderly persons (82.7 ± 6.2 years; male, n = 13) who underwent day-care service at two health service facilities for the elderly participated. We measured the home-based Life Space Assessment (Hb-LSA) [Maximal Life Space (Hb-M), Life space using equipment (Hb-E), Independent Life Space (Hb-I)], grip force, muscle strength of quadriceps, one-leg standing, Timed-Up and Go test (TUG), Barthel index (BI), Activities-of-Daily-Living Self-Efficacy Scale (ADLSES), depression scale and self-rated health. Subjects were divided into those who moved to outside with using equipment (outside group, N=25), those who moved to neighborhood with using equipment (neighborhood group, N=36).
Results: The results showed that neighborhood group had better TUG, BI and ADLSES compared with outside group.
Conclusion: The present findings suggest physical performance and confidence in performing activities of daily living are important for enhancing the life-space for disabled elderly at home.

Key Words: Disabled elderly at home, Life-Space, Activities-of-Daily-Living Self-Efficacy-Scale, Timed-Up and Go, Self-efficacy

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The Association between Moderate-to-vigorous Physical Activity and Falls in Independent Community-dwelling Older Adults Stratified by Balance Function

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Objective: The purpose of this study was to examine the association between objectively measured moderate-to-vigorous physical activity (MVPA) and falls in community-dwelling older adults stratified by balance function.

Methods: Subjects were independent community-dwelling older adults (n = 602) aged over 65 years, stratified by balance function at baseline. Daily time spent in MVPA, locomotive activity, and non-locomotive activity were measured using a tri-axial accelerometer. Self-reported incidence of falls at a 2-year follow-up survey was measured as the outcome.

Results: The risk of falls in the middle MVPA group was lowest among participants with high balance function. The risk of falls in the middle and high MVPA groups was significantly higher than that in the low MVPA group among participants with low balance function. Additionally, among low balance function participants, the risk of falls in the high locomotive activity group was significantly higher than that in the low locomotive activity group.

Conclusion: The association between MVPA and falls exhibited differences among independent community-dwelling older adults with different levels of balance function.

Key Words: Community-dwelling older adults, Physical activity, Fall, Balance function, Prospective cohort study

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Dynamic Spinal Alignment in Patients with Osteoarthritis of the Hip: Focusing on the Range of Motion of the Spine in the Standing and Crawling Positions

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Objective: The purpose of this study was to determine the spinal alignment and spinal range of motion in patients with end stage hip osteoarthritis (OA).
Methods: Eleven patients with end stage OA (OA group) and 16 healthy elderly individuals (control group) were included in this study. The static spinal alignment and dynamic range of motion were measured by the Spinal Mouse® on the standing position and all fours.
Results: The alignments of the thoracolumbar spine in the standing position were not significantly different between the two groups. A significant decrease in the lumbar spine range of motion was observed in the OA group in the standing and on all fours positions compared to that in the control group, but there was no significant difference in the thoracic spinal range of motion.
Conclusions: Patients with end stage hip OA showed no differences in static thoracolumbar alignment and reduced dynamic lumbar range of motion compared to those in healthy elderly patients.

Key Words: Hip osteoarthritis, Spinal alignment, Spinal mobility, Spinal mouse

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Examination of Predictors for Discharge Disposition in Patients Aged 60 Years or Older with Acute Exacerbation of Heart Failure

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Objective: To clarify the independent predictors of home discharge in patients with acute exacerbation of heart failure (HF) who underwent cardiac rehabilitation (CR).
Methods: This was a single-center retrospective cohort study. In this study, 305 patients aged 60 years or older, who were admitted with acute exacerbation of HF, were included in the analysis. The patients were divided into a Home group and Non-Home group based on discharge disposition. Basic characteristics, HF severity, knee extension strength (KES), Short Physical Performance Battery (SPPB) and Barthel Index (BI) at the commencement of rehabilitation and at hospital discharge were compared between groups. Additionally, multivariate logistic regression analysis and a receiver operating characteristic curve were used to evaluate independent predictors of home discharge and cut-off value.
Results: At the commencement of CR, KES, SPPB, and BI were significantly higher and age was significantly lower in the Home group. However, there were no significant differences in HF severity and nutritional status between the groups. At hospital discharge, KES, SPPB, and BI were significantly higher in the Home group. Multivariate analysis showed that predictors of home discharge and its cut-off value were KES at the commencement of CR (≥12.1 kg), SPPB at the commencement of CR (3/4 points), and BI at hospital discharge (≥80 points).
Conclusion: These results may contribute to the early detection of older patients who may be difficult to discharge to home and to setting appropriate CR goals.

Key Words: Heart failure, Home discharge, Predictor, Goal setting

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Effect of Physical Therapy for Prevention of Deep Vein Thrombosis on the Day after Total Knee Arthroplasty: A Randomized Controlled Trial

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Objective: It is important to prevent deep vein thrombosis (DVT) in patients who undergo total knee arthroplasty (TKA). However, few reports have described the usefulness of physical methods to effectively prevent DVT in this patient population. We investigated the role of same-day physical therapy (PT) in prevention of DVT after TKA.
Methods: This randomized controlled trial included 440 patients (stratified by sex) who underwent primary TKA at our hospital. Of these, 84 patients were randomly assigned to the PTcare and control groups. The PTcare group included patients who underwent simultaneous lower-limb massage and passive ankle motion during lower leg elevation on the day of surgery. The outcome was the DVT incidence rate observed on the day following surgery.
Results: The DVT incidence rate on the day following surgery was 11.9% (5 of 42) in the PTcare group and 40.5% (17 of 42) in the control group. The DVT incidence rate was significantly lower in the PTcare group than in the control group (risk ratio 0.29, 95% confidence interval 0.119–0.724).
Conclusion: Same-day PT was shown to be significantly effective for the prevention of DVT after TKA.

Key Words: Total knee arthroplasty, Deep vein thrombosis, Same-day Physical therapy

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Cortico-reticular Tract Integrity does not Predict Walking Ability in Acute Stroke Patients: A Diffusion Tensor Imaging Study

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Objective: This study intended to explain the relationship between the integrity of the cortico-reticular tract (CRT), a motor tract, and walking ability in stroke patients using diffusion tensor imaging (DTI).
Method: We enrolled 41 patients who had undergone DTI. Walking ability was assessed using the Functional Ambulation Category (FAC) during the inpatient stay following stroke. The participants were divided into two groups: the independent group (FAC $\geqq$ 3) and the dependent group (FAC<3). Neurological impairments were assessed using the Stroke Impairment Assessment Set (SIAS). We measured CRT and cortico-spinal tract (CST) integrity using DTI. In addition, logistic regression analysis determined whether neurological impairments and CRT and CST integrity predict walking ability.
Result: The SIAS hip flexion score on admission significantly predicted walking ability, while CRT integrity did not.
Conclusion: This study suggests that lower limb motor function is more important in predicting walking ability during the acute phase rehabilitation period following stroke than injury to the CRT.

Key Words: Diffusion tensor imaging, Predictor of the walking ability, Corticoreticular tract

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Impact of Delayed Rehabilitation on the Prognosis of Elderly Cardiac Surgery Patients One Year after Discharge

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Objective: To investigate the impact of delayed rehabilitation on the prognosis of elderly patients one year since their discharge after cardiac surgery.
Methods: Participants were 58 patients with heart disease (aged ≥ 65 years; average age: 73.8 years) who had undergone elective cardiac surgery (coronary artery bypass grafting, valvular disease surgery, or combined surgery). Those who achieved independent walking within postoperative day (POD) 5 were assigned to the early group (59%), while those who achieved it on or after POD 6 were assigned to the delayed group (41%). In addition, data collected from these groups were compared to the perioperative and postoperative data as well as prognosis data at one year after discharge.
Results: The delayed group had a longer operative time, anesthesia time, and ventilator intubation time, and their postoperative rehabilitation progress was delayed. However, the total rehabilitation time was longer and the SPPB at discharge recovered to the same level as the preoperative values. There were no significant differences in mortality, readmission rates, or vital functions between the two groups at one year after discharge.
Conclusion: Delayed postoperative rehabilitation progression in elderly postoperative cardiac surgery patients may have less impact on mortality, readmission rates, and vital function one year after discharge if physical functions are sufficiently restored during the hospitalization period.

Key Words: Cardiac surgery, Delayed rehabilitation, The prognosis

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(pp 180-188)

Predicting Decline in Activities of Daily Living at Discharge in Patients with Heart Failure

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Objective: The aim of this study was to predict the decline in activities of daily living (ADLs) at discharge in patients with heart failure based on motor function early during hospitalization.
Method: Ninety-six patients with heart failure whose ADLs were independent before hospital admission were enrolled in the present study. The patients' performances on the modified functional reach test (M-FRT) and standing from a seat height of 30 cm were measured early during hospitalization as indicators of motor function. We also evaluated the Katz index at discharge as an indicator of ADLs and created a formula to predict the decline in ADLs at discharge.
Result: The formula to predict the decline in ADLs at discharge based on the M-FRT and standing from a seat height of 30 cm was obtained from the results of multiple logistic regression analysis (sensitivity: 91.7%, specificity: 86.9%, area under the curve: 0.925, $p<0.05$).
Conclusion: We created a formula to predict the decline in ADLs at discharge based on motor function early during hospitalization.

Key Words: Activities of daily living, Heart failure, Motor function, Early during hospitalization

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Effect of Early Mobilization within 48 Hours on Activities of Daily Living after Pneumonia in the Elderly

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Purpose: Elderly people with pneumonia are more likely to experience functional deterioration upon hospitalization. The aim of this study was to examine the effect of mobilization within 48 hours on clinical outcomes, including the deterioration of ADLs, the discharge disposition, and the length of hospital stay of hospitalized elderly patients with pneumonia.
Methods: This retrospective observational study was conducted between April 2016 and March 2017. Elderly patients ($\geqq$ 65 years) who were consecutively admitted with pneumonia were studied. Eligible patients were divided into two groups based on whether the first mobilization was performed within 48 hours of admission or later. Propensity score matching was used to determine the relationship between early mobilization and the three clinical outcomes.
Results: Of the 376 patients who met the eligibility criteria, there were 55 matched patients in each group. It was found that a higher proportion of patients who were mobilized early maintained their ADL scores (64% vs. 26%, $p< 0.001$) and were discharged to prior residence (53% vs. 37%, $p< 0.001$). However, no significant difference was found in their length of stay (median of 15 days vs. 18 days, $p=0.099$).
Conclusion: After adjusting for propensity scores, early mobilization within 48 hours may have affected clinical outcomes among those studied, such as preventing the deterioration of their ADLs and influencing their discharge home. Further prospective study is needed to confirm the findings of the present study.

Key Words: Elderly people, Pneumonia, Early mobilization, Activities of daily living

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Investigation of Physical Function and Quality of Life Associated with Frailty in Patients with Hematological Malignancies during Outpatient Chemotherapy

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Purpose: To assess the frailty of patients with hematological malignancies during outpatient chemotherapy, it was investigated or are differed on the physical function and quality of life (QOL) by frailty.
Methods: Frailty classification was performed according to Japanese Cardiovascular Health Study index (J-CHS) criteria for 33 patients with hematological malignancies undergoing outpatient chemotherapy, and physical function, physical activity, QOL, and fatigue were compared.
Results: Of the subjects, the pre-frail and Frail groups combined were 66%. Physical activity was low and the percentage of activity was low in frail patients. The muscle strength of the pre-frail group was lower than that of the non-frail group, and the frail group also had lower cardiopulmonary functions and QOL. The Frail group had a slightly low Hb level of 9.0 g/dl.
Conclusion: Although there are no problems with Performance Status (PS), some hematological malignancies patients undergoing outpatient chemotherapy fall into the Pre-frail and Frail groups. In the Frail group, not only the amount of physical activity and physical function were low, but also the quality of life was low.

Key Words: Outpatient chemotherapy, Hematological malignancy, Frailty, Physical function, QOL

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Factors Associated with Decline in Hospital-acquired Instrumental Activities of Daily Living in Elderly Patients with Heart Failure

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Objective: The purpose of this study was to investigate the factors associated with decline in hospital-acquired instrumental activities of daily living (IADL) in elderly patients with heart failure (HF).
Method: We reviewed 485 elderly HF patients capable of independent basic ADL before hospitalization. The patients were divided into two groups based on changes in IADL during hospitalization (maintained ability and hospital-acquired disability groups). The National Center for Geriatrics and Gerontology-Activities of Daily Living (NCGG-ADL) scale was used as IADL parameter. Multivariate logistic regression analysis was used to determine significant factors associated with hospital-acquired disability.
Result: Using multivariate logistic regression analysis, the following factors were predictive of hospital-acquired disability: age (odds ratio [OR] 1.06, 95% confidence interval [CI] 1.02–1.11), diabetes mellitus (OR 0.98, CI 0.96–0.99), need for support or long-term care (OR 0.01, CI 0.00–0.08), a low level of albumin (OR 1.08, CI 1.02–1.14), and cognitive impairment (OR 1.08, CI 1.02–1.14).
Conclusion: Age, diabetes mellitus, need for support or long-term care, low level of albumin, and cognitive impairment were clinical predictors of hospital-acquired disability in elderly patients with HF.

Key Words: Elderly, Heart failure, Instrumental Activities of Daily Living

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(pp 214-221)

Effect of Types of Disease on Change in Care Levels in Home-visit Rehabilitation Users

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Objective: We investigated factors associated with changes in care levels of home-visit rehabilitation users and focused especially on the types of disease and the existence of comorbidity.

Method: Sixty-six patients (78.0 ± 9.3 years) who used home-visit rehabilitation for longer than three months and took the renewal survey of care levels more than once were included. We compared the difference in care levels between the beginning of home-visit rehabilitation and at the time of this investigation. Furthermore, a logistic regression analysis was conducted to investigate the factors associated with changes in care levels.

Result: Care levels did not significantly change at the time of investigation compared with at the start of home-visit rehabilitation ($p=0.72$). Factors that were associated with improvement in care levels were the presence of musculoskeletal diseases (odds ratio [OR] = 4.76, 95%confidence intervals [CI]: 1.05–21.50, $p < 0.05$) and, on the other hand as an inhibiting factor, the presence of internal failure, with the exception of cardiorespiratory disease (OR=0.19, CI: 0.05–0.83, $p<0.05$). A factor that deteriorated care levels was the presence of cognitive impairment (OR=8.82, CI: 1.08–72.20, $p<0.05$). Comorbidity did not affect changes in care levels.

Conclusion: The influence of difference in disease types on the changes in care levels should be considered.

Key Words: Home-visit rehabilitation, Changes in care levels, Types of disease, Factorial analysis

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Effects of a Self-management Program Based on Biopsychosocial Model on Physical Activity and Sedentary Behavior in Patients with Knee Pain: A Preliminary Trial

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Objective: A 12-week trial was conducted to examine the feasibility and preliminary effects of a biopsychosocial model-based self-management program (SMP) for knee pain on physical activity and sedentary behavior in patients with knee pain.
Methods: All forty-four patients with knee pain (age, 72.4 years; 93% female) received physical therapy and were divided into an intervention group willing to participate in SMP (n=24) and a control group not willing to participate (n=20). A SMP of nine 60-minute on pain, arthritis and lifestyle were provided over 12 weeks by physical therapists. Moderate-to-vigorous intensity physical activity (MVPA) and sedentary behavior (SB) time were assessed using a questionnaire at baseline and week 12.
Results: No adverse events occurred during the intervention. Seven of the 44 patients dropped out of the study, with a mean attendance rate of 78.8% in the SMP. The between-group difference in MVPA (METs・minute/weeks) change did not reach statistical significance, but the reduction in SB time (minutes/day) was significantly greater in the intervention group than in the control group (Mean difference: −190, 95%CI −262, −116. Cohen's d = 0.78).
Conclusion: Our study suggests that adding SMP to physical therapy was feasible and effective in reducing SB time in patients with knee pain.

Key Words: Osteoarthritis, Patient education, Physical therapist, Physical therapy, Pain management

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Reliability and Validity of the Two-step Test as an Assessment of Gait Performance in the Home Setting and Identifying the Cutoff Values for Independent Gait

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Objectives: To verify the reliability and validity of the two-step test as an assessment of gait performance in the home setting and to identify the cutoff values for independent gait.
Methods: A database (N = 226) was constructed from the results of a cross-sectional survey of home-visit rehabilitation users at 10 facilities, and data sets were extracted for analysis (reliability: n = 98, validity: n = 117, cutoff values: n = 209). The survey items comprised the demographic and clinical characteristic variables, knee extension strength, two-step values calculated from the two-step test, grade of gait independence, and Rivermead Mobility Index (Japanese version), among others. The intra-rater reliability and measurement error were examined for reliability, and validity was examined based on correlations among physical function, gait ability, and the two-step values. Twelve independent gait conditions from indoor gait with a cane to community ambulation of 800 m or more without assistive devices were set according to the gait means and gait distance, and the cutoff values for each condition were examined.
Results: The intra-rater reliability of the two-step test was high, with no fixed bias, but proportional bias was shown. The two-step value was more strongly correlated with gait ability than with the strength of the knee extensors, and the cutoff values were identified according to each independent gait condition.
Conclusions: The two-step test is a reliable and valid gait assessment tool in the home setting and has useful cutoff values for discriminating gait independence.

Key Words: Home, Home-visit rehabilitation, Gait, Assessment, Cutoff value

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Intramuscular Non-contractile Tissue of the Quadriceps is Associated with Swallowing Ability in Elderly Inpatients with Pneumonia: A Cross-sectional Study

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Objectives: This study aimed to examine the relationship between intramuscular non-contractile tissue of the quadriceps and swallowing ability in elderly inpatients with pneumonia.
Methods: Forty-seven elderly inpatients with pneumonia were included. Swallowing ability was assessed using the Food Intake Level Scale (FILS). The echo intensities of the ultrasound images were used to assess the intramuscular non-contractile tissue of the quadriceps. The mean echo intensities of the right and left quadriceps were analyzed. A higher echo intensity indicated greater amounts of intramuscular non-contractile tissue. We used multiple regression analysis to identify the factors that were independently associated with FILS. Echo intensity and muscle thickness of the quadriceps, subcutaneous fat thickness of the thigh, age, sex, length of hospital stay, Geriatric Nutritional Risk Index (GNRI) score, C-reactive protein level, updated Charlson comorbidity index score, and number of medications were independent variables.
Results: The echo intensity (standardized partial regression coefficient: −0.386; $p = 0.034$), GNRI (standardized partial regression coefficient: 0.529; $p = 0.014$), and subcutaneous fat thickness of the thigh (standardized partial regression coefficient: 0.339; $p = 0.043$) were significantly and independently associated with FILS ($R^2 = 0.484$).
Conclusions: Our results suggest that the amount of intramuscular non-contractile tissue of the quadriceps is more strongly related to swallowing ability than muscle mass in elderly inpatients with pneumonia.

Key Words: Intramuscular non-contractile tissue, Swallowing ability, Elderly inpatients with pneumonia

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Feasibility of Determining Low Skeletal Muscle Mass Using Digital Images of Lower Extremities in Elderly Women: A Preliminary Study Using Convolutional Neural Network Classification and Edge Detection

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Objective: To preliminarily test whether digital images of the lower leg and edge detection can be used to determine elderly women with low Skeletal Muscle Index (SMI).
Methods: An elderly woman who was hospitalized was the subject of this study. Digital images of the subject's lower leg taken with a digital camera were used for edge detection using the Canny method. The criteria for low SMI were grouped using the criterion of 5.7 kg/m^2 proposed by the Asian Working Group, and analysis by convolutional neural network was performed on digital and edge-detected images of the lower leg, respectively.
Results: Thirty-two subjects were included in the study. The C statistic for determining low SMI in digital and edge-detected images of the lower leg was 0.83 (95% CI: 0.83–1.00) and 0.92 (95% CI: 0.92–1.00), respectivel.
Conclusion: Digital images of the lower leg may be used to classify those with low SMI.

Key Words: Elderly, Skeletal muscle mass, Machine learning, Convolutional Neural Network

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Prevalence and Level of Urinary Incontinence and Pelvic Organ Prolapse Awareness in Women with End-stage Hip Osteoarthritis

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Objective: The purpose of this study was to determine the prevalence of urinary incontinence and pelvic organ prolapse in female patients who had end-stage osteoarthritis of the hip. The study also surveyed patient awareness of the conditions, the level of concern, and the expectations for care.
Methods: Thirty-eight female patients (mean age, 64.9 years) who had end-stage osteoarthritis before total hip arthroplasty were included in the study. The International Consultation on Incontinence Questionnaire-Short Form and the Pelvic Organ Prolapse Distress Inventory 6 were used to assess the prevalence of urinary incontinence and pelvic organ prolapse symptoms. In addition, awareness and concerns regarding urinary incontinence and pelvic organ prolapse, and expectations for care were surveyed using self-administered questionnaires.
Results: The prevalence of urinary incontinence and pelvic organ prolapse was 65.8% and 63.2%, respectively; 47.4% of patients had both symptoms. The prevalence of urinary incontinence and pelvic organ prolapse awareness was 58.5% and 29.3%, respectively. Greater than 70% of the patients were concerned about the disorders and approximately one-half expected guidance for care.
Conclusions: The prevalence of urinary incontinence and pelvic organ prolapse was high in female patients who had end-stage osteoarthritis of the hip. Many patients had an interest and expectation for guidance.

Key Words: Osteoarthritis of hip, Urinary incontinence, Pelvic organ prolapse, Prevalence, Awareness

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An Investigation of the Use of Rehabilitation Protocols before and after Total Knee Arthroplasty among Japanese Health Care Providers

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Objective: This study investigated the extent to which Japanese healthcare providers implemented rehabilitation protocols before and after total knee arthroplasty (TKA).
Methods: We sent a questionnaire to 442 hospitals and clinics that performed rehabilitation before and after TKA surgery. This questionnaire asked whether they implemented the rehabilitation protocol before and after TKA and whether the protocol was evidence-based. In addition to descriptive analysis, we used logistic regression analysis to examine differences in the number of hospitals and clinics that implemented the protocol considering the number of TKA surgeries.
Results: A total of 185 hospitals responded to the questionnaire. The number of hospitals that implemented the preoperative rehabilitation protocol (45.4%) was smaller than that of those that implemented the postoperative rehabilitation protocol (87.6%). Although we found no significant differences in the number of hospitals that implemented the preoperative rehabilitation by the number of TKA surgeries, there was a significant difference in the number of hospitals that implemented the postoperative rehabilitation by the number of TKA surgeries. Furthermore, we found no significant difference in the number of hospitals that implemented preoperative or postoperative rehabilitation by the location of the hospital.
Conclusions: Fewer hospitals implemented the rehabilitation protocol before TKA compared to after TKA. The number of hospitals that implemented the postoperative rehabilitation protocol varied with the number of TKA surgeries.

Key Words: Total knee arthroplasty, Evidence-practice gap, Rehabilitation protocols

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Effect of Mild Cognitive Impairment on Activities of Daily Living in Hospitalized Patients with Sub-acute Heart Failure

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Objective: This study aimed to clarify whether the presence of mild cognitive impairment (MCI) limits the effects of sub-acute phase physical therapy (PT) on activities of daily living (ADL) improvement in patients with heart failure.
Methods: This was a single-center case-control study. In total, 155 patients who performed ADL independently before hospital admission were included in the analysis. The patients were divided into an MCI and a control group. Physical function before and after PT in the hospital were compared between the groups. Additionally, multiple regression analysis was used to evaluate the associated factors of the Barthel index (BI) at hospital discharge.
Results: At the commencement of PT, short physical performance battery (SPPB) and BI were significantly lower in the MCI group. At hospital discharge, the MCI group had significantly lower SPPB and 6-minute walking distance. However, there were no significant differences in BI at hospital discharge between the groups. Multivariate analysis showed that SPPB was associated with BI at hospital discharge.
Conclusion: Heart failure patients with MCI had a higher risk of BI decline at admission than patients in the control group, but the effect of PT on BI improvement was found to be similar regardless of MCI status. This may allow heart failure patients with MCI to perform ADL independently again.

Key Words: Mild cognitive impairment, Heart failure, Activities of daily living, Physical Therapy

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Relationships between Physical Characteristics and Ultrasound and Physical Examination Findings of the Medial Epicondyle of the Humerus in Youth Baseball Players

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Objectives: This study aimed to investigate the relationships between ultrasound (US) and physical examination findings of the medial epicondyle of humerus based on baseball elbow screening conducted in Hakodate City, Hokkaido, in 2019.
Methods: The subjects were 259 elementary school baseball players. US findings were classified into positive and negative groups. The players were listening for their physical characteristics and conducted the physical examination. Items with significant differences between the two groups were investigated in a logistic regression analysis.
Results: Results indicated that 30 and 205 players had positive and negative US findings, respectively. There were significant differences between the two groups in the age, height, position, history of elbow pain, pain at end-range elbow flexion/extension, tenderness of the medial epicondyle of humerus (TD), moving valgus test (MVT). The logistic regression analysis extracted age, TD, and MVT.
Conclusions: Among players with positive US findings, high odds ratios were found for age, TD and MVT.

Key Words: Medical checkup, Baseball elbow injuries, Medial epicondyle of the humerus, Ultrasonography

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Relationship between Physical Activity and Apathy of Elderly Individuals Requiring Support and Nursing Care

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Objective: To investigate the association between apathy and physical activity in elderly individuals requiring support and nursing care.
Methods: The physical activity scale for the elderly, apathy, health locus of control, self-rated health, and short physical performance battery were evaluated in 65 elderly individuals requiring support and nursing care. In the statistical analysis, the physical activity scale for the elderly results were divided into three groups: low, moderate, and high. Then, each variable was compared among the three groups. Additionally, multiple regression analysis was performed with physical activity scale for the elderly as the dependent variable and each evaluation item as independent variables.
Results: Compared with the high physical activity group, the low physical activity group showed significantly worse values for the apathy score, health locus of control scale, and measured 4-m walking time in the short physical performance battery. The apathy score and 4-m walking time remained significant factors even on multiple regression analysis.
Conclusion: Apathy and 4-m walking time were associated with the physical activity in elderly individuals requiring support and nursing care.

Key Words: Elderly individuals requiring support and nursing care, Physical activity, Apathy, Health locus of control, Physical function

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Trunk Alignment of Elite Male Swimmers with a History of Low Back Pain during a Streamlined Position

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Objectives: By contrasting elite male swimmers without a history of low back pain, the aim of this study is to explain the characteristics of trunk alignment during a streamlined position in elite male swimmers with a history of low back pain.
Methods: A total of 24 male elite swimmers were divided into two groups: one with a history of low back pain and the other without (LP: 9 swimmers with low back pain, NP: 15 swimmers without low back pain). The trunk alignments during a stance and a streamlined position on the ground were assessed to investigate the differences in the flexibilities of the shoulder girdle, ribcage, and hip. To compare the outcomes of the two groups, a T-test was performed.
Results: During the streamlined position, there was a significant difference in the pelvis, trunk, and lumbar angle, while there were no significant differences during the stance position. In comparison with NP, the lumbar lordosis angle, pelvic anterior tilting angle, upper trunk posterior tilting angle, and upper trunk extension angle were all greater in LP. Moreover, the flexibility of the lower ribcage was also found to be slightly lower in LP during the streamlined position, with no differences in the stance position.
Conclusions: We clarified that swimmers with a history of low back pain were unable to control their trunk alignment during a streamlined position. In LP, the lack of flexibility in the lower ribcage was shown, implying that it may be a major contributor to excessive lumbar lordosis in a streamlined position.

Key Words: Competitive swimming, Lumbar lordosis, Low back pain, Streamlined position

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Efficasy of Combined Exercise with Gait Exercise Assist Robot on Chronic Hemiplegic Stroke Patient: A Single-case Study ABAB Design

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Purpose: The purpose of this study was to examine the effects of low-frequency intervention combining exercise therapy with the Gait Exercise Assist Robot (GEAR) in patients with chronic hemiplegic stroke.
Methods: The participant was a 47-year-old male patient with stroke with right hemiparesis (13 months post-stroke). This study used an ABAB single-case design. The participant underwent a combination of ground-based walking exercise and physical therapy during the A period and exercise with the GEAR and physical therapy during the B period. Both periods were conducted twice a week for 4 weeks for a total of 16 weeks. The walking speed, step length, cadence, physical and cognitive function, and gait pattern were evaluated.
Results: The walking speed improved during the initial and secondary B period, cadence increased during the secondary B period, and gait pattern improved before and after the intervention.
Conclusion: Low-frequency intervention combining exercise with the GEAR and physical therapy appears to improve gait ability in patients with chronic stroke hemiplegia.

Key Words: Chronic stroke, Gait exercise, Robot

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Effects of Body Weight-Supported Treadmill Training on Ambulatory Function in Stroke Patients with Cerebellar Ataxia: A Single-case Design Study

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Objective: This study aimed to describe the effects of body weight-supported treadmill training (BWSTT) on two stroke patients with cerebellar ataxia.
Methods: Two inpatients post cerebellar infarction (a female, about 50 years old; and a male, about 60 years old) participated in this study. This study was conducted in an A-B-A single-subject research design. The baseline phase (A) and intervention phase (B) lasted for 10 days. The patients received physical therapy focusing on limb and trunk coordination, standing balance, and overground walking training in phase A. In phase B, these patients underwent BWSTT in conjunction with the therapies performed in phase A. Outcome measures included maximum walking speed, step length, cadence, the Timed Up and Go test, the Scale for the Assessment and Rating of Ataxia (SARA), the Berg Balance Scale (BBS), the Functional Assessment for Control of Trunk, and the Functional Ambulation Category.
Results: In both cases, maximum walking speed was significantly improved in the intervention phase (B) compared to the baseline phase (A). On the other hand, there was no difference in the SARA (gait, stance, and heel-shin slide) and BBS between phases A and B.
Conclusions: BWSTT can improve ambulatory function in stroke patients with cerebellar ataxia.

Key Words: Stroke, Cerebellar ataxia, Body weight-supported treadmill training, Single-case design study

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Relationship between Mental Health and Lower Back Pain Relating to Labor Productivity of Ward Nurses: A Study of Work Engagement, Workaholism, and Lower Back Pain

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Objective: This research sheds light on the relationship between work engagement, workaholism, and lower back pain in nurses from a perspective of mental health. The study focused on the labor productivity of nurses in real-world settings.
Methods: Seventy-three female ward nurses participated in this study. An anonymous, self-administered questionnaire survey was conducted with the participants. Survey items were as follows: labor productivity, work engagement, workaholism, the presence and duration of lower back pain.
Results: In terms of absolute presenteeism, a significant positive correlation was observed between the work engagement scores, but no significant correlation was observed between the workaholism scores. Significantly lower scores for work engagement were observed in the lower back pain group than in the non-lower back pain group. No significant difference was observed between these groups in terms of workaholism.
Conclusion: The presence or absence of non-specific low back pain and work performance were independent factors explaining work engagement, suggesting the importance of positive mental health.

Key Words: Labor Productivity, Work Engagement, Workaholism, Lower Back Pain

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Examination of Motor Function and Changes Over Time in Patients with Fukuyama Congenital Muscular Dystrophy

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Objectives: We examined changes in motor function over time in Fukuyama congenital muscular dystrophy (FCMD) patients.
Methods: The subjects were 57 FCMD patients. Motor functions were evaluated using the gross motor function measure (GMFM). The subjects were grouped according to genotype, and GMFM score transitions were observed for each individual. We determined each GMFM score monthly and performed a regression analysis for all data obtained, using a least-squares method. The age at peak GMFM score (peak age) was also studied based on regression analysis results for all cases and for each clinical severity.
Results: The monthly course of GMFM scores showed a biphasic pattern comprised of a rapidly increasing phase, followed by a slowly decreasing phase. According to genotypes, the range of GMFM scores was greater in compound heterozygotes than in homozygotes. The peak motor function ages of severe, typical and mild cases, based on an approximated graph for each, were 20, 48 and 68 months, respectively. The peak GMFM score in typical cases was 28 for homozygous and 18 for compound heterozygous cases.
Conclusion: Changes in FCMD motor function over time showed a rapidly increasing phase, followed by a slowly decreasing phase. The peak ages, in the approximated graphs, differed according to clinical severity. Among typical cases, compound heterozygotes tended to have poorer motor skills than homozygotes.

Key Words: Fukuyama congenital muscular dystrophy, Motor function, Genotype, Gross motor function measure

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Effects of Posture Differences on the Thickness of Abdominal Trunk Muscles in the Final Range of Continuous Vocalization

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Objective: To examine the effects of posture differences on the thickness of the abdominal trunk muscles in the final range of continuous vocalization.
Methods: Thirty healthy individuals (15 men and 15 women) were included in this study. The transversus abdominis, internal oblique, and external oblique muscles were measured in the final range of resting expiration and continuous vocalization using ultrasonography. The vocal task was the vowel /o/ sound and the amount of vocalization was controlled at 60–70 dB. The three postures were supine, sitting, and standing. The thickness of the three abdominal muscles were compared between tasks and between postures. The rate of change in thickness of these muscles was also compared between postures and between genders.
Results: The thickness of the transversus abdominis and internal oblique muscles was significantly greater during the vocalization task than during resting expiration in all the postures for both men and women. The rate of change in thickness of the transversus abdominis muscle was significantly higher in the supine posture than in standing posture in men. In addition, in both men and women, the rate of change in thickness of the transversus abdominis muscle was higher than that of the internal oblique and external oblique muscles. No significant difference was observed in the rate of change in thickness of the transversus abdominis and internal oblique muscles between men and women.
Conclusions: Continuous vocalization was observed a significant increase in the thickness of the transversus abdominis in all postures regardless of gender.

Key Words: Thickness of the transversus abdominis, Continuous vocalization, Posture

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Influence of Mobility Independence and Mobility Method on the Positivity of Attitude during Leisure Activity in Outpatient Rehabilitation Service for Long-term Care

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Objective: The purpose of this study was to investigate the effects of independence and methods of mobility on positivity of attitude during leisure activity in an outpatient rehabilitation service for long-term care.
Methods: Ninety-seven elderly persons (mean age, 83.2 ± 7.3 years; 30 men, 67 women) who underwent outpatient rehabilitation service for long-term care participated in this study. Positivity of attitude during leisure activity was assessed by one evaluator using items related to activity and interpersonal relationships in a behavioral rating scale for the elderly. Mobility independence was classified as assistance, supervision, or independence, and method of mobility was classified as wheelchair or walking. Age, sex, diagnosis, required care level in daily living, upper limb function, cognitive function, posture during leisure activity were recorded as other independent variables. The odds ratio was calculated by generalized estimating equations to analyze the effects of these independent variables on the positivity of attitude during leisure activity.
Results: High mobility independence and high cognitive function were significantly associated with high activity and enhanced interpersonal relationships during leisure activity. Having a wheelchair for mobility significantly increased activity. The odds ratios were greater for mobility independence than for cognitive function.
Conclusion: Even when taking method of mobility and level of cognitive function into consideration, independence of mobility influenced positivity of attitude in leisure activity.

Key Words: Outpatient rehabilitation service for long-term care, Leisure activity, Mobility independence, Mobility methods

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Epidemiology of Anterior Cruciate Ligament Injury in Female Gymnasts

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Objective: While anterior cruciate ligament injury in female athletes are generally well documented, there are a lack of reports for female gymnasts. The purpose of this study was to clarify the occurrence of anterior cruciate ligament (ACL) injuries in female gymnasts.
Method: The subject number were 283 female gymnasts who visited in Funabashi Orthopedic Hospital and were diagnosed with knee joint diseases and disorders. The incidence and age of each disease were investigated. We investigated the height, weight, Body Mass Index, complications, level of competition, event (vault, uneven bars, balance beam, floor exercise) at the time of injury, injury mechanism, injured side, direction of twist at the time of skill execution, and type of skill performed at the time of injury in patients with anterior cruciate ligament injuries, and examined the relationship between injured side and direction of twist.
Results: ACL injuries occurred at the second highest rate among knee joint diseases, with the most common age of occurrence being 16 and 17 years old. The majority of injuries occurred on the floor exercise, and the majority of injuries occurred on the landing. The most common complication was lateral meniscus injury. The relationship between the injured side and the direction of the twist was observed, and the injury on the opposite side of the twist direction was significantly more frequent.
Conclusion: The relationship between the injured side and the direction of twist was characteristic of ACL injuries in female gymnastics, reflecting the specificity of the sport.

Key Words: Female gymnastics, Anterior cruciate ligament injury, Epidemiology

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Examination of Physical and Psychosocial Factors of Elderly that Improve the Life Space Based on the Type of Neighborhood Environment

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Objectives: This study aimed to categorize neighborhood environment and examine the factors of the elderly that improve the life space in each environment.
Methods: A total 106 elderly people attending day care facilities participated in this study. Life-space assessment (LSA), abbreviated neighborhood environmental walkability scale, basic attributes, and physical, and psychosocial factors were measured. A cluster analysis was used to categorize the neighborhood environment. The LSA scores were divided into two groups, a high-score group and a low-score group under each environment, with cutoff score of 56. The factors of the elderly were compared between the two groups.
Results: The neighborhood environment was classified into three types using cluster analysis. On comparison between the high and low-score groups, a significant difference was found in the long-distance mobility in the poor-status environment, whereas a significant difference was found in the hobbies and social support scale in the good-status environment.
Conclusion: These results suggested that the physical and psychosocial factors of the elderly that the life space differ in each environment.

Key Words: Elderly, Life-space assessment, Neighborhood environment, Physical and psychosocial factors

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Examination of the Factors Related to Walking Independence at Discharge in Patients who Required Mechanical Ventilation

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Objectives: This study examines the related factors and cut-off values for determining walking independence at discharge in patients who required mechanical ventilation in the critical care ward.
Methods: We enrolled 100 patients who had been on mechanical ventilation for > 24 h. The patients were divided into the independent and dependent groups as per their walking ability at discharge. Outcome measures for determining the walking independence were examined with multiple logistic regression analysis for factors, such as patient characteristics and blood test data on admission in the critical care ward and the mental function, physical function, and physical activity status during their stay in the critical care ward. Moreover, the cut-off values for each extraction factor and the prediction model score were calculated from the receiver operating characteristic curve.
Results: Multiple logistic regression analysis showed that age, serum total protein (TP) value, and intensive care unit mobility scale (IMS) were significantly associated with the walking ability at discharge. Furthermore, the cut-off value of each parameter and score were as follows: age, 79 y; TP value, 6.1 g/dL; and IMS, level 6 (marching on spot); and the prediction model score, 0.72.
Conclusions: The results of this study suggest that age, TP, and IMS might be related to walking independence at discharge in patients who required mechanical ventilation in the critical care ward.

Key Words: Mechanical ventilation, Critical care ward, Walking ability

Vol. 48, No. 5 (pp 515-522)

Factors Associated with Walking Ability Evaluated 2 Weeks after Hip Fracture Surgery in Elderly Patients

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Objective: We investigated the association between perioperative factors, including the postoperative Cumulated Ambulation Score for 3 days after operation (3-day CAS) and walking ability evaluated 2 weeks postoperatively in elderly patients with hip fracture.
Methods: The study included 187 patients with hip fractures, who were categorized into two groups based on their walking ability evaluated 2 weeks postoperatively. One group included 99 patients who could not walk or could walk only with the use of parallel bars, and the other group included 88 patients who could walk using a walker. Multiple logistic regression analysis was performed based on preinjury and preoperative patient information, surgical factors, and 3-day CAS. Additionally, we calculated cutoff values based on the receiver operating characteristic curve.
Result: Preinjury Barthel Index (BI), fracture type, and 3-day postoperative CAS as variables associated with walking ability that was evaluated 2 weeks postoperatively. The cutoff values used to determine patients' walking ability using a walker 2 weeks postoperatively were 92.5 points for the preinjury BI and 3.5 points for the 3-day CAS.
Conclusion: We observed that in addition to the preinjury BI and fracture type, the 3-day CAS was useful to determine patients' walking ability using a walker, 2 weeks postoperatively.

Key Words: Hip fracture, Early postoperative functional evaluation, CAS, Walking ability

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Comparative Study of the Carrying Angle Measured from the Body Surface by Goniometry and Radiography

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Objective: This study aimed to highlight the differences between the measurements of the carrying angle from the body surface by goniometry and radiography.
Methods: The carrying angle of 194 elbows of 97 healthy subjects was measured. From the body surface, the angle between the upper arm and forearm was measured using a goniometer. For radiological measurement, two methods were adopted: one measured the angle between the humeral and ulnar axes, whereas the other measured the angle between the humeral axis and line connecting the superior radioulnar joint and the radial tuberosity. The carrying angles measured by each method were compared, and the effects of the body shape factors on each method were analyzed.
Results: There was a significant difference in carrying angle measurement between the methods, and the angle in the body surface method was the smallest. In the analyses of the body surface method, the maximum circumference of the forearm and upper arm length were statistically significant contributors. In the analyses of the radiological methods, the forearm length was a statistically significant contributor.
Conclusion: It should be considered that body shape factors affect the carrying angle measurement; a significant difference was noted in the measurements between the body surface and radiological methods. For use in sports medicine, the development of a measurement method from the body surface similar to that of the radiological methods is necessary.

Key Words: Carrying angle, Body surface, Radiograph, Normal elbow

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Dynamic Three-dimensional Lower Limb Mechanical Axis According to the Severity of Knee Osteoarthritis

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Objective: To clarify the relationship between three-dimensional mechanical axis (3D-MA) passing points on the proximal tibial surface and the knee joint kinematics and radiographic coronal alignment.
Methods: Seventy-five participants (93 knees) with knee osteoarthritis (OA) (Hokkaido University classification, stage II-V) were included. Three-dimensional motion analysis was performed using an optical motion capture system while walking to examine the knee joint kinematics and the trajectory of 3D-MA passing points.
Results: The displacements of the x-component of the 3D-MA passing points (3D-MAx) were qualitatively similar to varus and valgus knee kinematics and demonstrated a significant moderate correlation with the radiographic alignment. There was an increase in the 3D-MAx medial displacement between the initial contact and peak value in severe cases, along with a decrease in the change in knee flexion angle during the loading response phase.
Conclusion: 3D-MA is a multiplex index that reflects static knee alignment and dynamic knee kinematics. Evaluation of the load axis dynamics during gait may help clarify the mechanism that underlies the progression of OA.

Key Words: Knee osteoarthritis, Knee joint kinematics, Three-dimensional mechanical axis

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Associations of Instrumental and Affective Attitudes with Exercise Behavior: Examining the Mediating Roles of Self-efficacy and Self-regulation

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Objective: The present study aimed to examine whether instrumental and affective attitudes are associated with exercise behavior, mediated by self-efficacy and self-regulation.
Methods: A baseline internet survey was conducted with 500 individuals aged 50–74 years. Among them, 394 individuals responded to the six-month follow-up survey. After adjusting for demographic factors, the associations between instrumental attitude, affective attitude, self-efficacy, self-regulation, and exercise behaviors were examined using path analyses.
Results: In the cross-sectional and longitudinal models of path analyses, both self-regulation and self-efficacy significantly regressed on exercise behavior. Furthermore, affective attitude was significantly associated with both self-regulation and self-efficacy, whereas instrumental attitude was significantly associated with self-regulation but not with self-efficacy.
Conclusions: The present study indicated that affective attitude influenced exercise behavior, mediated by both self-regulation and self-efficacy. However, the influence of instrumental attitude on exercise behavior, mediated by self-regulation and self-efficacy, remains unascertained.

Key Words: Attitude to health, Self-efficacy, Self-control, Exercise, Healthy aging

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Effect of Skeletal Muscle Mass on Functional Prognosis in Patients with Proximal Femur Fractures

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Objective: This study investigated the relationship between skeletal muscle mass, estimated by the psoas muscle area on abdominal computed tomography, and functional prognosis, in proximal femur fracture patients.
Methods: One hundred and thirteen recovery ward patients were divided into the skeletal muscle mass loss group and a control group. We compared their clinical history and functional prognoses. Multiple regression analysis, with Functional Independence Measure (FIM) gain as the objective variable, was performed to examine the relationship between skeletal muscle mass and the results.
Results: The mean age of the patients was 83.5 ± 8.3 years. Thirty-five patients were males, and 78 were females. There were a total of 56 patients in the skeletal muscle mass loss group. Compared to the control group, the skeletal muscle mass loss group members were older, more, had significantly lower cognitive FIM at admission, lower total FIM at discharge, and FIM gain. Multivariate analysis showed a significant association between skeletal muscle mass loss and FIM gain.
Conclusion: Skeletal muscle mass loss, estimated by the area of the psoas muscle in patients with proximal femur fractures, may be associated with a poor functional prognosis.

Key Words: Proximal femur fractures, Psoas Muscle mass Index, Skeletal muscle mass, FIM gain

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The Effects of Temporal and Spatial Changes in Motor Imagery of Walking on Brain Neural Activity: Using the Microstate Segmentation Method

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Objective: The purpose of this study was to investigate the neural activity in the brain during the temporal and spatial changes of a gait image by EEG analysis.
Methods: We examined the characteristics of neural activity in the brains of eight healthy young subjects under the conditions of temporal and spatial changes of a walking image by EEG microstate segmentation method.
Results: The supplementary motor area and the anterior segment of the wedge were commonly activated during the temporal and spatial changes in the gait image. The frontal eye area and the superior parietal lobule were predominantly activated during the temporal change, and the frontal eye area, frontal pole, and superior parietal lobule were predominantly activated during the spatial change.
Conclusion: It was suggested that different brain regions were activated when the gait image was changed spatially and temporally. These results suggest that the temporal and spatial characteristics of the gait image need to be considered when it is used as an optimized intervention method.

Key Words: gait imagery, microstate segmentation method, EEG, brain neural activity

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Prevalence and Clinical Impact of Hospital-acquired Disability in Patients with Interstitial Lung Disease: A Two-center Prospective Observational Study

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Objectives: Patients with interstitial lung disease are known to show functional decline due to dyspnea on exertion. However, the incidence of hospital-acquired disability (HAD) associated with hospitalization and its impact on clinical outcomes remains unclear.
Methods: A prospective observational study was conducted by two study participating hospitals. Patients were hospitalized for respiratory failure who had been diagnosed with interstitial lung disease before, or who had been diagnosed with interstitial lung disease by a physician on high-resolution computed tomography at admission and underwent rehabilitation between June 2018 and December 2020. HAD was defined as a decrease of more than 5 points in the total Barthel index score at discharge compared to that before admission. Multiple regression analysis was performed to examine the influence of HAD on the length of hospital stay.
Results: Of 66 patients analyzed (median age 77 years, 47 males), 32 (48%) had HAD. In multiple regression analysis, HAD was identified as an independent determinant of the length of hospital stay (β = 0.34, 95% confidence interval = 3.86–25.52).
Conclusion: We found that HAD occurred at a high rate in patients with interstitial lung disease and affected clinical outcomes, including the length of hospital stay.

Key Words: Interstitial lung disease, Hospital-acquired disability, Length of hospital stay

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Prediction of Walking Independence 3 Months after Onset by Deep Residual Network from Acute Computed Tomography Images in Patients with Capsular and Thalamic Hemorrhage: A Retrospective Cohort Study

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Objective: To predict walking independence in patients with capsular and thalamic hemorrhage three months after symptom onset using acute phase computed tomography (CT) images.
Methods: A total of 134 patients with capsular and thalamic hemorrhage, who were admitted to a rehabilitation ward, were included in the study. CT images were taken within 12 hours after symptom onset, and a deep residual network was used to predict walking independence three months after symptom onset. The C statistic, sensitivity, specificity, F value, and Matthews Correlation Coefficient (MCC) were calculated to determine prediction accuracy.
Results: The prediction accuracy [mean value (95% CI)] calculated from the C statistic, sensitivity, specificity, F value, and MCC was 0.89 (0.70 – 0.94), 0.91 (0.76 – 0.95), 0.83 (0.69 – 0.88), 0.87 (0.80 – 0.92), and 0.82 (0.76 – 0.89), respectively.
Conclusion: Acute phase CT image findings of patients with capsular and thalamic hemorrhage can be used to predict walking independence three months after symptom onset.

Key Words: Stroke, Gait, Machine learning, Deep Residual Network, Prediction

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Effects of Neuromuscular Electrical Stimulation as an Assistance to Outpatient Cardiac Rehabilitation in a Heart Transplant Patient: Single-case Data Analysis

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Objective: We examined whether neuromuscular electrical stimulation (NMES) in outpatient cardiac rehabilitation (CR) assists physical function and performance in a heart transplant patient.
Method: A 40-year-old patient underwent heart transplantation due to hypertrophic cardiomyopathy followed by outpatient CR after discharge. The study design was A (basic level period)–B (intervention period)–A (basic level period), and each period was of 8 weeks. The patient underwent outpatient CR once weekly for the entire study period. NMES was performed on the thighs and lower legs for 50 min/day, 5 times/week at home only during the intervention period. The objective variables in this study were exercise capacity, muscle strength, and usual walking speeds. The measurement points were the 0th week (M1), 8th week (M2), 16th week (M3), and 24th week (M4).
Results: Changes in oxygen consumption at anaerobic threshold (AT) were 16.7 mL/min/kg, 20.6 mL/min/kg, 22.8 mL/min/kg, and 17.9 mL/min/kg, and lower limb muscle strength was 0.69%, 0.70%, 0.76%, and 0.74 % body weight; the usual walking speeds were 1.17 m/s, 1.36 m/s, 1.41 m/s, and 1.37 m/s (M1, M2, M3, and M4, respectively).
Conclusion: NMES may have synergistic effects on outpatient CR in patients following transplantation.

Key Words: Heart transplant, Outpatient cardiac rehabilitation, Neuromuscular electrical stimulation

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Factors Associated with Walking Independence during Hospitalization in Patients with Acute Ischemic Stroke: Multivariate Analysis of the Berg Balance Scale, Moss Attention Rating Scale, and Stop Walking When Talking Test

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Objectives: Although accurately evaluating the independence of walking in acute-phase patients with ischemic stroke is important, no quantitative study has been performed on attentional deficit. The purpose of this study was to clarify factors associated with walking independence of patients during hospitalization using the Moss Attention Rating Scale (MARS), Stop Walking When Talking test (SWWT), and Berg Balance Scale (BBS).
Methods: Eighty-six patients with ischemic stroke within two weeks after onset were enrolled. Discriminant accuracy of walking independence was compared between the BBS score and discriminant score calculated by multivariate logistic regression analysis.
Results and Conclusion: The BBS, MARS, and SWWT were selected as determinant factors of walking independence. Discriminant accuracy based on the discriminant score calculated using the BBS, MARS, and SWWT was higher than that based on the BBS alone.

Key Words: Berg Balance Scale, Moss Attention Rating Scale, Stop Walking When Talking test, Acute phase of ischemic stroke, Walking independence

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Psychological Stress among Frontline Physical Therapists during the Coronavirus (COVID-19) Pandemic in Japan

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Objective: The purpose of this study was to identify psychological stress among physical therapists who provide physical therapy to patients with novel coronavirus disease (COVID-19) in the containment zone.
Methods: A survey was conducted using an internet-based questionnaire system. In addition to basic personal information, the content of the physical therapy, the burden of infection control, and psychological stress were surveyed.
Results: Of the 584 individuals analyzed, only six physical therapists did not state that they feel "stressed" about physical therapy conducted in the containment zone. In addition to anxiety over the possibility of being infected, social stress – such as being discriminated against due to prejudice from others – were also identified. The most common types of psychological stress were "infection of family members and others" (88.5%) and "infection of oneself" (82.0%).
Conclusion: Almost all physical therapists who provide direct physical therapy in the containment zone to patients with COVID-19 showed signs of psychological stress.

Key Words: Physical therapists, COVID-19, Containment zone, Psychological stress

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