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REVIEW

Recent Advances in the Neural Control of Movements: Lessons for Functional Recovery

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ABSTRACT. We review the current views on the control and coordination of movements following the traditions set by Nikolai Bernstein. In particular, we focus on the theory of neural control of effectors - from motor units to individual muscles, to joints, limbs, and to the whole body - with spatial referent coordinates organized into a hierarchy with multiple few-to-many mappings. Further, we discuss synergies ensuring stability of natural human movements within the uncontrolled manifold hypothesis. Synergies are organized within the neural control hierarchy based on the principle of motor abundance. Movement disorders are discussed as consequences of an inability to use the whole range of changes in referent coordinates (as in spasticity) and an inability to ensure controlled stability of salient variables as reflected in indices of multi-element synergies and their adjustments in preparation to actions (as in brain disorders, including Parkinson's disease, multiple-system atrophy, and stroke). At the end of the review, we discuss possible implications of this theoretical approach to peripheral disorders and their rehabilitations using, as an example, osteoarthritis. In particular, "joint stiffening" is viewed as a maladaptive strategy, which can compromise stability of salient variables during walking.

Key words: Synergy, Stability, Agility, Referent coordinate, Osteoarthritis

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The fields of the neural control of movements and movement disorders have always been tightly intertwined. Indeed, observations of neurological patients have led to a number of influential concepts such as those of hierarchical control of movements, multiple cortical representations, and synergy[1,2)]. The highly influential theoretical views of Nikolai Bernstein[3,4)] have been largely based on observations of patients with a variety of motor disorders and also produced important insights for motor rehabilitation. In particular, Bernstein emphasized the importance of plastic changes within the central nervous system leading to adaptive adjustments in movement patterns.

These insights have important implications for a number of issues related to practice of motor rehabilitation. These include the following: Should the goal of therapy be bringing the movement patterns of a patient back as close as possible to those observed in healthy persons ("normal movements")? Should therapy emphasize functional recovery even at the expense of apparently abnormal movement patterns being used to solve everyday motor problems? In cases of a localized injury, should therapy be focused on that locus or involve the whole body?

Discussions of these issues have been ongoing over the past years with the accumulation of knowledge about the neural mechanisms of the production of voluntary movements[5-7)]. Indeed, the importance of basic knowledge for motor rehabilitation has become obvious for both researchers and practitioners. Hence, the main purpose of this review is to present an update on the current understanding of the neural mechanisms involved in the production (and, sometimes, perception) of human voluntary movements with an emphasis on most recent developments. Of course,

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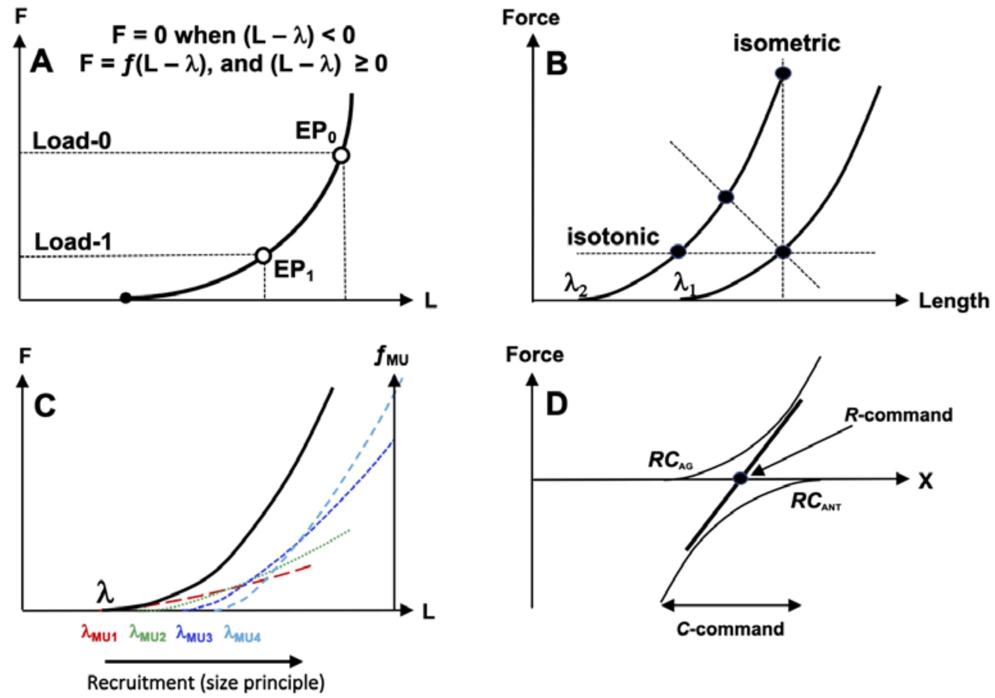

Fig. 1

A: Setting a value of stretch reflex threshold, λ produces a dependence of muscle active force on muscle length, F (L). A change in external load leads to movement from the initial equilibrium point (EP_0) to another one, EP_1. B: The production of voluntary movements is associated with changes in λ, for example from λ_1 to λ_2. The same shift of λ can lead to different mechanical effects depending on the external load. C: Each motor units (MU) can be described with a corresponding λ value resulting in a dependence of its firing frequency (*f*) on muscle length. D: The control of an effector can be described with time-varying referent coordinates RC_{AG} and RC_{ANT} (for the agonist and antagonist muscles). Alternatively, *R*-command (reciprocal command) and *C*-command (coactivation command) can be used.

this review reflects the subjective opinions of the authors and may not be shared by all of our respected colleagues.

We accept, as an axiom, that the human body, including the brain, is a product of natural evolution and, as such, it has to obey laws of nature[8,9]. Some of those laws are described in physics textbooks. They are common across the inanimate world and biological objects. These laws are very powerful in predicting behavior of inanimate objects, but not so - for biological objects. Indeed, they only constrain biological behaviors but do not prescribe them. As a result, biological objects, including humans, commonly show movements, which are not observed in the inanimate world. Obvious examples include walking uphill and swimming against the current. This means that some of the laws of nature are specific to biological objects, and we see discovering such biology-specific laws as imperative for progress in the field of the neural mechanisms of behavior.

We begin this review with a brief exposition of the theory of motor control with time-varying spatial referent coordinates for the effectors[8,10], explain how this theory can be applied to objects ranging from motor units to the whole body, and then describe recent applications of this theory to clinical issues such as spasticity and its treatment. Further, we shift emphasis to the issue of movement stability and introduce the principle of abundance, the notion of performance-stabilizing synergies, and the toolbox associated with the uncontrolled manifold hypothesis[11-13]. We review recent studies documenting changes in the ability to control stability of movements in task-specific manner in a variety of neurological patients. At the end, we consider osteoarthritis as a pathological condition, which has not been discussed within the introduced theoretical frameworks.

Control of Biological Movement with Referent Coordinates

The theory of motor control with spatial referent coordinates (RCs) originates from the classical equilibrium-point hypothesis (EP-hypothesis)[14,15]. According to the EP-hypothesis, the neural control of a muscle with its intact connections to the spinal cord can be adequately described as setting time changes in the threshold of the stretch reflex, λ. Note that setting a value of λ produces a dependence of muscle active force on muscle length, F(L) (Fig. 1A),

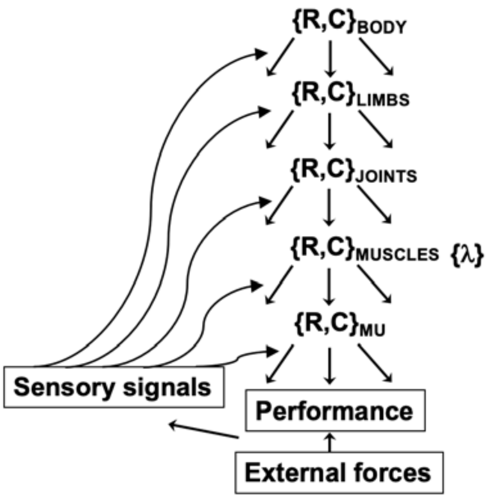

Fig. 2

At the task level, the control of action can be described with a low-dimensional set of *R* and *C* commands. Further, a sequence of few-to-many transformations leads to the emergence of the *R* and *C* commands at the hierarchically lower levels corresponding to the involvement of joints, muscles, and motor units (MUs).

which can be viewed as a law of nature valid across all skeletal muscles. This law links the two salient variables for the muscle, its length and force (consider only static conditions, for simplicity), with the help of a single parameter λ: $F = f(L - \lambda)$, when $L > \lambda$. Since muscles always act against an external load, the system "muscle + reflexes + load" will come to an equilibrium at a point with certain values of L and F, when muscle force exactly balances the load (equilibrium point, EP).

If λ = const., movements can happen as a result of changes in the external load, for example from EP_0 to EP_1 in Figure 1A. The production of voluntary movements is associated with changes in λ, for example from λ_1 to λ_2 in Figure 1B. Note that the same change of λ can lead to different peripheral consequences, depending on the external load: From force change in isometric conditions, to movement in isotonic conditions, and to changes in both F and L when the muscle acts against a more realistic load. In neurophysiological terms, λ has been associated with subthreshold depolarization of the corresponding alpha-motoneuronal pool. As a result, λ is a neurophysiological variable expressed in millivolts, which is converted by the stretch reflex mechanism into a mechanical variable expressed in units of muscle length (meters). Note that λ may be viewed as muscle RC because, if the external load is removed, the muscle will change its length until $L = \lambda$.

The scheme of control with λ can be extended both inside the muscle (to control of individual motor units) and to multi-muscle effectors. Figure 1C illustrates the control of a few motor units (MUs) with the corresponding λ values; for a given MU, its firing frequency (f_{MU}) increases with muscle length leading to an increase in the contribution of that MU to muscle force. Note that muscle λ equals the smallest of MU λs, and muscle active force is the sum of the contributions of all the MUs.

Any effector in the human body is controlled with opposing muscle groups, agonists and antagonists. The control of an effector can be described with time-varying λ_{AG} and λ_{ANT} (the subscripts stay for agonists and antagonists, Fig. 1D). Alternatively, these two variables can be replaced by an equivalent pair, *R*-command (reciprocal command) and *C*-command (coactivation command). The *R*-command defines a value of the coordinate (e.g., joint angle) where the resultant force variable (moment of force, M, for a joint) is zero. The *C*-command defines the spatial range where the two opposing muscle groups are activated simultaneously. Changing the *C*-command effectively leads to changes in the apparent stiffness[16,17] of the effector. So, the control of any effector, up to the whole body may be viewed as setting the {*R*; *C*} pair at the task-specific level. For example, for an arm reaching movement, *R* and *C* are set for the endpoint of the arm. Then, a sequence of few-to-many transformations (Fig. 2) leads to the emergence of {*R*; *C*} pairs at the hierarchically lower levels corresponding to the involvement of joints, muscles, and MUs. Note that all natural movements involve abundant sets of elements: More joints, muscles and motor units as compared to the number of task-related constraints. This offers an exciting opportunity to organize the transformations illustrated in Figure 2 in a way that leads to stabilization of salient, task-specific variables (this issue is described in more detail in the next section).

The idea of muscle control with changes in λ has been developed to analyze movements in certain groups of neurological patients, in particular those suffering from spasticity[18,19]. Healthy humans can relax their muscles within their whole anatomical range and also produce high levels of muscle force also within the whole range. This is illustrated in Figure 3A. Note that relaxing a muscle implies moving its λ beyond the longest possible value of muscle length. Producing a very large force with a short muscle requires moving λ beyond the anatomical range in the opposite direction. The whole healthy range of λ changes is shown as λ_{MIN} to λ_{MAX}.

Patients with spasticity typically display two groups of signs: An inability to activate the affected muscle voluntarily (paresis) combined with unintentional muscle activation leading to spasms and high resistance to external motion (imprecisely addressed as increased muscle tone). The two groups of signs can show parallel changes with treatment, as shown for example in studies of the effects of intrathecal baclofen[20]. Figure 3B illustrates that both paresis and spasms can originate from a single cause: Lost ability to shift λ within its whole range. Indeed, if a patient cannot shift λ to the left of λ_{min}, no active muscle force can be pro-

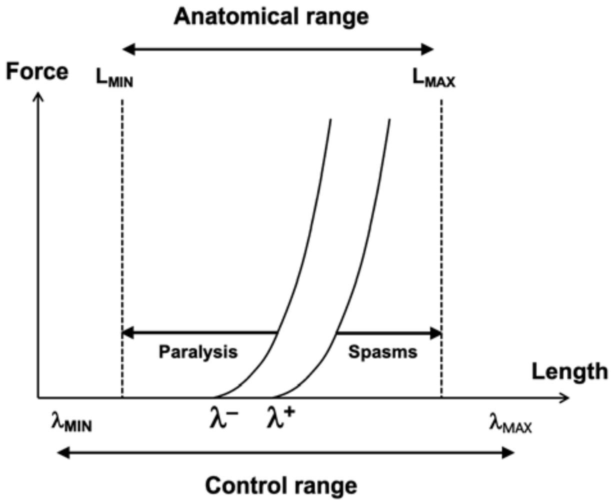

Fig. 3
Healthy humans can shift λ over a control range larger than the anatomical range of muscle length. This allows relaxing the muscle within its anatomical range and also producing high levels of muscle force within this range. Spasticity is caused by loss of the ability to shift λ within its whole range, e.g., only within λ_{min} to λ_{max}. No active muscle force can be produced (paralysis) for the muscle when its length $L < \lambda_{min}$. The muscle cannot relax (spasm) when $L > \lambda_{max}$.

duced for the muscle when its length $L < \lambda_{min}$. If the same patient cannot shift λ to the right of λ_{max}, the muscle will be unable to relax when its length $L > \lambda_{max}$. Recent studies have shown that, indeed, stroke survivors with spasticity show a reduction in the range of voluntary λ changes and this reduction correlate with the clinical severity of their disorder[21,22].

Motor Variability: A Crucial Feature of Healthy Movements

Before moving to the topic of synergies, we have to consider briefly the phenomenon of motor variability, which has been studied at least since the end of the XIXth century. Currently, motor variability is viewed not simply as a result of "noise" within the body but as a crucial, functionally important feature of biological movements[23]. Indeed, a number of studies have shown that elevated motor variability at the level of involved elements is typical of highly-experienced workers, whereas low motor variability is a predictor of chronic pain emergence[24]. Along similar lines, very low postural sway may be seen in patients with advanced-stage Parkinson's disease[25] who display seriously compromised ability to maintain vertical posture.

The current understanding of motor variability can be traced back to the seminal study by Nikolai Bernstein of hammering by professional blacksmiths. These subjects were arguably best trained to perform the movement of hitting the chisel held by the non-dominant hand by the hammer moved by the dominant hand. So, if there was an optimal solution to problems associated with performing this task, Bernstein's subjects were the ones to have it. Nevertheless, Bernstein reported high motor variability at the level of trajectories of both individual joints and the tip of the hammer. His most surprising observation was that the variability of the tip of the hammer was much lower compared to the variability of individual joint trajectories.

Obviously, the brain could not send signals to the hammer, only to muscles that produced joint rotations. How come that the signals to muscles produced highly variable trajectories of the joints, whereas the trajectory of the hammer produced by those joint rotations was much more reproducible? Bernstein introduced the notion of a kinematic synergy stabilizing the hammer trajectory by co-varying joint trajectories, an insight that waited for over 50 years to become the foundation of the uncontrolled manifold (UCM) hypothesis[26].

Synergies: Ensuring Dynamical Stability of Action

Bernstein[3] emphasized two main functions of the "Level of Synergies" in his multi-level hierarchical system for the control of movements. First, this level was responsible for uniting numerous elements (e.g., muscles) into groups thus alleviating the problem of motor redundancy (reducing the number of degrees-of-freedom) and facilitating control. Second, this level was responsible for ensuring dynamical stability of movements, which is crucial given the unpredictably varying external forces and intrinsic body states.

The first feature of synergies has received much attention recently with various matrix factorization techniques used to identify stable groups of elements, including principal component analysis, factor analysis, non-negative matrix factorization, etc.[27,28]. Bernstein thought of synergies organized in multi-muscle spaces, and this insight has been developed in future studies[29-31]. This idea has also been applied to both multi-muscle systems, such as those involved in moving individual joints[32] and intra-muscle systems such as muscle compartments viewed as constellations of motor units as elements[33]. We would like to emphasize that the idea of grouping elements is far from trivial. Indeed, imagine that a person co-contracts muscles acting at the major joints of a limb. This can be viewed as the means of reducing the number of effective kinematic degrees-of-freedom. But obviously this strategy would increase muscle activation levels and the number of recruited motor units thus making the problem worse at those levels of analysis.

The other feature of synergies is of obvious importance for everyday movements. For example, while walking, we commonly step on small pebbles or other uneven parts of the road. Given the inherently unstable bipedal pos-

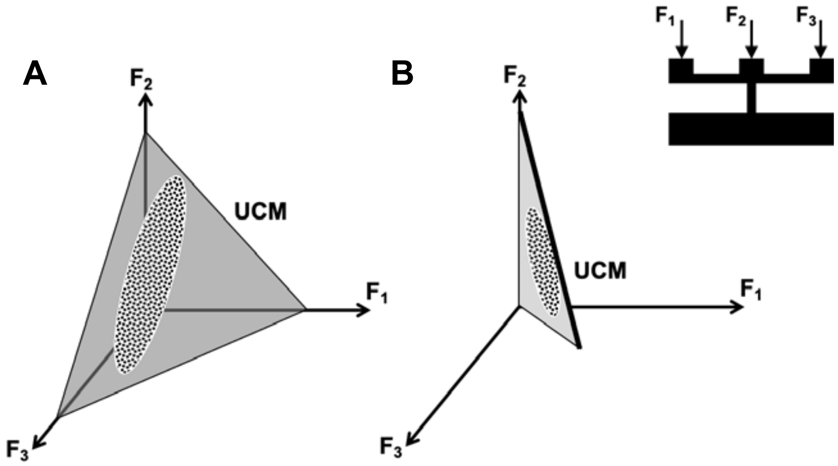

Fig. 4

An illustration of a three-finger task pressing on a rigid surface (the insert). A: The solution space (uncontrolled manifold, UCM, gray) for accurate force production. Data points across repetitive trials are expected to be constrained primarily to the UCM. B: If the task is to produce a certain magnitude of the total moment of force with respect to the pivot, the UCM changes. Both tasks can be accomplished simultaneously: the UCM becomes one-dimensional (the thick line in panel B).

ture, the importance of dynamical stability of walking patterns is obvious. This is also true for other everyday tasks. Bernstein assumed that, in the processes of both evolution and personal experience, the central nervous system elaborates dynamically stable patterns of movements, which do not require continuous corrections by the brain. Note also that, depending on the task, humans stabilize different performance variables, even when those are produced by the same sets of effectors. For example, the human hand can stabilize the resultant force and/or moment of force on the hand-held object. The concept of task-specific stability has formed the foundation of the UCM hypothesis[12,34)].

According to the UCM hypothesis, the controller acts in a multi-dimensional space of elemental variables and stabilizes a salient performance variables to which all the elemental variables contribute. Consider tasks performed by three effectors (e.g., fingers) pressing in parallel on a rigid surface (the insert in Fig. 4). If the task is to produce a certain magnitude of total force, the solution space is shown in panel A of Figure 4. One can expect data points across repetitive trials to be constrained primarily to the solution space (the UCM) for this task shown as the gray triangle. If the same system is required to produce a certain magnitude of the total moment of force with respect to a pivot (e.g., located under effector E2), the solutions space changes, and the inter-trial data distribution is expected to be constrained to another planar UCM shown in panel B of Figure 4. Note that both tasks can be accomplished simultaneously. Then, the UCM becomes one-dimensional: It is a line formed by the intersection of the two planes (the thick line in panel B).

The illustration in Figure 4 suggests that inter-trial variance can be analyzed to produce an index of stability. Indeed, stabilization of a salient variable implies higher variance within the corresponding UCM as compared to the orthogonal to the UCM space (ORT). If both indices are quantified per dimension in the corresponding spaces, $V_{UCM} > V_{ORT}$ is expected. One can use an index reflecting the normalized difference between V_{UCM} and V_{ORT} and use it as an index of a synergy stabilizing the selected performance variable: $\Delta V = (V_{UCM} - V_{ORT})/V_{TOT}$, where V_{TOT} stands for total variance.

Let us emphasize a few important features of the UCM concept. First, low variability of performance does not necessarily imply a strong synergy stabilizing this performance. Performance may be stereotypical (very low V_{TOT}) without a difference between V_{UCM} and V_{ORT} or even with $V_{UCM} < V_{ORT}$. Such behavior may be accurate in perfectly predictable conditions in the absence of unexpected perturbations, but it is expected to show major deterioration as soon as conditions become more natural and less predictable. Second, while performance accuracy, by definition depends only on V_{ORT} but not on V_{UCM}, large V_{UCM} is important: It reflects channeling effects of unexpected perturbations into the UCM where deviations of elemental variables do not affect the salient performance variable. For example, when you walk down the hallway with a cup of coffee in the hand, you would like the cup to be close to vertical at all times. The cup orientation depends on many factors including all the joint angles. Note that every step is associated with large varying forces between the foot and the floor, which are transmitted to all body parts and perturb all the joints. We can also move the cup with respect to the body while walking without spilling its contents. This is achieved by organizing the relevant joints into a multi-joint synergy stabilizing the cup vertical orientation. The synergy is associated with low stability along the UCM, which accepts all the joint angle deviations and protects the cup from excessive tilting.

When a person plans to perform a movement associated with a quick change of a performance variable, having a strong synergy stabilizing that variable may be counterproductive: The actor will have to overcome the resistance to a change in the variable by the synergy. In other words, stability and agility compete with each other. The brain has an ability to attenuate synergies in preparation to quick actions. These anticipatory synergy adjustments (ASAs) have two components. The first is observed when a person knows that a quick action may be required, e.g. to a signal or to a perturbation, but no signal and no perturbation emerge. In such conditions, the synergy index is reduced as compared to a similar task performed in conditions when no quick action can happen[35-37]. The other component of ASAs is linked to planning a self-paced quick action; it is associated with a drop in the synergy index 300-400 ms prior to then action initiation[38,39] While the synergy index, ΔV, can be used as an index of stability, ASA characteristics (their timing and magnitude) can be used as an index of agility[40].

The UCM-based method of analysis of stability has been used to quantify synergies in various spaces of elemental variables, kinetic, kinematic, and electromyographic[13,16]. Recently, the method of analyzing synergies has been developed to spaces of hypothetical control variables, such as the *R*-command and *C*-command introduced earlier[41,42]. The first studies on multi-finger force production tasks have documented strong performance-stabilizing synergies in the $\{R; C\}$ space, but expanding this method to other tasks has been challenging. This approach has also not been able to quantify ASAs, which slows down its possible application to clinical studies. There has also been progress in applying this method to analysis of synergies in spaces of individual motor units[33], but this approach is in its infancy.

Indices of both stability and agility are sensitive to mild impairments of movements. For example, healthy aging is associated with a drop in both ΔV and ASA indices[43,44]. Changes in synergy index have been reported under fatigue in healthy persons[45] and in healthy welders[46] who are at high risk for developing movement disorders resembling parkinsonism due to the accumulation of manganese in the basal ganglia. Synergies can be improved with practice[47], which carries an optimistic message to the field of motor rehabilitation.

Impaired Control of Stability in Neurological Patients

Problems with controlled movement stability are highly prevalent across the spectrum of neurological disorders. They can be classified into two groups. The first is impairment of dynamical stability leading to disruptions of functional movement patterns by variations in the external forces and intrinsic body states. Loss of postural stability in Parkinson's disease (PD) and ataxia in cerebellar disorders may be seen as most obvious examples. The second is impairment in the ability to initiate a movement or to switch from an unsuccessful movement pattern to an alternative one. Freezing in PD may be viewed as an example of this group. In other words, impaired control of stability may involve impaired stability and impaired agility as its components. These can be studied quantitatively using indices of synergies (ΔV) and of ASAs, respectively.

Both impaired stability and impaired agility have been documented in PD patients[40]. Both signs can be observed in early-stage PD and even in sub-clinical cases. Indeed, similar changes in both indices have been reported during studies of multi-finger synergies in both hands of PD patients at stage-I (Hoehn and Yahr 1967), which is defined as the stage with PD symptoms limited to one side of the body only[48]. Along similar lines, impaired synergies and ASAs in whole-body standing tasks have been reported for stage-II PD patients[49], i.e., when clinical examination fails to detect signs of postural instability. Recent studies of drug-naïve PD patients have confirmed that problems with synergic control are consequences of the disease itself, not of long-term drug exposure[50]. Note that the reduced ASA may be viewed as a predictor of episodes of freezing. Indeed, if one cannot destabilize vertical posture during standing, one's feet may feel as if glued to the grounds.

Indices of both stability and agility are sensitive to dopamine-replacement drugs[51,52]. In contrast, a study of the effects of deep-brain stimulation (DBS) applied to the globus pallidus and to the subthalamic nucleus has confirmed an improvement in indices of agility but not of stability[53]. These observations suggest caution with the DBS because it can lead to more agile movements in a person with poor stability resulting in undesired effects on fall incidence[54].

PD is not the only disorder showing problems with the two aspects of the synergic control. In particular, similar results have been reported in patients with multi-system brain atrophy[55] and with multiple sclerosis[56]. In contrast, observations in stroke survivors are less consistent. These patients have been reported to show minimal, if any, differences in indices of stability (such as ΔV), but significantly reduced ASA indices[57,58]. Taken together, studies of patients point at subcortical loops as potentially crucial elements of both aspects of the synergic control, ensuring proper stability of actions and being able to attenuate stability prior to a planned quick action.

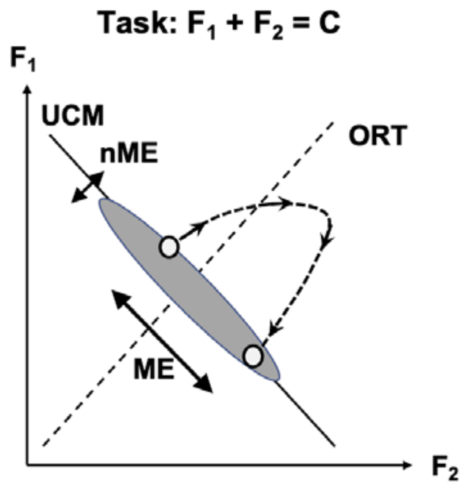

Fig. 5

The task is to produce accurate total force by pressing with two fingers. Larger inter-trial variance along the UCM is expected as compared to that along the orthogonal direction (ORT). If the subject is asked to increase the force quickly and then return to the initial force magnitude, at the end of actions deviations within-the-UCM (motor equivalent, *ME*) will be larger than along ORT (non-motor equivalent, *nME*).

Challenges of Clinical Studies

The reviewed studies suggest that exploring synergic control may be of high clinical importance, in particular for making clinical decisions related to drug therapy, tracking disease progression, and estimating effectiveness of rehabilitation. Quantifying aspects of the synergic control has been truly eye-opening. Broad application of these methods to clinical studies has been slow due to both the conceptual and technical difficulties associated with quantitative studies of action stability and to the necessity to collect multiple trials to compute indices of stability and agility. The former problem can only be solved by education of clinical researchers, in particular by writing reviews targeting clinical professionals, such as this one.

The problem of collecting multiple trials is more challenging. Indeed, patients are less likely to be able to perform a motor task multiple times "in the same way". They typically fatigue faster that healthy persons, and there is limited time they can spend being tested. Indices of synergic control typically show good-to-excellent indices of reliability[59], which is a positive sign. On the other hand, to estimate such indices as V_{UCM} and V_{ORT} (and indices computed based on those, such as ΔV and ASA indices), one has to collect a cloud of data points. But how many data points form a "cloud"? This question has been explored recently[60,61], and the conclusion is that the minimal number of data points ranges between 12 and 24.

There have been several attempts to overcome the problem of collecting multiple trials in clinical studies. One of such attempts has been based on the phenomenon of motor-equivalent movement, i. e. movement within the UCM[62,63]. For example, if a person performs a task of accurate total force production by pressing with two fingers (Fig. 5), larger inter-trial variance along the UCM is expected reflected in the cloud of data points elongated along the UCM. If this person is now asked to increase the force quickly and then return to the initial force magnitude, at the end of this action, deviations both within-the-UCM (motor equivalent, *ME* in Fig. 5) and within-the-ORT (non-motor equivalent, *nME*) are expected. Larger deviations along the UCM are expected, *ME* > *nME* (similar to $V_{UCM} > V_{ORT}$). Note that *ME* and *nME* can be measured in individual trials. Estimation of the number of trials needed to obtain reliable estimate of *ME* and *nME* indices has suggested that these indices require half as many trials as needed for reliable estimate of V_{UCM} and V_{ORT}[59]. This is a promising result, but *ME* and *nME* cannot be used to estimate ASAs, which limits their usefulness for clinical studies.

There have also been attempts to improve the situation by using cyclical tasks that allow collecting multiple cycles within a relatively short time[33,64]. This method, unfortunately, is also unable to quantify ASAs. Combining within-a-trial and across-trials analyses has also been used[65], but this method has not been developed for clinical studies. A potentially important development has been suggested recently based on bootstrapping techniques that allow overcoming the problem of having relatively few trials and can potentially be used to analyze performance of individual patients[61].

Implications for Synergic Control in Osteoarthritis

While most reviewed studies have focused on impaired synergic control in neurological patients, few studies pay attention to that in peripheral disorders such as osteoarthritis (OA). OA is the most common form of arthritis, causing chronic pain and motor impairment[66]. Earlier studies have shown that OA patients display a reduction in the gray matter in areas related to the transmission of pain, including prefrontal cortex, precentral, and postcentral cortices[67-69]. Plasticity in the brain has also been observed following the improvements of both pain and the motor function[67,70,71]. Given plastic brain changes following chronic pain and motor impairment[67,70,71], important changes in the synergic control in OA patients can be expected.

The treatments for OA patients have been focused on relieving pain and preventing undesired mechanical stress in the affected joints, which can cause OA progression[72,73]. Resistance training, mainly for quadriceps muscle strengthening, has been viewed as an effective intervention for improving pain and physical function in patients with knee OA[74,75], and is also recommended as a core treatment in the

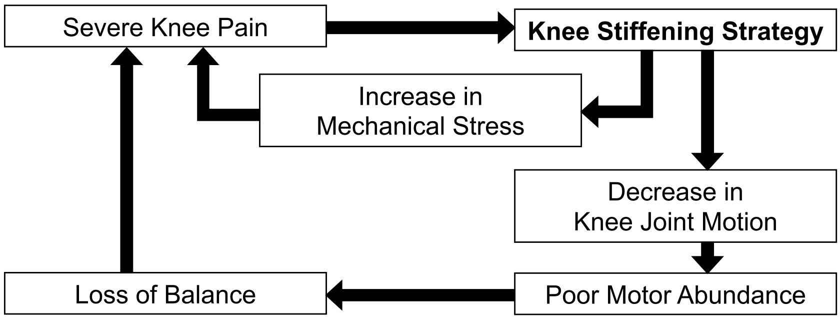

Fig. 6

An illustration of a "vicious circle" due to knee symptom. Knee pain will cause the knee stiffening strategy resulting in the increased mechanical stress at the joint and stronger knee pain. Additionally, the knee stiffening strategy is associated with poor motor abundance, leading to the possibility of the loss of balance (also contributing to knee pain) and, potentially, other comorbidities.

clinical guidelines[76]. Gait modifications (e.g., the lateral trunk lean walking) have also been used to avoid the pain and undesired mechanical stress[77-80].

In addition to the pain and undesired mechanical joint stress, impaired gait stability is also a problem for OA patients. OA is viewed as an important risk factor for falls[81,82], and an earlier study has reported the greater risk of falls in patients with knee OA, compared to healthy older adults[83]. Given that impaired multi-segmental synergy stabilizing the center of mass (CoM) trajectory during gait has been associated with elevated fall risk[84], analysis of the synergic control related to gait stability could be useful for guiding treatment of OA patients. So far, however, few studies have evaluated possible changes in the synergic control in OA.

One study explored the synergic control in patients with knee OA during gait[85]. These authors evaluated the kinematic synergies controlling CoM trajectory during lateral trunk lean walking, a common gait modification to reduce undesired mechanical stress at the knee[85]. During walking, real-time visual feedback on the angle of lateral trunk lean was provided, and the patients were instructed to lean the trunk by a certain angle during the stance phase. The lateral trunk lean walking allowed the patients to reduce the undesired knee loading while maintaining the CoM-stabilizing synergy, similar to that during normal walking. These results suggest that the lateral trunk lean walking could be a reasonable treatment strategy for both gait stability and desired knee loading. However, future studies are needed to address such issues as changes in the CoM-stabilizing synergy with OA progression and with long-term treatment, including gait modification.

Gait pattern in patients with knee OA include, in particular, a large reduction in the knee flexion excursion[86,87]. Such stereotypical motor patterns have been viewed as a compensatory strategy to avoid knee pain and reduce the knee joint motion[88,89]. However, excessive muscle forces required to "stiffen" the knee are expected to increase the mechanical stress at the joint[90,91] leading to a possibility of OA progression and/or increased pain severity. Given the recent results suggesting that muscle co-activation compromises postural stability in young healthy adults[92], the "knee stiffening" strategy should probably be discouraged as it might lead to increased incidence of loss of balance and falls.

Note also that an earlier study has explored the effects of joint immobilization, including knee immobilization, on the posture-stabilizing synergy during standing and showed impaired synergic control of posture, especially for tasks with increased complexity[93]. Given that walking may be viewed as a more complex task compared to standing, the "knee stiffening" strategy in patients with knee OA may lead to undesired consequences through the poor use of the kinematic abundance, resulting in elevated fall risk and other pain comorbidities.

To prevent such a "vicious circle" (shown in Fig. 6 as a potential combination of two circles), we have to consider all the salient variables during gait in patients with knee OA. In healthy adults, trajectories of the CoM and swing foot have been viewed as salient performance variables for successful gait[84,94]. In OA patients who typically show proprioceptive deficits and joint laxity[95,96], additional salient performance variables related to the affected joint may need to be stabilized during gait. It is possible that studies of gait in healthy subjects with additional constraints, e.g., reduced knee joint excursion, could provide useful information on possible adaptive gait strategies able to ensure stability of all the salient variables. Such studies would avoid the mentioned "vicious circle", because healthy persons would not experience pain and potentially could explore a broader range of muscle activation patterns. Such studies could provide important insights into treatment strategies of OA directed at optimizing stability of functionally important behaviors such as walking.

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PHYSICAL
THERAPY
RESEARCH

SCIENTIFIC RESEARCH ARTICLE

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

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ABSTRACT. Objective: It is important for hemodialysis patients to exercise while their nutritional status is being monitored. This study aimed to examine the difference in physical exercise function and the effect of exercise intervention in hemodialysis patients who were divided into two groups (high-nutrition and low-nutrition groups) based on the serum albumin levels.
Method: A total of 26 outpatients (18 men and 8 women) undergoing hemodialysis (age: 66 ± 10 years) were included in this study. The patients' body composition data (weight, body mass index, percentage of body fat, fat-free mass, and total body water) and physical functions (grip strength, knee extensor strength, open-eyed one-legged standing time, long sitting trunk anteflexion, and 6-minute walking distance [6MWD] test) were measured. The intervention was supine ergometer exercise during hemodialysis, and the patients exercised for 30 minutes during hemodialysis thrice a week. The intervention period was three months.
Results: Compared to the high-nutrition group, the low-nutrition group showed a significant decrease in muscle strength. Furthermore, long sitting trunk anteflexion in the high-nutrition group and 6MWD in the low-nutrition group improved significantly after the intervention.
Conclusion: The result of this study may indicate that 6MD can be improved by exercise during dialysis, regardless of nutritional status. It is said that low nutritional status has a negative impact on survival rate; thus, considering the impact on survival rate, it is hemodialysis patients with a low nutritional status that should be considered to introduce more active exercise during dialysis.
Key words: Intradialytic exercise, Renal rehabilitation, Serum albumin, Muscle strength, 6-minute walking distance

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Since the 1990s, the number of dialysis patients in Japan has been increasing in tandem with the number of patients with diabetes. According to a report by the Japanese Society for Dialysis Therapy, there were more dialysis patients aged ≥65 years than those aged ≤64 in 2017[1)]. In older patients undergoing hemodialysis, there is a decline in physical function or increased mortality due to sarcopenia and cachexia[2,3)]. The high mortality rate and decreased physical function in dialysis patients can be improved by a variety of exercise programs[4)]. Therefore, exercise intervention is important, and it needs to be supported by appropriate nutritional support. Further, serum albumin level, which is an indicator of nutritional status, is negatively affected by inflammation, and the effect is said to be greater in long-term dialysis patients[5)]; hence, it is a valuable indicator in hemodialysis patients. Various studies have reported hypoalbuminemia to be a strong predictor of mortality in dialysis patients[6,7)]. Therefore, it is important to maintain a high serum albumin level in hemodialysis patients. In a study of hemodialysis patients by Johansen et al., frailty scores decreased as serum albumin levels increased, and patients whose serum albumin levels increased over time were less likely to

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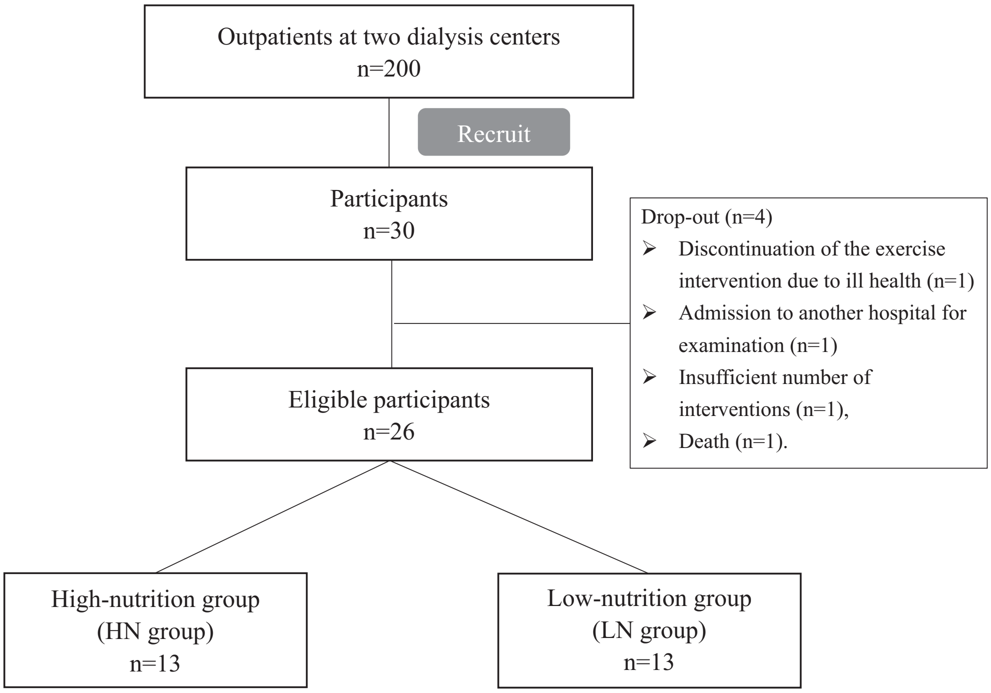

Fig. 1. Participants' tree
The figure shows the process of recruitment, selection, dropout, and grouping of participants.

become frailty[8]. Serum albumin levels have a positive impact on frailty scores; thus, further verification of the association between albumin levels and exercise is needed. A systematic review examining the combined effects of exercise and nutrition in healthy older adults found that exercise had a positive effect on muscle strength and muscle mass in many studies and that nutrition had a positive effect in some studies[9]. A meta-analysis examining the effects of oral nutritional supplements on muscle fitness of dialysis patients reported that supply of a mixture of macronutrients and an intervention duration of 48 weeks had some effects on increasing lean body mass[10].

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

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

Method

Study design and participants

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

Physical therapy assessment

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

Exercise Intervention

The method of exercise and discontinuation criteria were prototyped in accordance with the American College of Sports Medicine exercise guidelines[12] and renal rehabilitation guidelines[11]. The exercise intervention consisted of a supine ergometer exercise during dialysis for 12 weeks. The exercise equipment used was an electric cycle machine Escargot PBE-100 (Meisei Co., Ltd., Tokyo, Japan). The physical therapists set up the equipment and checked the physical condition of the patients each time. The exercise was performed for 30 minutes during the first half of dialysis. The participants were instructed to row to a metronome at 120 beats per minute for the rotation speed, and a drive of 60 rotations per minute was used as the standard. Participants rowed 1800 revolutions/30 minutes based on 60 rotations/minute for 30 minutes and recorded the actual number of rotations they were able to drive on that day after exercise of each day. During the exercise, patients were allowed to train independently. Blood pressure and pulse rate were measured before and after each exercise intervention using a dialysis machine. The number of interventions and the number of rotations on the ergometer were also recorded during the intervention period. After the exercise, the rating of perceived exertion (RPE) during exercise was measured using the Borg Scale[13].

Statistical analysis

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

Results

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

The physical functions of the HN and LN groups are shown in Table 3. A two-way analysis of variance showed

Table 1. Characteristics of participants

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

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

Table 2. Exercise intervention data

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

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

Table 3. Results of physical functions

	HN group		LN group	
	pre-intervention	post-intervention	pre-intervention	post-intervention
Grip strength (kg)	31.38 ± 8.75	31.25 ± 10.25	22.92 ± 9.95$^+$	22.58 ± 9.37$^+$
Knee extensor strength (kg)	27.99 ± 13.63	30.44 ± 17.22	17.11 ± 7.90$^+$	18.91 ± 6.67$^+$
One leg standing time (s)	33.85 ± 24.93	38.27 ± 25.37	26.42 ± 22.74	24.96 ± 22.30
Long sitting trunk anteflexion (cm)	31.65 ± 9.82	34.96 ± 10.54*	28.50 ± 17.39	29.65 ± 14.86
6MD (m)	459.85 ± 146.37	494.69 ± 126.08	374.69 ± 127.01	406.85 ± 124.64*

Compared between pre and post intervention: *p<0.05, Compared between HN group and LN group: $^+$p<0.05
HN group: High nutrition group; LN group: Low nutrition group; 6MD: 6-minute walking distance test

no interaction between pre- and post-intervention and nutritional status, and grip strength, KES, and 6MD were found to have significant differences between HN and LN groups. Since the results of the Shapiro-Wilk test assumed that there was no normal distribution for open-eyed one-legged standing time before and after the intervention and the KES after the intervention, a non-parametric test was used for these analyses. Grip strength and KES were significantly higher in the HN group than in the LN group both before and after the intervention ($p<0.05$). In comparison before and after the intervention, long sitting trunk anteflexion improved significantly after the intervention in the HN group ($p<0.05$), and the 6MD improved significantly after the intervention in the LN group ($p<0.05$).

Discussion

The results of this study revealed that grip strength and KES were significantly lower in patients with low nutritional status than in those with high nutritional status. A previous study examining the effects of exercise on the nutritional status and body composition of hemodialysis patients reported that physical activity could have a beneficial impact on the nutritional status of hemodialysis patients and help prevent sarcopenia[14]. Although this study only investigated albumin levels before the intervention, it was found that dialysis patients with originally high albumin levels maintained high muscle strength after the intervention. This study may have a positive effect on sarcopenia in terms of muscle strength.

As for the exercise intervention, the number of driving rotations for the supine ergometer during 30 minutes of intradialytic exercise was approximately 1600 in the HN group and approximately 1400 in the LN group. Souweine et al. discovered a relationship between physical activity, serum albumin levels, and quadriceps muscle weakness[15]. Therefore, this difference in the number of driving rotations may be attributed to the difference in original muscle strength, which had a significant effect on the driving force. Silva et al. reported that biarticular muscles such as quadriceps and biceps femoris have a significant influence on lower limb movements during cycling[16]. It is suggested that the difference in the strength of the quadriceps muscle, which is a knee extensor, had a significant effect on this driving force. In the future, maintaining a high nutritional status and training the quadriceps and other biarticular muscles of the lower extremities may lead to more effective supine ergometer exercise during dialysis.

In the comparison before and after the intervention, long sitting trunk anteflexion in the HN group improved significantly after the intervention. Reportedly, ergometer exercises during dialysis improved flexibility which is similar to the present study[17]. Studies that looked at the effects of cycling on spastic muscles such as cerebral palsy and spinal cord injury showed a decrease in muscle tone[18,19]. In the present study, it is possible that the bicycle ergometer exercise reduced muscle tone in the lower limb muscles. In particular, the improvement was observed in the HN group, suggesting that the nutritional status and the amount of exercise may affect the improvement. Furthermore, 6MD in the LN group improved significantly after the intervention. Long-term nutritional supplementation has been reported to increase skeletal muscle anabolic effects, thigh fat cross-sectional area, and skeletal muscle mitochondrial content[20]. Therefore, we hypothesized that a more effective exercise effect would be obtained in the HN group. However, 6MD significantly improved even in patients with low nutritional status. This may indicate that 6MD can be improved by exercise during dialysis, regardless of nutritional status. It has been reported that 6MD is related to the survival rate of hemodialysis patients and that every 100 m of walking is associated with approximately 5.3% of life expectancy[21]. It is said that low nutritional status has a negative impact on survival rate; thus, considering the impact on survival rate, it is hemodialysis patients with a low nutritional status that should be considered to introduce more active exercise during dialysis.

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

Conclusion

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

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PHYSICAL THERAPY RESEARCH

SCIENTIFIC RESEARCH ARTICLE

The Feasibility of a Newly Developed Local Network System for Cardiac Rehabilitation (the CR-GNet) in Disease Management and Physical Fitness after Acute Coronary Syndrome

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ABSTRACT. Objective: To examine the Cardiac Rehabilitation Gifu Network (CR-GNet) feasibility in managing diseases and assisting patients in attaining physical fitness, and its impact on long-term outcomes after acute coronary syndrome (ACS). Methods: In this prospective observational study, we enrolled 47 patients with ACS registered in the CR-GNet between February 2016 and September 2019. 37, 29, and 21 patients underwent follow-up assessments for exercise capacity (peak oxygen uptake) at 3 months, 6 months, and 1 year after discharge, respectively. Major adverse cardiac events (MACE) were compared with controls not registered in the CR-GNet. Results: The coronary risk factors, except blood pressure, improved at 3 and 6 months, and 1 year after discharge. These risk factors in each patient significantly reduced from 2.9 at admission to 1.6, 1.4, and 1.9 at 3 months, 6 months, and 1 year after discharge ($p<0.05$), respectively. Peak oxygen uptake was significantly higher at 3 months (17.5±4.9 ml/kg/min), 6 months (17.9±5.1 ml/kg/min), and 1 year (17.5±5.5 ml/kg/min) after discharge than that at discharge (14.7±3.6 ml/kg/min) ($p<0.05$). During follow-up, there was no significant difference; MACE did not occur in any patients in the CR-GNet but occurred in controls. Conclusion: CR-GNet is a feasible option for the long-term management of ACS patients.

Key words: Cardiac rehabilitation, Disease management, Physical fitness, Motivational enhancement, Acute coronary syndrome

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Recurrent major adverse cardiovascular events (MACEs) such as atherothrombotic events occur in a substantial proportion of patients after acute coronary syndrome (ACS)[1,2]. In Japan, the incidence of MACEs from 31 days to 3 years after ST-elevation myocardial infarction was 19.8%, indicating that one out of five patients experienced recurrence within 3 years[2]. Therefore, over the past few decades, many researchers have shown an interest in the effects of cardiac rehabilitation (CR). Several studies have proven that CR is superior to vital medications and has advantages over percutaneous coronary intervention (PCI) in terms of mortality[3,4]. However, the participation rate in CR, especially for

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outpatients, is estimated to be low in most hospitals in Japan despite the well-established benefits of CR[5-7].

In Gifu Prefecture, a region in central Japan, medical facilities implemented the Cardiac Rehabilitation Gifu Network (CR-GNet) in 2016 to create a regional alliance network of CR. CR-GNet provides seamless support for patients with cardiovascular disease by rendering medical facilities in core hospitals, such as university hospitals, district general hospitals, cardiovascular hospitals, or primary care clinics, and fitness clubs. The CR-GNet system is equipped with a high-quality patient education system, an interactive information-sharing nexus between medical facilities, a periodic follow-up system including medical and physical examinations, and education using standardized disease management material and an alliance notebook. This is a new method for supporting patients with cardiovascular diseases and is the first such attempt in Japan.

This study aimed to examine the feasibility of CR-GNet for managing disease and physical fitness in patients after ACS. We hypothesized that CR-GNet would aid in improving coronary risk factors and physical fitness and would be feasible for long-term prognosis.

Methods

Patients and study design

In this prospective observational study, we analyzed the data of consecutive ACS patients who were admitted to Gifu University Hospital and enrolled in CR-GNet between February 2016 and September 2019. At the Gifu University Hospital, all patients admitted for ACS underwent cardiac rehabilitation. Patients are encouraged to participate in CR-GNet and transfer to outpatient maintenance cardiac rehabilitation when discharged from the hospital. We excluded patients with poor physical fitness due to advanced age or physical deconditioning from the CR-GNet group, in addition to those who were followed up at another facility. Patients who completed the 1-year follow-up examination were assigned to the CR-GNet group. Patients without poor physical fitness but ineligible for enrollment in CR-GNet due to difficulty of access, unavailability of the regional alliance, or other reasons were classified as the control group. They were pursued for more than 1 year to confirm their outcome.

Management system for CR-GNet

Patients who could undergo symptom-limited exercise tests and had no cognitive impairment were registered in CR-GNet. After they were enrolled, disease management material and an alliance notebook, consisting of healthcare knowledge from healthcare professionals such as physicians, physical therapists, nurses, registered dietitians, and pharmacists, were provided to each patient. During disease management education, the psychobehavioral approach was used to address readiness and enhance motivation for behavioral changes towards a favorable lifestyle. The information obtained during the education sessions was shared with the entire healthcare team and used to improve the efficacy of patient education. The patients set specific goals for disease management and recorded them in an alliance notebook at discharge. Patients were referred to primary care doctors from Gifu University Hospital at discharge and received prescription medicines after discharge by these doctors. Medicine dose and management was at the discretion of the primary care doctors. Follow-up assessments were scheduled at Gifu University Hospital 3 months, 6 months, and 1 year after discharge and annually thereafter. Physical and blood examinations, transthoracic echocardiography, and disease management education, including nutritional guidance, checking goal status, and setting new goals, were conducted during the follow-up assessments. The goals and status of disease management and clinical data, such as exercise prescriptions, were shared with the primary care doctors.

The physical therapists' role was mainly to provide behavioral psychology-based disease management and exercise guidance, provide assistance in goal setting and resetting, ensure information sharing with other professionals, and conduct periodic assessment of physical functions during hospitalization and follow-up examinations.

Clinical data

The following data were collected at discharge: patient characteristics, coronary risk factors, alcohol consumption, blood examination results, and physical function test results such as peak oxygen uptake (peak VO_2) measured by cardiopulmonary exercise testing (CPX), grip strength, and knee extension strength. The following risk factors were assessed as items related to coronary risk factor status: hypertension, diabetes, serum lipid levels, body mass index (BMI), smoking status, and physical activity.

Blood pressure was measured at rest on the day of CPX. Patients with diabetes or chronic kidney disease were considered hypertensive if this measurement was >130/80 mmHg, whereas a threshold of >140/90 mmHg was used for other patients, according to the 2014 Japanese Guidelines for the Management of Hypertension[8]. Dyslipidemia was defined as low-density lipoprotein cholesterol (LDL-C) level >100 mg/dL, high-density lipoprotein cholesterol (HDL-C) level <40 mg/dL, or triglyceride (TG) level <150 mg/dL, which are the target levels of cholesterol management. Diabetes was assessed using the hemoglobin A1c (HbA1c) level. An HbA1c level <7% was considered a favorable status for diabetes management[9]. BMI was calculated from the height and weight measured on the day of CPX. Patients were classified as overweight if their BMI was ≥25 kg/m^2. Smoking status was assessed by asking the patients whether they had smoked before and/or after discharge, including the number of cigarettes smoked per day. Patients were considered non-smokers if they had never smoked or if they had stopped smoking completely for at least 1 month before completing the survey[10]. Physical activity was determined using the Japanese version of the International Physical Activity Questionnaire, which is widely used in the Japanese population[11]. Patients were classified as active if they engaged in ≥150 min of moderate and/or vigorous activity per week. Patients whose ethanol consumption was <30 mL/day or less than one drink per day were considered to have a favorable status of alcohol consumption.

Blood investigation data at admission were used as parameters for CPX. At the 3-month, 6-month and 1-year follow-ups after discharge, coronary risk factors, alcohol consumption, blood test results, and physical function parameters were re-assessed.

Exercise test

Symptom-limited exercise testing was performed using an ergometer (BE250; Fukuda Denshi Co., Tokyo, Japan) to measure peak VO_2. The patients rested for 3 min on an ergometer. The exercise began with a 3-minute warm-up at a work rate of 10 W, followed by a ramped increase of 10 W/min. During the exercise test, the subjects were coached to maintain a constant pedaling speed of 60 rpm until a symptom-limited endpoint was attained[12]. A 12-lead electrocardiogram (ML-9000; Fukuda Denshi Co., Tokyo, Japan) was used for continuous monitoring, and blood pressure was measured every minute using an automatic blood pressure monitor (FB-300; Fukuda Denshi Co., Tokyo, Japan). Throughout the test, expired gas was sampled using a breath-by-breath method with a gas analyzer (ML-9000; Minato Ikagaku Co., Tokyo, Japan).

Outcomes

MACEs were defined as the composite of death owing to cardiac causes, cardiac arrest, myocardial infarction, and rehospitalization due to unstable or progressive angina.

Statistical analysis

Assuming the incidence of adverse events to be very low in the CR-GNet group and 19.8-33.6% in the control group based on previous studies[2], 17-52 cases in both groups were needed to obtain a significant difference in the incidence; this was the basis for determining the sample size for this study.

To compare the clinical and demographic characteristics between the two groups, unpaired t-tests were used to compare continuous variables. If the variables were not normally distributed, the Mann-Whitney U test was used. Non-continuous and categorical variables were compared using the chi-squared test. With regard to the comparison of MACEs between the CR-GNet group and the control group, time-to-event curves were constructed using the Kaplan-Meier method and compared using the log-rank test.

Peak VO_2 and knee extension strength were calculated based on body weight. Data relating to coronary risk factor status, alcohol consumption, and physical function between different time points (i.e., at admission or at discharge and at 3 months, 6 months and 1 year after discharge) were compared using the Friedman test in all patients who completed the 1-year follow-up examination in the CR-GNet group.

All analyses were performed using EZR on R commander (version 1.35)[13]. Comparisons were considered statistically significant at $p<0.05$.

Ethical considerations

Written informed consent was obtained from all patients included in this study. The study was approved by the ethics committee of the Gifu University Graduate School of Medicine (Permission number: 27-417) and registered in the UMIN Clinical Trials Registry (UMIN ID: UMIN 000021908).

Results

Clinical and demographic characteristics of the patients

The number of patients enrolled in CR-GNet during the study period was 47; of these, two patients underwent follow-up examinations at another facility (Fig. 1). During the study period, 37, 29, and 21 patients completed the follow-up assessments at 3 months, 6 months, and 1 year after discharge, respectively. The completion rates, calculated as (the number of patients who completed the follow-up examinations divided by the number of patients who were expected to participate in the follow-up examinations) multiplied by 100, were 82.2% (37/45), 78.4% (29/37), and 72.4% (21/29), respectively. Table 1 shows the clinical and demographic characteristics of the patients, including the coronary risk factors at admission. There were no significant differences in clinical demographics between the CR-GNet and control groups.

Coronary risk factor status and alcohol consumption

Table 2 shows the proportion of patients in the CR-GNet group who achieved optimal control for each coronary risk factor and alcohol consumption target. The proportion of patients who achieved control of all coronary risk factors and alcohol consumption, except blood pressure, improved at 3 months, 6 months, and 1 year after discharge compared with that at admission. Additionally, the average number of coronary risk factors per patient significantly decreased to 1.6 ($p=0.004$) at 3 months and 1.4 ($p=0.001$) at 6 months compared to 2.9 at admission. Conversely, the number at 1 year significantly increased to 1.9

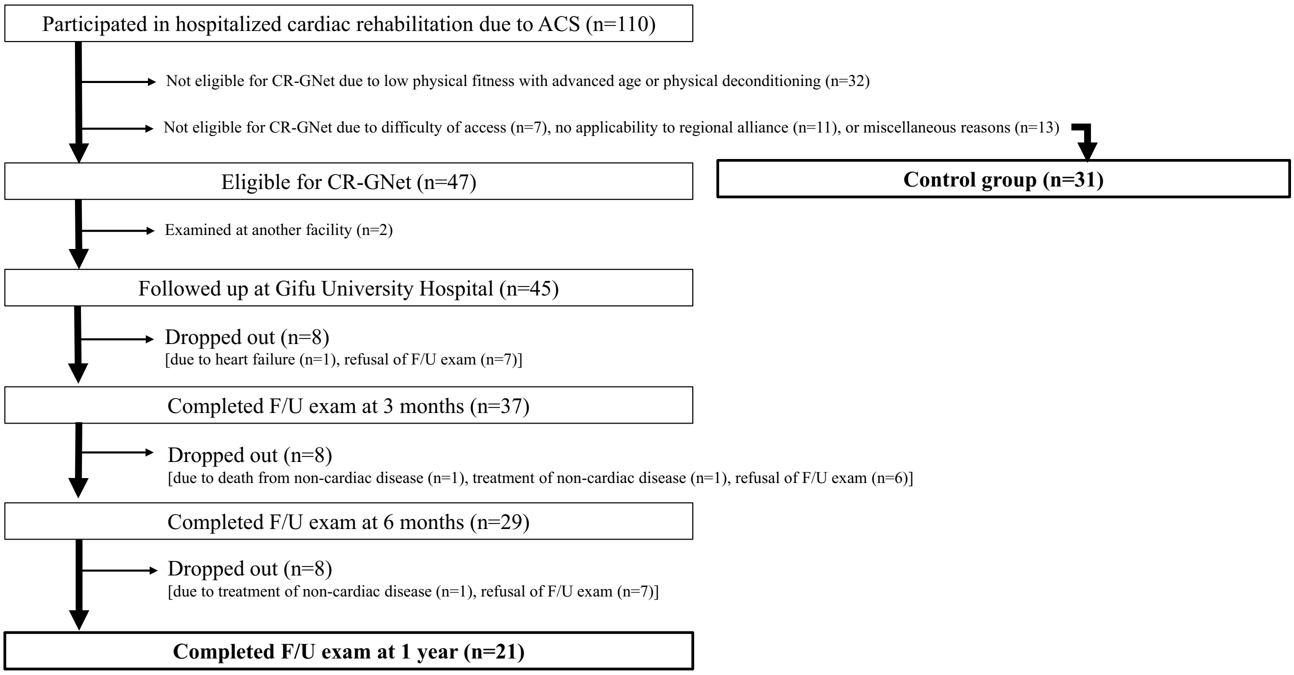


Fig. 1. Flowchart of patients throughout the study.
ACS, acute coronary syndrome; F/U, follow-up; MACE, major adverse cardiovascular events; exam, examination.

($p=0.035$) compared with that at 6 months, though it remained significantly lower than that at admission ($p=0.011$).

Physical function

The number of patients whose respiratory exchange ratio, indicating whether there was a maximum volitional effort during CPX, reached >1.1 were 17 (80.1%) at discharge, 18 (85.7%) at 3 months, 18 (85.7%) at 6 months, and 16 (76.2%) at 1 year in the CR-GNet group. Figure 2 shows temporal changes in exercise tolerance. In the CR-GNet group, peak VO_2 significantly increased from 14.7±3.6 mL/kg/min at discharge to 17.5±4.9 mL/kg/min ($p=0.02$) at 3 months, 17.9±5.1 mL/kg/min ($p=0.001$) at 6 months, and 17.5±5.5 mL/kg/min ($p=0.04$) at 1 year. Similarly, right grip strength increased significantly from 31.1±8.0 kg at discharge to 33.3±6.6 kg at 3 months, 33.3±6.6 kg at 6 months, and 34.1±6.6 kg at 1 year and right knee extension strength increased significantly from 0.44±0.11 kgf/kg at discharge to 0.49±0.12 kgf/kg at 3 months, 0.49±0.13 kgf/kg at 6 months, and 0.45±0.13 kgf/kg at 1 year.

Clinical outcomes

MACEs did not occur in any patient in the CR-GNet group (median [interquartile range] follow-up: 2.0 [1.4-3.0] years) but occurred in one patient in the control group (median follow-up: 1.4 [1.9-1.9] years) at the 3-year follow-up period (log-rank, p=ns) (Fig. 3). The patient was rehospitalized for unstable angina on the 117th day after discharge and had been previously ineligible for enrollment in CR-GNet owing to difficulty of access. The patient had five coronary risk factors during the first hospitalization, as follows: hypertension, diabetes, dyslipidemia, obesity, and smoking.

Discussion

This study demonstrates the feasibility of CR-GNet in disease management and the achievement of physical fitness in patients after ACS, though its clinical impact remains uncertain because of the small sample size and low event rates in our study population.

A previous study investigated the long-term outcomes of patients with ACS, reporting that the event rate from 31 days to 3 years was 19.8-33.6%; this was higher than that in our results[2]. This difference might be attributed to the effect of education on the disease, which was provided to all patients in our facility, including those in the control group before or after discharge. Regardless, although a type II error cannot be eliminated because of the low number of adverse events and the power to detect such a minor difference was 40.5% when the non-event rate of the CR-GNet group at the 3-year follow-up was set at 99%, the feasibility of CR-GNet in determining long-term outcomes compared with a conventional model was demonstrated in this study.

The proportion of patients who achieved control in all seven items related to coronary risk factors, namely diabetes, LDL-C, HDL-C, TG, BMI, smoking, and physical activity, improved at 3 months, 6 months, and 1 year after discharge. Moreover, the average number of risk factors per patient decreased at all checkpoints for over 1 year.

A previous study claimed that the management of

Table 1. Clinical demographics in patients in the CR-GNet group (n=21) and patients in the control group (n=31)

Characteristics	CR-GNet (n=21)	Control (n=31)	p value
Sex: male	19 (90.5)	27 (87.1)	1.00
Age (years)	65.8±10.5	64.6±8.9	0.655
Body mass index (kg/m^2)	24.1±3.5	23.5±3.0	0.507
Peak CK (IU/L)	1,263 (1,033–1,917)	2,100 (1,152–3,664)	0.183
Infarct-related artery			0.307
Left anterior descending artery	11 (52.4)	11 (35.5)	
Left circumflex artery	5 (23.8)	5 (16.1)	
Right coronary artery	5 (23.8)	14 (45.2)	
Left main coronary artery	0 (0)	1 (3.2)	
PCI			0.970
POBA	3 (14.3)	6 (19.4)	
BMS	3 (14.3)	3 (9.7)	
DES	12 (57.1)	17 (54.8)	
DCB	3 (14.3)	3 (9.7)	
Aspiration	0 (0)	1 (3.2)	
Untreated	0 (0)	1 (3.2)	
LVEF (%)	58.5±12.5	53.4±9.4	0.102
Length of hospital stay (d)	18.0 (14.0–24.0)	18.0 (13.5–25.0)	0.787
First day of rehabilitation (d)	3 (3–4)	3 (2–5)	0.637
Coronary risk factors			
Hypertension	17 (81.0)	26 (83.9)	1.00
Diabetes	9 (42.9)	16 (51.6)	0.582
Dyslipidemia	16 (76.2)	27 (87.1)	0.457
Obesity	10 (47.6)	11 (35.5)	0.405
Smoking	7 (33.3)	13 (41.9)	0.575
Physical inactivity	9 (42.9)	N/A	
Alcohol consumption	6 (28.6)	5 (16.1)	0.318
Medication			
Beta blocker	15 (71.4)	28 (90.3)	0.133
Angiotensin-converting enzyme inhibitor	9 (42.9)	13 (42.0)	1.000
Angiotensin receptor blocker	10 (47.6)	8 (25.8)	0.185
Calcium channel blocker	6 (28.6)	6 (19.4)	0.512
Aldosterone antagonist	7 (33.3)	13 (42.0)	0.738
Nitrovasodilator	9 (42.9)	21 (67.7)	0.135
Statin	20 (95.2)	28 (90.3)	0.639
Oral hypoglycemic agent	6 (28.6)	9 (29.0)	1.000
Insulin preparation	1 (4.8)	3 (9.7)	0.639
Antiplatelet agent	21 (100.0)	30 (96.8)	1.000
Anticoagulant	3 (14.3)	3 (9.7)	0.675
Hyperuric acid treatment	1 (4.8)	3 (9.7)	0.639

Categorical variables are expressed as n (%), and continuous variables as mean±standard deviation or median (interquartile range). CR-GNet, Cardiac Rehabilitation Gifu Network; CK, creatine kinase; PCI, percutaneous coronary intervention; POBA, plain old balloon angioplasty; BMS, bare metal stent; DES, drug-eluting stent; DCB, drug-coated balloon; LVEF, left ventricular ejection fraction; N/A, not available.

modifiable risk factors among post-PCI participants at 12-18 months after revascularization was inadequate, wherein the average number of coronary risk factors was 1.9 among the five items and approximately one-third of the participants had at least two modifiable risk factors despite having taken medications for these risk factors[14]. Although it is difficult to compare their data directly with our findings due to differences in the study period, race of selected patients, and medications, our study sets the number of items related to coronary risk factors at seven, which was higher than

Table 2. Achievement of target levels for the management of coronary risk factors and alcohol consumption, and average number of coronary risk factors for all patients (n=21)

Coronary risk factors and alcohol consumption	Target level	At admission	3 months	6 months	1 year
Hypertension	BP <140/90 mmHg§	95% (20/21)	81% (17/21)	86% (18/21)	76% (16/21)
Diabetes	HbA1c <7.0%	71% (15/21)	80% (16/20)	86% (18/21)	81% (17/21)
LDL-C	LDL-C <100 mg/dL	25% (5/20)	90% (19/21)	80% (16/20)	81% (17/21)
HDL-C	HDL-C ≥40 mg/dL	70% (14/20)	81% (17/21)	85% (17/20)	71% (15/21)
TG	TG <150 mg/dL	62% (13/21)	71% (15/21)	67% (14/21)	81% (17/21)
BMI	BMI <25.0 kg/m^2	57% (12/21)	62% (13/21)	71% (15/21)	62% (13/21)
Smoking	Non-smoking	67% (14/21)	95% (20/21)	95% (20/21)	95% (20/21)
Physical activity	Exercise time ≥150 min	57% (12/21)	76% (16/21)	86% (18/21)	61% (13/21)
Alcohol consumption	Daily alcohol consumption <30 mL	71% (15/21)	90% (19/21)	90% (19/21)	81% (17/21)
Average number of coronary risk factors		2.9	1.6*	1.4**	1.9***†

LDL-C, low-density lipoprotein cholesterol; HbA1c, hemoglobin A1c; HDL-C, high-density lipoprotein cholesterol; TG, triglyceride; BMI, body mass index; BP, blood pressure.

§Target level of BP is <130/80 mmHg for patients with diabetes or chronic kidney disease.

*p=0.004 vs. at admission; **p=0.001 vs. at admission; ***p=0.011 vs. at admission; †p=0.035 vs. at 6 months

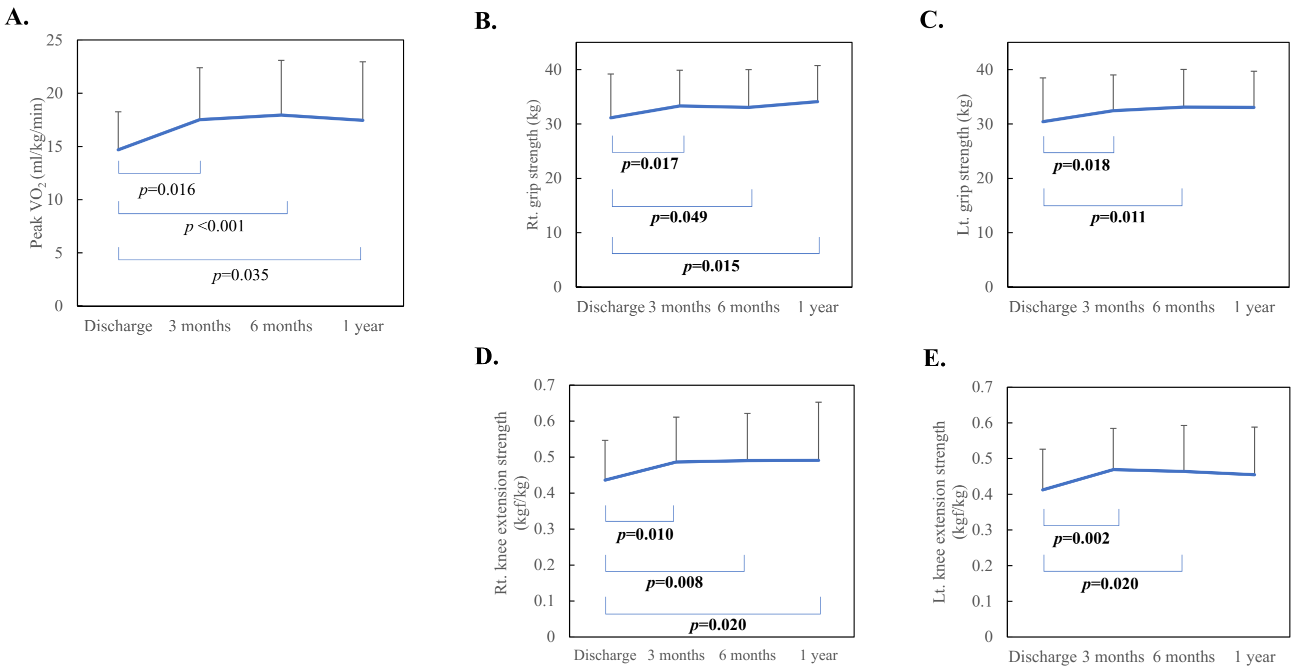
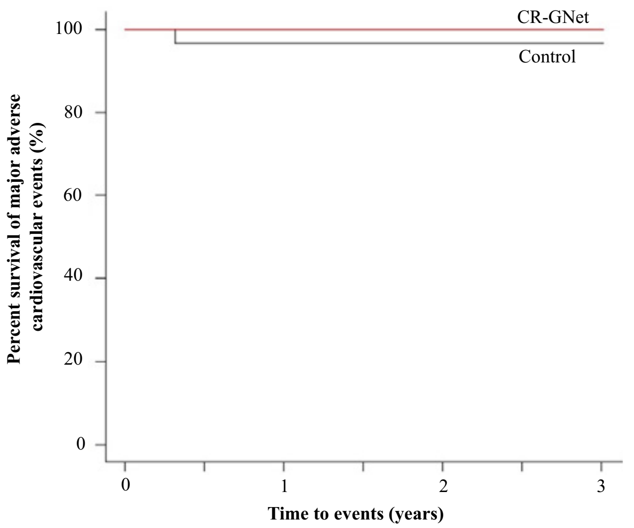


Fig. 2. Comparison of peak oxygen uptake (VO_2) (A; n=15), grip strength (B and C; n=19) and knee extension strength (D and E; n=19) among different time points, including at discharge and at 3 months, 6 months, and 1 year after discharge. Rt., right; Lt., left.

that in the previous study. Hence, our system could result in a more favorable disease management status.

However, coronary risk factor management worsened at 1 year compared with that at 6 months, despite the fact that it had improved compared with that at admission. Thus, the discussion should be extended to include the methods by which the patient support system can be involved in bringing long-lasting motivation and effects on disease management.

Physical function was significantly enhanced at all the follow-up time points. The proportion of patients who participated in outpatient CR was 86%, with most participating less than once a week. Additionally, 76%-86% of patients established a favorable frequency of physical activity in their routine at 3 and 6 months after discharge. Thus, it can be presumed that the improvement in physical function observed in this study resulted not only from outpatient CR but also from the increase in home exercise.



Number at risk

CR-GNet	31	29	26	11	6	5	4
Control	21	21	21	15	14	12	10

Fig. 3. Time-to-event curves for major adverse cardiovascular events after discharge in the CR-GNet (n=21) and control (n=31) groups.
CR-GNet, Cardiac Rehabilitation Gifu Network

Previous findings have indicated that the proportion of patients who receive outpatient CR after discharge is extremely low. The participation rate of patients with acute myocardial infarction was estimated to be 4.8%-11.7% in Japan and 34.7% in hospitals approved for CR[5]. Even in studies of relatively proactive CR facilities, the rate was only 47%-60.3%[6,7]. The predominant causes for the low participation rate are busy work schedules and difficulty in hospital visits, along with the preference for self-exercise. In such circumstances, CR programs that are flexible, convenient, and have reduced temporal restrictions, such as home-based arrangements and periodic follow-up systems, including psychobehavioral support, can be helpful for patients who plan to return to work and simultaneously undergo CR or who prefer self-exercise[15,16].

In CR-GNet, follow-up assessments including medical and physical examinations and assessment of disease management status are conducted periodically in late phase II and phase III; these results are beneficial for health education. With respect to prolonged disease control, some researchers have demonstrated that long-term disease management of patients with coronary disease in routine clinical practice by the CR program staff is feasible and effective in achieving and maintaining secondary preventive goals[17]. Therefore, it is evident that the follow-up system in CR-GNet is important.

Furthermore, the CR-GNet has several psychobehavioral functions that could contribute to motivational enhancement, in addition to offering patients psychobehavioral education for disease management. First, patients set at least three personal goals on their own at discharge and during follow-up assessments; these were monitored with the help of the healthcare staff during the next follow-up visit. As a result, “the commitment and consistency principle” is practiced effectively[18-21]. This principle states that once we make a decision, we experience pressure from others and ourselves to behave consistently. Especially when the commitment is active, public, and freely chosen, people are more likely to behave in ways that are congruent with that position. In CR-GNet, patients set their goals and shared them with healthcare staff, demonstrating “public commitment.” Hence, goal attainment is enhanced by this effect.

The second factor to be considered is education using disease control material that is standardized region-wide. All healthcare personnel, regardless of profession, provide guidance that leads to motivational enhancement. According to the principle of “social proof,” individuals determine the appropriate behavior by examining the behavior of others, especially of those in similar situations[21,22].

Despite the overlooked effects of medications on coronary risk factors, items unrelated to medication intake, such as alcohol consumption, smoking, physical activity, and BMI, all improved. This indicates that lifestyle and behavioral changes could have affected the management of each coronary risk factor.

Considering the favorable effects on disease control and physical function, CR-GNet may continuously enhance the patients’ motivation after discharge and improve adverse event rates; as previous studies have shown, exercise capacity, physical activity, and correction of coronary risk factors improve life expectancy[23-26].

Additionally, the enrollment of patients with heart failure is currently being implemented in CR-GNet, wherein the material for disease management for heart failure has been introduced. Further research on the long-term effects of CR-GNet would be invaluable in the field of disease management after cardiovascular disease.

Study limitations

This study has some limitations that should be noted. First, while comparing the controls for coronary risk factors, we could not examine the data of patients who did not undergo CPX or periodic follow-up assessments. This includes those who were not enrolled or who dropped out from the follow-up. Second, the participants enrolled in this study had a relatively small infarction size, suggesting bias in the inclusion criteria for CR-GNet. Therefore, our results may not be applicable to patients with severe conditions. Third, we could not demonstrate the extent of the influence of medications on risk factors in the results. Fourth, data after the 2-year follow-up were not analyzed; thus, the long-term effects have not been investigated. Fifth, the data of patients with cardiovascular diseases other than myocardial infarction were not explored. Sixth, a multicenter study was not conducted. Finally, although we demonstrated the feasibility of CR-GNet in determining long-term outcomes, the effectiveness of this network could not be revealed because of the low statistical power. Nearly twice the total number of patients analyzed in this study will be required to achieve a statistical power of >80%. The prognostic impact of CR-GNet requires further investigation with a larger sample size and a longer follow-up duration.

Conclusion

CR-GNet is feasible and useful for achieving continued patient education, better long-term risk factor management, improved exercise capacity, and, possibly, better clinical outcomes.

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PHYSICAL THERAPY RESEARCH

BRIEF REPORTS

Cutoff Value for a Nutritional Indicator Related to Gait Independence in Elderly Fracture Patients: A Preliminary Study

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ABSTRACT. Objective: Previous studies have reported the relationship between nutritional status and gait independence in elderly fracture patients. However, the degree to which nutritional indicators are related to gait independence is unclear. The purpose of this study is to calculate a cutoff value for a nutritional indicator related to gait independence in patients with hip and vertebral compression fractures. Method: This study included 69 patients (33 hip fracture, 36 vertebral compression fracture) who underwent rehabilitation at a convalescent rehabilitation ward. The relationships between nutritional indexes (Mini-Nutritional Assessment-Short Form [MNA®-SF] and skeletal muscle mass index [SMI]) at admission and gait independence at discharge were analyzed using logistic regression. In addition, receiver operating characteristic analysis was performed to calculate a cutoff value that predicts gait independence. Results: Among the nutritional indicators used in this study, only MNA®-SF was significantly able to predict gait independence at discharge, and this association was maintained, even after adjustment for confounders. The calculated MNA®-SF cutoff values were 5.5 (sensitivity 100%, specificity 46.3%) and 7.5 points (sensitivity 67.9%, specificity 78.0%). Conclusion: This study suggests that MNA®-SF may be an index for predicting gait independence in patients with hip or vertebral compression fractures in the convalescent rehabilitation ward. The cutoff values calculated in this study were simple and useful index for physical therapists to interpret the results of MNA®-SF.

Key words: Nutrition, Gait, Cutoff

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Hip fractures and vertebral compression fractures are common in the elderly population. Japan's aging population is the largest in the world and, in 2017, there were an estimated 193,400 hip fracture patients[1)]; vertebral fractures—reported to be >10 times more frequent than femoral fractures—have been estimated at 1-1.5 million per year[2)]. After such fractures, patients often present with gait disturbance and receive physical therapy aimed at improving their gait ability.

In order to perform effective physical therapy, it is important to understand the factors related to gait ability and to predict the prognosis accordingly. In recent years, the relationship between nutritional status and the effect of rehabilitation has gained attention. For example, previous studies reported that nutritional states were related to functional outcomes in elderly patients[3)] and those with various diseases, such as stroke[4)], Parkinson's disease[5)], distal radius fracture[6)], and pneumonia[7)]. Similarly, it has been reported that nutritional status is associated with improvement in activities of daily living (ADL) and gait ability in patients with hip and vertebral compression fractures[8-12)]. Although there are some reports that nutritional interventions have not had significant impacts on long-term outcomes after hip fractures[13,14)], other studies have shown that nutritional inter-

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ventions are effective for improving ADL and gait ability in patients with hip fractures[8].

These findings suggest that it is important for physical therapists to understand nutritional status, in order to consider intervention plans and predict prognosis when treating patients with hip and vertebral compression fractures. However, previous studies have not established the degree to which nutritional indicators relate to gait independence, i. e., cutoff values; it is difficult to interpret the results of nutritional assessments. Therefore, the purpose of this study is to calculate the cutoff value of a nutritional indicator related to gait independence in patients with hip and vertebral compression fractures. The findings of this study can provide a reference for interpreting nutritional indicators when predicting the prognosis of gait independence.

Method

Study design and patients

This study was a retrospective observational study including 69 patients (33 hip fracture, 36 vertebral compression fracture) who underwent rehabilitation at a convalescent rehabilitation ward between August 2018 and July 2020. The inclusion criteria were for patients aged >65 years, evaluated as not independent in gait at the time of their admission. Those with missing data, who transferred to another hospital, or who died were excluded. The Research Ethics Committees of Fukushima Medical University and Kita- Fukushima Medical Center reviewed and approved the study (No 94, general 2020-236), which was carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki).

Assessments

In order to examine the relationship between nutritional status at admission and gait independence at discharge, Mini-Nutritional Assessment-Short Form (MNA®-SF)[15,16] and skeletal muscle mass index (SMI) were used as indicators of nutritional status. MNA®-SF is a shortened version of the Mini-Nutritional Assessment, a nutritional screening tool for the elderly. MNA®-SF is based on six items: decrease in food intake over the past 3 months, weight loss during the last 3 months, mobility, psychological stress or acute disease in the past 3 months, neuropsychological problems, and body mass index or calf circumference. In its original use, MNA®-SF scores of 12-14 points are judged as "normal nutritional status," scores of 8-11 points are judged as "at risk of malnutrition," and scores of 0-7 points are judged as "malnourished." However, for this study's purpose, MNA®-SF scores were treated as continuous variables. The patients included in this study inevitably scored 0 points for the items of "mobility" and "psychological stress or acute disease in the past 3 months." SMI was measured using a body composition analyzer (InBody S10, InBody Japan, Tokyo, Japan). Gait independence at discharge was determined using the Functional independence measure (Locomotion: Walk), with ≥6 points being independent and ≤5 points being non-independent. In addition, we collected data on age, cognitive function, and knee extension strength, which were considered as confounding factors and have been reported to be associated with gait independence in previous studies[17,18]. The revised Hasegawa's Dementia Scale (HDS-R) was used as an indicator of cognitive function. The knee extension strength was measured using a hand-held dynamometer (μTas F1, Anima Co., Tokyo, Japan) in the sitting position, and the index in Nm/kg was calculated based on body weight and lower-limb length. MNA®-SF, HDS-R, and knee extension strength were assessed by physical therapists or occupational therapists within two weeks after admission to the convalescent rehabilitation ward. Other subject attributes at admission were obtained from medical records, including: gender, period from onset to admission, and intervention period.

Statistical analysis

Comparisons of nutritional status and other variables were performed between the two groups of patients, who were gait-independent at discharge (independent) or not (non-independent), using the t-test, Mann-Whitney test, and chi-square test. Next, in order to determine a nutritional index suitable for calculating a cutoff value, forced input method logistic regression analysis was performed using group (independent or non-independent) as a dependent variable, and MNA®-SF and SMI as independent variables (crude model). We also created a model in which age, HDS-R, knee extension strength, and fracture site (hip or vertebral) were used as adjustment variables (adjusted model). When the correlation coefficient among the independent and adjustment variables was 0.7 or higher, two variables with high correlation coefficient were input into the model separately to avoid multicollinearity.

For nutritional indicators that were significantly associated by logistic regression analysis with gait independence at discharge, receiver operating characteristic (ROC) analysis was used to calculate a cutoff value for distinguishing gait independence. The area under the ROC curve (AUC) was calculated with gait independence at discharge as the dependent variable and nutrition index as the independent variable. When the AUC was ≥0.7 (moderate accuracy), a cutoff value was calculated using Youden's index. The level of significance was set at 5% for all tests, and all analyses were performed using SPSS Statistics version 25 (IBM, Armonk, NY, USA).

Results

Table 1 shows the subjects' attributes and nutritional

Table 1. Attributes, nutritional status, and gait capacity of the subjects

	Overall (n = 69)	Independent (n = 28)	Non-independent (n = 41)	*p* value
Age (years)	83.4 ± 7.8	80.0 ± 7.2	85.7 ± 7.4	<0.01
Gender (Men, %)	23.2	17.9	26.8	0.39
Bone fracture site (n)	Femur 33	Femur 8	Femur 25	<0.01
	Vertebral 36	Vertebral 20	Vertebral 16	
Period from onset to admission (days)	20.6 ± 10.2	18.0 ± 7.7	22.3 ± 11.4	0.08
Intervention period (days)	57.9 ± 18.2	56.0 ± 19.9	59.1 ± 17.1	0.49
Knee extension strength (Nm/kg)				
Stronger side	0.72 ± 0.3	0.82 ± 0.3	0.65 ± 0.3	<0.01
Weaker side	0.55 ± 0.3	0.65 ± 0.3	0.48 ± 0.2	<0.01
HDS-R (points)	20.0 ± 6.6	22.9 ± 5.0	18.0 ± 6.8	<0.01
MNA®-SF (points)	6.7 ± 2.0	8.0 ± 1.6	5.8 ± 1.8	<0.01
SMI (kg/m^2)	4.9 ± 1.0	5.3 ± 1.1	4.6 ± 0.8	<0.01

Mean ± Standard deviation

Abbreviation: HDS-R, revised Hasegawa's Dementia Scale; MNA®-SF, Mini Nutritional Assessment-Short Form; SMI, Skeletal Muscle Mass Index

Table 2. Logistic regression analysis of gait independence at discharge and nutritional indicators at admission

	Crude model		Adjusted model			
	OR (95% CI)	*p*	OR (95% CI)	*p*	OR (95% CI)	*p*
MNA®-SF	1.96 (1.36, 2.87)	<0.01	2.39 (1.43, 4.02)	<0.01	2.27 (1.39, 3.71)	<0.01
SMI	1.51 (0.78, 2.94)	0.22	1.01 (0.42, 2.43)	0.98	1.12 (0.48, 2.62)	0.79
Moderators						
Age			0.91 (0.82, 1.01)	0.07	0.91 (0.82, 1.01)	0.06
HDS-R			1.04 (0.91, 1.19)	0.53	1.05 (0.92, 1.19)	0.51
Bone fracture site (0: femur, 1: vertebral)			5.29 (1.15, 24.28)	0.03	4.24 (0.89, 20.14)	0.07
Knee extension strength on stronger side			17.21 (0.65, 454.93)	0.09		
Knee extension strength on weaker side					7.07 (0.36, 140.15)	0.20

Abbreviation: MNA®-SF, Mini Nutritional Assessment-Short Form; SMI, Skeletal Muscle Mass Index; HDS-R, revised Hasegawa's Dementia Scale

status. There were 28 (40.6%) patients in the independent group and 41 (59.4%) in the non-independent group. Comparisons between the independent group and non-independent group found significant differences for all items except gender, period from onset to admission, and intervention period (Table 1). In logistic regression analysis of crude model, the nutrition indicator MNA®-SF was able to significantly predict gait independence at discharge (OR: 1.96; 95% confidence interval: 1.4-2.9; P < 0.01) (Table 2). In the adjusted model, knee extension strength on the stronger and weaker side was input into the model separately because the correlation coefficient was ≥0.7. MNA®-SF was significantly associated with gait independence at discharge in both the adjusted models (with age, fracture site, HDS-R, and knee extension strength on the stronger or weaker side as adjustment variables). In the ROC analysis, the AUC of MNA®-SF was 0.81, and the cutoff values based on a high Youden's index were 5.5 (sensitivity 100%, specificity 46.3%, Youden's index 0.463) and 7.5 points (sensitivity 67.9%, specificity 78.0%, Youden's index 0.459) when gait independence was set to "positive".

Discussion

This study used MNA®-SF and SMI as indicators of nutritional status; only MNA®-SF was associated with gait independence at discharge. Since this association was maintained even after adjustment for fracture site in the multivariate analysis, it is considered that MNA®-SF and gait independence are related, regardless of whether the patient had a hip fracture or vertebral compression fracture. A previous study has already reported an association between MNA®-SF and gait ability in patients with hip fractures[19]; the results of our study coincide.

Few other previous studies have compared multiple nutritional indicators as predictors of outcomes in patients with fractures. Helminen et al.[20] compared MNA® and serum albumin as predictors of outcomes in patients with hip fractures, and reported that MNA® (long-form) and MNA®-SF were useful for predicting mobility and living environment. Their finding suggested that MNA®-SF may be a better index for predicting gait independence in patients with fracture.

In previous studies that have used MNA®-SF, the original cutoff values of the index were used to classify subjects (12-14 points, "normal nutritional status"; 8-11 points, "at risk of malnutrition"; and 0-7 points, "malnourished"). Our study has taken an original approach by treating nutritional indexes as continuous variables, attempting to calculate a more accurate and reliable cutoff value relating to prognosis of gait independence in fracture patients. The cutoff values calculated in this study were 5.5 and 7.5 points in MNA®-SF. We believe that 7.5 points is a reasonable cutoff value because of the balance between sensitivity and specificity. In other words, when the MNA®-SF score at admission is 7 points or less, gait independence at discharge may be difficult. The cutoff value (7.5 points) calculated in this study was consistent with the original MNA®-SF range for "malnourished." Prior to this study, the degree of nutritional status that affected gait independence was unknown. For example, it was unclear within which range of MNA®-SF gait independence would be affected. As a result of this study, it was clarified for the first time that MNA®-SF is related to the gait independence of patients with fractures, regardless of whether or not it corresponds to the original MNA®-SF range for "malnutrition," i. e., 0-7 points.

However, it should be noted that some items of MNA®-SF become 0 points in patients with fractures, such as those included in this study. This indicates that it is important that the total score of "decrease in food intake over the past 3 months," "weight loss during the last 3 months," "neuropsychological problems," and "body mass index or calf circumference" reaches 8 points for gait independence in patients with fractures.

Since our cutoff value (7.5 points in MNA®-SF) had sensitivity of 67.9% and specificity of 78.0%, it may be clinically realistic to use it in combination with other variables for predicting prognosis. However, our cutoff value may be a simple and useful index for physical therapists to interpret the results of MNA®-SF.

On the other hand, the odds ratio in the logistic regression analysis revealed that the bone fracture site had a very strong effect on gait independence. A previous study reported that 40%-60% patients with hip fractures regained their prefracture level of mobility within 1 year[21]. To the best of our knowledge, there are no large-scale studies investigating the rate of regaining gait independence in patients with vertebral fractures. However, patients with vertebral fractures are more likely to recovery gait independence than patients with hip fractures in general. Considering that the association between MNA®-SF and gait independence was maintained even after adjustment for fracture site in the logistic regression analysis, MNA®-SF and gait independence can be considered to be associated, regardless of whether the patient has a hip fracture or a vertebral fracture. However, considering the magnitude of the impact of the fracture site on gait independence, it cannot be denied that the factors related to gait independence may differ between patients with hip fractures and those with vertebral fractures. In other words, the degree of influence of MNA®-SF on gait independence may be different in patients with hip fractures and in those with vertebral fractures.

One limitation of this study is that it contained only a small sample. Therefore, not all potential confounders, including pain and operative procedures, which are critical factors, could be included in multiple logistic analysis. Also due to the small sample size, it was difficult to perform detailed analysis, such as calculating the respective influence of MNA®-SF for hip and vertebral compression fractures. Therefore, this study is only a preliminary study, in future it will be necessary to increase the sample size and perform more detailed analysis.

Conclusion

MNA®-SF score at admission to a convalescent rehabilitation ward is associated with gait independence at discharge in patients with hip and vertebral compression fractures. The MNA®-SF cutoff value associated with gait independence is 7.5 points.

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

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PHYSICAL
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BRIEF REPORTS

Gait-related Self-efficacy is Low in Older Adults with Knee Osteoarthritis: A Preliminary Study

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ABSTRACT. Objective: To investigate the differences in self-efficacy (SE) for walking tasks between older patients with knee osteoarthritis (OA) and older adults without knee OA. Methods: A cross-sectional design was employed. Older patients with radiographic knee OA and community-dwelling older adults without knee OA as controls were enrolled in the study. SE for the walking task was assessed using the modified gait efficacy scale (mGES). A Wilcoxon rank-sum test was used to compare the mGES between the groups of participants. A Tobit regression model was used to estimate the difference in mGES. The presence of radiographic knee OA was used as an independent variable. Sex (women), age, and body mass index were used as potential confounding variables in the model. Results: After exclusion, 78 participants (n=40 with knee OA, n=38 controls) were included. The mGES was lower in patients with knee OA than in controls. In the Tobit regression model adjusted for confounding factors, mGES in patients with knee OA was estimated to be 26.8 (95% confidence interval [CI]: 15.8-37.8) points lower than in controls. Conclusion: This study demonstrated that mGES was lower in older patients with knee OA than in older adults without knee OA.

Key words: Knee osteoarthritis, Older adult, Self-efficacy, Gait efficacy scale

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Knee osteoarthritis (OA) is one of the most common joint diseases and is clinically characterized by chronic pain, functional disability, and limitations in activities of daily living. There are many studies that have investigated physical problems such as gait kinematics in patients with knee OA[1)]. However, recent studies focusing on psychological aspects such as pain catastrophizing and self-efficacy (SE) have also been investigated[2,3)]. Several SE scales have been used for patients with knee OA, including fear of falling and SE for disease-specific symptoms, such as the fall efficacy scale and the arthritis self-efficacy scale, respectively[3,4)]. The modified gait efficacy scale (mGES), which is specifically used for self-reporting confidence in carrying out 10 common walking tasks, was developed[5)]. Walking is the most important for mobility and is essential for many daily activities. Walking-related symptoms (i. e., pain) and dysfunction are common problems for patients with knee OA; therefore, SE scales for walking tasks will be very informative. Consequently, reductions in SE for walking tasks can adversely affect various activities of daily living, occupations, as well as general physical activity (PA). However, it is unclear how much lower the SE for walking tasks is in patients with knee OA when compared to without knee OA. The purpose of this preliminary study was to provide basic data on the SE for walking tasks among patients with knee OA, comparing it with that in people without knee OA.

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Materials and Methods

Study design and ethics

The present study employed a cross-sectional design. All participants underwent the following measurements: measurement of SE for the walking task, objective measurement of PA, and measurement of gait speed. The present study was approved by the medical ethics committee of Akita City Hospital, 2017 (approval No. 6), and the study was conducted in accordance with the Declaration of Helsinki. The objectives and procedures used in the study were orally explained to the participants, and explanatory documents were also provided. Written consent was obtained from the participants after they were informed that participation in the study was voluntary and that their privacy would be protected.

Participants

Patients aged 65 years or older with radiological knee OA (Kellgren-Lawrence [K-L] grade ≥ 2) who visited the Department of Orthopedics at Akita City Hospital between April 2017 and March 2019 were enrolled. As a control group, community-dwelling older adults were recruited by poster at a local community center as an opportunity to assess physical performance. Participants as the control group who had symptoms of knee pain or had been diagnosed with knee OA were excluded from the analysis. The common exclusion criteria for participation were as follows: diagnosis of severe and/or unstable cardiac diseases, hip or ankle osteoarthritis, mental disorders, disorders other than OA that could affect PA level (i.e., chronic obstructive pulmonary disease), not living independently, being wheelchair-bound, and the inability to operate the activity monitor.

Measurements

Self-efficacy for walking task

The SE for the walking task was assessed using the Japanese version of the mGES, which has been established reliability[5,6]. The mGES, which represents the SE for performing safe walking tasks, consists of 10 items that address an individual's perception of their level of confidence in each task. The items include level-ground walking, climbing stairs, and long-distance walking. The items were scored individually on a 10-point scale, with one indicating no confidence and 10 indicating perfect confidence. The total score ranged from 10 to 100 points.

Other characteristics

A ten-meter walking test was performed to measure gait speed (GS). The participants were instructed to walk at a comfortable pace. The test was performed twice for each subject, with a 10-second break between the trials. The faster speed of the two trials was accepted as GS. The intensity of knee pain for level-ground walking was assessed after the trials using the visual analog scale (VAS) in patients with knee OA.

The objective measurement of PA was performed using an accelerometer-based activity monitor (Lifecorder GS 4, Suzuken Co., Ltd., Tokyo, Japan). The validity and reliability of this activity monitor has been previously demonstrated[7]. Participants wore the monitor on the belt or waistband of their clothing for at least nine consecutive days. The device was worn throughout the day, except during bathing and at bedtime, and data on the participants' daily activities for at least 7 days were obtained. Days with at least 10 hours of wearing time were considered valid[8]. The participants' average daily step count was calculated as their PA level.

The participants' sex, age, height, weight, and body mass index (BMI) were assessed or retrieved from medical records. The K-L grade and femorotibial angle (FTA) were assessed by a physician using a full-length standing radiograph from the hip to the ankle joints in patients with knee OA.

Statistical analysis

Statistical analysis was performed using R ver. 3.6.1 (The R Foundation for Statistical Computing, Vienna, Austria) and RStudio ver. 1.2.5042 (RStudio, PBC., MA, US). Statistical significance was set at $P < 0.05$. The assumptions of normality were assessed using the Shapiro-Wilk test. We performed Welch's t-tests or Wilcoxon rank-sum tests for interval and ordinal variables, respectively, and Pearson's chi-squared tests for categorical variables to assess differences between the two groups of participants. A general linear regression model or generalized linear regression model was used to estimate the difference in mGES between the two groups. Radiographic knee OA was adopted as an independent variable in the initial model (Model 1). In the second model (Model 2), sex (women) and age as demographic factors and BMI as obesity level were adopted as confounding variables and added to Model 1. Categorical variables (the presence of radiographic knee OA and sex) were transformed into dummy variables.

Results

Eighty-eight participants were enrolled in this study. Ten patients with knee OA were excluded for the following reasons: previous history of knee surgery (n=2), unwilling to participate in the study (n=1), inability to walk independently (n=1), and a lack of available PA data (n=6). In the control group, there were no individuals excluded from the analysis. Consequently, 78 participants (n=40 with knee OA; n=38 controls) were included in the study.

Comparisons of the clinical and demographic data for the participants in the two groups are presented in Table 1. The mGES was lower in patients with knee OA than the

Table 1. Comparison of the clinical and demographic characteristics and measurement values for patients with knee osteoarthritis and controls

	All (n=78)	Knee OA (n=40)	Control (n=38)	p-value
Sex, women (n)	58 (74)	34 (85)	24 (63)	0.051
Age (years old)	74 ± 6	76 ± 6	72 ± 5	0.008
Height (cm)	153.2 ± 7.4	152.7 ± 7.7	153.9 ± 7.0	0.475
Weight (kg)	58.5 ± 9.8	61.4 ± 11.3	55.6 ± 6.8	0.007
BMI (kg/m^2)	24.9 ± 3.3	26.2 ± 3.6	23.5 ± 2.2	< 0.001
K/L grade (n)				
III		14 (35)	—	
IV		26 (65)	—	
VAS (mm)		55.8 ± 24.1	—	
mGES	74 (40, 91)	42 (30, 72)	88 (79, 100)	< 0.001
GS (m/sec)	1.28 ± 0.37	0.99 ± 0.25	1.59 ± 0.19	< 0.001
Daily step counts (steps/day)	4716 (2691, 7004)	3093 (2256, 4950)	6486 (4690, 9595)	< 0.001

The data are presented as mean ± standard deviation, median (25, 75 percentile), or number (%).
The p-values are results of Welch's t-test, Wilcoxon rank-sum test, or chi-squared test.
The K/L grade and VAS in the control group were not evaluated.
Abbreviations: OA, osteoarthritis; BMI, body mass index; K/L grade, Kellgren-Lawrence grade; VAS, visual analog scale of knee pain; mGES, modified gait efficacy scale; GS, gait speed.

Table 2. Results of the Tobit regression analysis

	Variables	B	95% CI lower	95% CI upper	SE	β	z-value	p-value	AIC
Model 1	Knee OA	-36.612	-46.187	-27.036	4.886	-0.647	-7.494	< 0.001	664.032
Model 2	Knee OA	-26.793	-37.778	-15.809	5.605	-0.474	-4.781	< 0.001	659.715
	Women	-10.734	-21.600	0.132	5.544	-0.166	-1.936	0.053	
	Age	-1.154	-2.139	-0.169	0.503	-0.226	-2.295	0.022	
	BMI	-1.352	-2.834	0.131	0.757	-0.155	-1.786	0.074	

The dependent variable is modified gait efficacy scale
Abbreviations: B, partial regression coefficient; CI, confidence interval; SE, standard error; β, standardized partial regression coefficient; AIC, Akaike information criteria; OA, osteoarthritis; BMI, body mass index.

controls. In the controls, 6 individuals (15.8%) were full score of the mGES. Patients with knee OA were older and had higher body weight and BMI than the controls. GS was faster, and the daily step count was higher in the control group compared to the patients with knee OA.

The Shapiro-Wilk test determined that a normal distribution was not present for mGES ($W = 0.905$, $p < 0.001$). The distribution of mGES was slightly skewed (−0.330) and censored (range: 16-100); some participants were at the upper limit. As a result of the above reasons, a Tobit regression model was used (Table 2). In Model 1 (chi-square = 42.165, $p < 0.001$), mGES was lower in patients with knee OA than in the controls (Table 2). These findings were similar for Model 2 (chi-square = 52.481, $p < 0.001$), which was adjusted for sex, age, and BMI. Model 2 estimated that mGES was 26.8 (95% confidence interval [CI]: 15.8-37.8) points lower in patients with knee OA than in the controls (Table 2).

Discussion

The results of this study demonstrate that mGES was lower in patients with knee OA than in the controls. Additionally, gait speed and the daily step count were lower in patients with knee OA, as shown in previous studies[9].

Patients with knee OA who have various challenges related to walking, such as pain, poor balance and lower gait function, may also have problems with SE for walking tasks. The influence of psychological aspects, such as pain catastrophizing, has been studied. A previous study showed that pain catastrophizing is associated with physical function, activities of daily living, and PA[10-12]. The current study found that patients with knee OA may have psychological problems as well as pain and poor gait function during walking. Physical function was associated with pessimism, SE for walking tasks, and activity-related balance efficacy, but the association with pessimism was attenuated after controlling for both SE in older adults[13]. Additionally, one study found that the SE for walking tasks has a partially mediating role in the pathway from PA to functional limitations in older adults[14]. Thus, the SE for walking tasks was associated with physical function and PA in older adults. Future studies are therefore warranted among patients with knee OA.

Total knee arthroplasty (TKA) is one of the methods used to improve pain and physical function in patients with knee OA. Hiyama et al. reported that although there were improvements in physical function and pain in patients 6 months after TKA, there was no difference compared with the preoperative scores for life-space mobility and mGES[15]. These results suggest that improving pain and physical function alone is not enough to improve the SE for walking tasks and that interventions to improve confidence in the walking task itself (e.g., task-oriented training) are needed. The mGES can assess the SE for walking tasks in 10 different situations, including level surface walking, rough terrain walking, stair climbing, and more[5]. Consequently, we might be able to assess not only overall confidence in walking, but also more specific problems in SE for individual walking challenges. These findings are informative for personalized, task-oriented gait training conducted by physicians, physical therapists, and others.

This study was subject to several limitations that merit mentioning here. First, because this study was conducted at a single center, the participants with knee OA had the following characteristics: 74% of the subjects were female; and all patients had severe radiographic OA changes. These limitations might have imposed selection bias and might limit the validity and generalizability of our findings. Further study is needed, particularly on mild and moderate radiographic knee OA. Second, we did not perform radiological examinations among the community-dwelling participants. Lastly, the community-dwelling participants was recruited with posters, so their interest in health may have been higher than average, and their gait speed was faster than in previous studies. There was no knee pain in controls and median mGES was comparable to that reported in previous studies[5]. However, the number of participants with full score was twice that of the previous study, which may be due to differences in physical function[5]. Therefore, the controls in this study may have higher physical function and the SE for walking tasks than the general community-dwelling older adults.

In summary, the present preliminary data support that older patients with severe knee OA have lower SE for walking tasks compared to older adults without knee OA. The impact of lower SE for walking tasks on physical function, PA, and patient-reported outcome measures requires further study.

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PHYSICAL THERAPY RESEARCH

BRIEF REPORTS

Maximum Phonation Time is a Useful Assessment for Older Adults Requiring Long-term Care/support

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ABSTRACT. Objective: The maximum phonation time (MPT) is used to assess simple respiratory functions and can be performed anywhere without special instruments. We investigated the association between MPT and respiration, considering the future utilization of simple respiratory assessments during home-based physical therapy. Method: This cross-sectional study included 140 older adults enrolled in Japanese long-term care insurance (77 men, 63 women; mean age, 77.9±8.0 years). The participants performed the MPT, followed by spirometry. We analyzed the MPT of the three age groups, relative reliability of the MPT values, and the association between MPT and respiratory function. Results: We found that the MPT of older men requiring long-term care or support was related to age. The intraclass correlation coefficient of MPT was >0.8 for all groups. Only forced vital capacity was associated with MPT in the partial correlation and multiple regression analyses. Conclusion: MPT could be an alternative assessment of respiratory function in home-based physical therapy for older adults requiring long-term care or support.

Key words: Day care, Elderly, Home care services, Maximum phonation time, Respiration

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Decreased respiratory function as one ages is associated to a decline in activities of daily living and quality of life and is a common problem in older adults[1)]. According to a statistical survey, pneumonia is a common cause of death in Japan and has a high number of cases of lower respiratory infections worldwide[2,3)]. It has also been reported that aspiration pneumonia accounts for approximately 80% of pneumonia cases in patients aged ≥70 years[4)]. Since decreased respiratory function is a risk factor for aspiration pneumonia, it is crucial to assess this in older adults, especially in those receiving medical care at home[5)].

The maximum phonation time (MPT) is a comprehensive assessment of vocal function, which include respiratory factors[6)]. The use of MPT was frequently reported during the 1960s-1980s, and evidence from previous reports, such as that on the association of MPT with respiration, is currently being used[7-9)]. Thus, MPT has been established as a simple spirometry technique and is used as a clinical tool[9)].

In Japan—an aging society—the number of persons certified for long-term care insurance has increased[10,11)]. In addition, most older people have decreased respiratory function but have not been diagnosed with respiratory diseases[12)], prompting an increase in the frequency of respiratory function assessment during home care visits. Usually, respiratory function should be assessed using a spirometry in a specialized clinic. Since MPT can be measured anywhere without special tools, it can be used to assess respiration during physical therapy on home care visits. However, most evidence regarding the association between MPT and respiration is outdated[7-9)], and there are no studies on their measurement among current Japanese older adults requiring long-term care and support who might be eligible for home-care visits.

Due to changes in life expectancy and advances in equipment, the association between MPT and respiration

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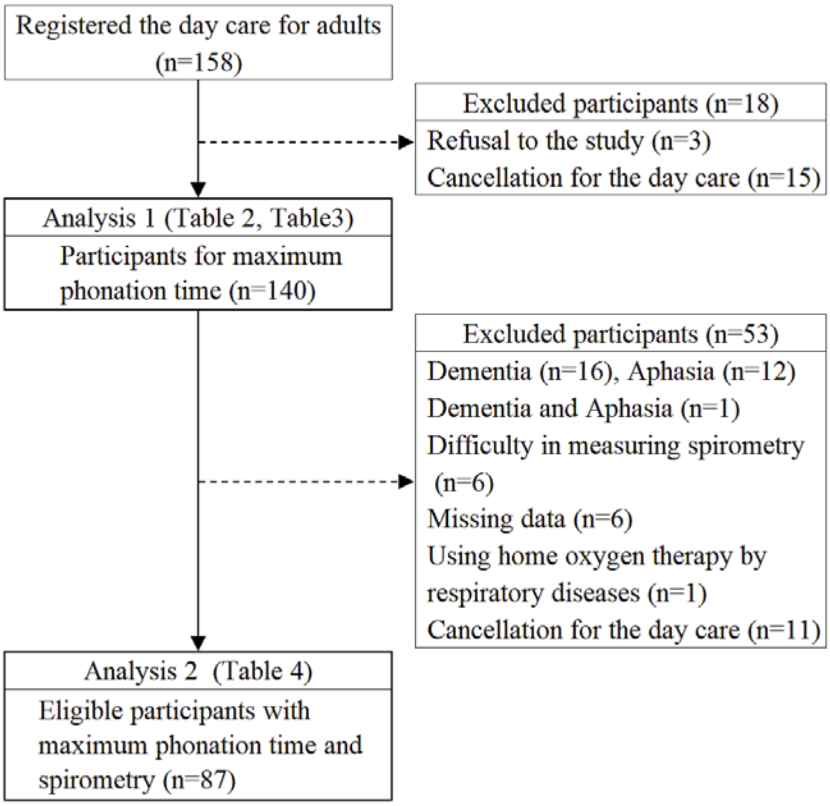

Fig. 1. Flow chart of participant selection

should be investigated in the current older population. As a preliminary study, we primarily investigated the association between MPT and respiratory function for the future utilization of simple respiratory assessments during physical therapy on home-care visits. Considering frequently reported in the past, we hypothesized that the association between MPT and respiration could be proven, even now, that life expectancy has increased.

Method

Study design

This cross-sectional study was conducted as a complete survey of daycare in March 2018, with the approval from the Ethics Review Committee of International University of Health and Welfare (approval number: 17-Io-189-7) in compliance with the Declaration of Helsinki. We recruited participants through announcements at the daycare center or through face-to-face encounters with their families. Written informed consent was obtained from all participants or their family members.

Participants

All participants were enrolled in a daycare facility through the Japanese long-term care insurance system. They were certified as requiring long-term care and support with similar care levels and physical function, such as those who receive home-care visits[10,11]. Our daycare services for older adults include rehabilitation, bathing, meals, and shuttle services to and from their homes.

Figure 1 shows the flowchart of the participants in this study. The inclusion criterion was age ≥60 years for the analysis of age groups. All 158 participants aged ≥60 years old in a single day care were included; however, three of them refused to provide consent, 15 skipped daycare for a long period. Finally, a total of 140 participants were included. The MPT was measured initially, followed by spirometry. Considering fatigue, MPT and spirometry were measured on separate days. A two-step analysis was used in this study. In the first phase, only MPT data from all consenting participants were analyzed. In the second phase, MPT and spirometry data were analyzed in 87 participants after applying the exclusion criteria. The exclusion criteria for spirometry were as follows: (1) those who had been diagnosed with dementia or aphasia; (2) required home oxygen therapy for severe respiratory diseases; and (3) difficulty in understanding detailed spirometry instructions, such as several repetitive breaths of varying intensities, despite the absence of dementia and aphasia.

Maximum phonation time

MPT measurements were performed in a sitting position while the vowel /a/ was pronounced, according to the methods of previous studies[13,14]. Measurements were taken twice, with ample breaks between them. The pitch and loudness of voice were set to a natural level, and the dura-

Table 1. Characteristics for participants

	Total (n=140)	Men (n=77)	Women (n=63)	P value
Age (years)	77.9 ± 8.0	76.6 ± 7.4	79.6 ± 8.4	0.023*
Height (cm)	157.3 ± 8.3	162.7 ± 6.2	150.7 ± 4.9	<0.001*
Body weight (kg)	55.6 ± 11.4	61.4 ± 10.0	48.6 ± 8.9	<0.001*
Body mass index (kg/m^2)	22.4 ± 3.7	23.2 ± 3.5	21.4 ± 3.6	0.003*
Certification level (1–7)	3 (3–4) †	3 (3–4) †	3 (3–4.5) †	0.852
Morbidity				
Hypertension	52	27	25	0.602
Dementia	17	8	9	0.605
Aphasia	13	9	4	0.383
Cerebrovascular dis	70	48	22	0.002**
Cancer	21	15	6	0.152
Intractable neurological dis	14	9	5	0.576

* Significant for un-paired t test.
** Significant for Fisher's exact test.
† Median (25 percentile–75 percentile). Ordinal scale with ranking 1 (mild) –7 (severe) by Japanese long-term care insurance.
Dis, diseases.

tion of phonation was measured using a stopwatch by the speech-language therapist[13,14]. The higher value of the two measurements was taken as the representative value.

Spirometry

Respiratory function was measured using a spirometer (Autospiro AS-507, Minato, Osaka, Japan) and an attached unit (AAM377, Minato, Osaka, Japan). The measured parameters were forced vital capacity (FVC), forced expiratory volume in one second (FEV 1.0), percentage (FEV 1.0%), peak expiratory flow rate, maximal expiratory pressure (PEmax), and maximal inspiratory pressure (PImax). The highest of the three measured values was taken as the representative value. Measurements were performed by a physical therapist following the guidelines[15].

Statistical analysis

Sex differences in characteristics were analyzed using an unpaired t-test, Mann-Whitney U test, and Fisher's exact test. Participants were then divided into three groups according to age: 60-69, 70-79, and ≥80 years old. The maximum values of MPT were analyzed using an unpaired t-test, one-way analysis of variance without repetition, and the Bonferroni method. The normal distribution of MPT values was confirmed using the Kolmogorov-Smirnov test/Shapiro-Wilk test. Next, to examine the relative reliability, the intraclass correlation coefficient (ICC) (1,1) of MPT for trials 1 and 2 was calculated for the total population, dementia, and aphasia groups. The association between MPT and respiratory function was analyzed using partial correlation and multiple regression analyses. Both partial correlation and multiple regression analyses were adjusted for sex, age, body mass index, certification level, and morbidity (cerebrovascular diseases, cancer, and intractable neurological diseases), which were expected to affect respiratory function decline[6,16-18]. MPT was the dependent variable, and respiratory function items were the independent variables for the stepwise method after considering multicollinearity. All statistical analyses were performed using IBM SPSS Statistics 25 (IBM, Tokyo, Japan), and the only power analysis was performed using G*Power version 3.1.9.2[19]. Statistical significance was set at $p < 0.05$.

Results

Table 1 shows the characteristics of the study participants. Table 2 lists the maximum MPT values according to age and sex. Significant age-related differences were found between the total study population and the male participants. Significant differences were found between men and women in the ≥80 years group. Table 3 shows that the ICC (1,1) was >0.8 for the total study population, dementia, and aphasia groups. Table 4 shows the association between MPT and spirometry. In the partial correlation analysis, MPT had a significant positive association with three respiratory parameters (FVC, FEV 1.0, and PEmax). Since the partial correlation coefficient between FVC and FEV 1.0 was 0.831, FEV 1.0 was excluded from the independent variables in the multiple regression analysis. In their analysis, MPT was associated with FVC only. The R square of the regression equation is 0.179.

Post-hoc power analysis was performed for ICC and multiple regression analyses. Regarding the ICC results, the power was 1.00 for each of the three groups in the bivariate

Table 2. Maximum value of maximum phonation time by age groups and gender (n=140)

	Total (n=140)		Men (n=77)		Women (n=63)		P value
	n	MPT (sec)	n	MPT (sec)	n	MPT (sec)	
60–69 years	17	16.8 ± 10.3	10	18.7 ± 12.7	7	14.2 ± 5.5	0.404
70–79 years	63	11.4 ± 5.9	40	10.8 ± 5.5	23	12.5 ± 6.4	0.256
≥80 years	60	11.2 ± 5.5	27	9.5 ± 6.0	33	12.6 ± 4.8	0.028*
Total	140	12.0 ± 6.6	77	11.3 ± 7.4	63	12.8 ± 5.5	0.208
P value	0.005**		0.002**		0.752		
60–69 vs 70–79 years	0.007***		0.006***		—		
60–69 vs ≥80 years	0.005***		0.002***		—		
70–79 vs ≥80 years	1.000		1.000		—		

* Significant for un-paired t test of men vs women.
** Significant for one-way analysis of variance without repetition among total, men and women included three age groups.
*** Significant for Bonferroni method.
MPT, maximum phonation time.

Table 3. Results of intraclass correlation coefficient for maximum phonation time

	Trial 1 (sec)	Trial 2 (sec)	ICC (1,1)	95%CI	P value
Total (n=140)	10.4 ± 5.6	11.2 ± 6.4	0.817	0.754–0.866	<0.001*
Dementia (n=17)	10.0 ± 4.2	10.5 ± 5.7	0.852	0.646–0.943	<0.001*
Aphasia (n=13)	9.8 ± 6.2	9.9 ± 6.2	0.903	0.722–0.969	<0.001*

* A p value < 0.05.
ICC, intraclass correlation coefficient; CI, confidence interval.

Table 4. Association between MPT and respiratory function without dementia and aphasia (n=87)

	Mean ± SD	Partial correlation		Multiple regression analysis		
		R	P value	β	95%CI	P value
FVC (L)	1.89 ± 0.66	0.370	0.001*	0.490	2.203–7.963	0.001*
FEV1.0 (L)	1.49 ± 0.60	0.278	0.013*	—		—
FEV1.0% (%)	79.1 ± 15.2	−0.083	0.462			
PEFR (L/sec)	3.21 ± 1.68	0.125	0.269			
PEmax (cmH_2O)	50.1 ± 22.0	0.241	0.031*			
PImax (cmH_2O)	37.2 ± 18.8	0.091	0.424			

* A p value < 0.05.
SD, standard deviation; CI, confidence interval; MPT, maximum phonation time; FVC, forced vital capacity; FEV1.0, forced expiratory volume in one second; PEFR, peak expiratory flow rate; PEmax, maximal expiratory pressure; PImax, maximal inspiratory pressure.

normal model of the Exact tests. For the linear multiple regression of F tests, the power was 0.86, based on an effect size of 0.22, calculated from the R square of the regression equation.

Discussion

Proving the reliability and association between MPT and respiration among older adults requiring long-term care and support will provide further evidence that it is an option for respiratory function assessment during physical therapy on home care visits. Therefore, we analyzed the following: (1) MPT with respect to age groups, (2) relative reliability of MPT values, and (3) the association between MPT and respiratory function.

We found that the MPT in older adults requiring long-term care and support had an ICC (1,1) of >0.8 for the total study population, dementia, and aphasia groups. This ICC means high relative reliability and corresponds to “good” or “great” from previous studies[13)]. There are some reports of high relative reliability of MPT in young and healthy older adults[13,20)]. Hence, MPT might be a relatively reliable assessment, even for older adults who have lower instructional understanding, such as those with dementia and aphasia. Due to the simplicity of MPT, it was possible to assess the MPT of almost all older adults, even those who needed care. When the same older adults requiring long-term care/support were evaluated, several of them could not perform tests for gait speed and body composition, which are typical findings on physical assessment[21)].

This study showed that MPT in older adults requiring long-term care or support was associated with FVC among various respiratory functions. Even with the current older adults and latest spirometry, this result was similar to previous reports including the 1960s-1980s, as expected[7-9,22,23)]. MPT could be an alternative method of measuring FVC during physical therapy on home care visits where spirometry is not available. However, the partial correlation coefficient and R^2 in this study were not high. Therefore, MPT is not a reliable representative of respiratory function. Since respiration is affected by a variety of explanatory variables, further analysis, especially on patient sex, is needed; this could be achieved by increasing the number of study participants.

In Japan’s aging society, aspiration pneumonia is associated with high mortality[2)]. In terms of swallowing factors, FVC is reportedly associated with aspiration pneumonia and peak cough flow, such as the index of cough strength[24,25)]. Considering the coordination and linkage between swallowing and respiration[26)], MPT could be useful as a comprehensive, simple assessment during physical therapy on home care visits.

During MPT in adults ≥65 years old, a review reported that (1) the decline of MPT with age was not clear, and (2) men had a longer MPT than women in all age groups[14)]. However, this study showed a significant age-related change in men and a significantly longer MPT in women aged ≥80 years. This result may be a characteristic of older adults requiring long-term care/support with comorbidities and disability.

This study has some limitations. First, MPT and respiratory function may be affected by diseases[6,16-18)]. However, considering the application to home-care visit users with multiple diseases and medical histories, participants with comorbidities who use home care visits were comprehensively included. Second, participants were excluded solely based on a diagnosis of dementia or aphasia, and the severity of these conditions was not categorized. In addition, since it was difficult to measure a large amount of data from real home-care visit users, daycare users with similar levels of physical function were included. In recent years, MPT has been used as a simple tool for several patients before and after surgery, as well as in patients with chronic diseases. Our study may be useful in general practice for older adults needing care. Further studies are needed to analyze the association between MPT and the history and development of aspiration pneumonia.

Conclusion

Based on the high relative reliability and association with FVC, MPT could be an alternative assessment of respiratory function in home-based physical therapy for older adults requiring long-term care and support.

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Conflict of Interest: None.

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PHYSICAL THERAPY RESEARCH

CASE REPORTS

Action Observation Training to Improve Activities of Daily Living and Manipulation Skills in Children with Acquired Brain Injury Secondary to an Oncologic Process: A Prospective Case Series Clinical Study

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ABSTRACT. Objective: Among solid tumours, medulloblastoma is the most common of the posterior fossa neoplasms, given that it represents 15%-20% of childhood brain tumours. The main aim of the present study was to assess the effects of action observation training on the activities of daily living (ADL) and the manipulation skills of children with acquired brain injury secondary to an oncological process. Methods: We recruited a consecutive convenience sample of 5 patients diagnosed with acquired brain injury secondary to an oncological process. ADL and manipulation skills were assessed using the ABILHAND-Kids and Jebsen-Taylor Hand Function Test, respectively. After conducting the initial evaluation, we planned the intervention, which lasted 10 weeks and consisted of 40 sessions for each participant, 10 in the occupational therapy department and 30 at home. After completing the intervention, we re-evaluated the main variables. Results: Overall, the results of the postintervention ABILHAND-Kids questionnaire showed a 5-point improvement, with a statistically significant difference and a large effect size. Eighty per cent of the sample showed better results in the total score, with differences between 4 and 8 points. In relation to manual dexterity, as measured by the Jebsen-Taylor Hand Function Test, there were no significant changes, except in one of the participants. Conclusion: It appears that action observation training can elicit positive changes with respect to the development of ADL, but the influence on manual dexterity was almost nonexistent.

Key words: Medulloblastoma, Action observation, Activities of daily living, Brain injury

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The Central Brain Tumor Registry of the United States reports that the incidence of medulloblastoma in patients up to 19 years of age is up to 48 for girls and 75 for boys per 100,000 patient-years and accounts for 16% of all paediatric brain tumours, with medulloblastoma accounting for 40% of all paediatric cerebellar tumours. The peak incidence of medulloblastoma occurs between 3 and 4 years of age and between 8 and 9 years of age [1)]. Each year in Spain, 1500 new cases of cancer are diagnosed in children younger than 15 years, 15%-20% of which are central nervous system tumours. The annual incidence of these tumours is 2-5 per 100,000, with a similar distribution for both sexes[2)].

Among solid tumours, medulloblastoma is the most

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common of the posterior fossa neoplasms, given that it represents 15%-20% of childhood brain tumours. The approach to these patients is multidisciplinary and begins with surgical resection, with the objective to establish a diagnosis and reduce the tumour volume. Subsequently, patients undergo radiotherapy and/or chemotherapy, the aim of which is to eliminate the cancer cells that persist after surgery and prevent a possible recurrence [3]. After the surgery phase, complications are treated in other departments, such as the paediatric intensive care unit and the rehabilitation unit. Although survival rates for this type of tumour are high, approximately 25% of survivors have motor and cognitive complications, including ataxia, balance problems, functional motor deficits, emotional lability and speech dysfunction, which typically appear between the first and second day after the surgery. Together, these symptoms comprise posterior fossa syndrome [4].

Among the most affected functional motor deficits are manual skills and abilities and the ability to perform activities of daily living (ADL), which are addressed by occupational therapy. Although few studies have described the role of occupational therapy in treating patients with brain tumours, it is important to achieving the maximum independence possible for children in terms of their ADL. Posture, movement and practical activities are compromised in children with acquired brain damage [5], which, together with sensory difficulties, makes it difficult for them to properly relate to their environment and they will therefore need help performing their ADL. The activities of occupational therapists are therefore essential in facilitating functional recovery, thereby helping children autonomously recover their abilities.

Movement representation techniques, such as action observation (AO) training, are a set of sensorimotor neurotraining tools widely employed in the field of neurorehabilitation [6]. AO training evokes an internal, real-time simulation of what the observer sees [7] and can lead to an activation of areas related to the planning, adjustment and automation of voluntary movements in a manner similar to when the movement actually occurs. AO has been previously proposed for arm motor rehabilitation after stroke [8] due to the neurophysiological properties of AO and its rehabilitative potential. Our hypothesis is that AO training can help improve ADL and manipulation skills in children with acquired brain injury secondary to an oncologic process.

The main aim of the present study was therefore to assess the effects of AO training on ADL and the manipulation skills of children with acquired brain injury secondary to an oncologic process.

Materials and Methods

Study Design

The present study was a prospective case series clinical study.

Participants

The study protocol was approved by the ethics committee of the Niño Jesús University Children's Hospital (Madrid, Spain; CI: R-0011/19). We recruited a consecutive convenience sample of 5 patients diagnosed with acquired brain injury secondary to an oncologic process, specifically a brain tumour (medulloblastoma), from the Niño Jesús University Children's Hospital. Prior to enrolment, all patients were explained the study's objectives and implications and agreed to participate by signing an informed consent document. We reviewed case records dated between October 2018 and June 2019.

The inclusion criteria for this prospective case series were as follows: age between 6 and 18 years; brain tumour diagnosis; undergoing partial or complete tumour resection surgery no more than 30 months prior to the completion of this project; undergoing oncologic therapy and standard occupational therapy at the Niño Jesús University Children's Hospital; an acquired brain injury as a consequence of the oncologic process; and a score of 1 or 2 on the Manual Ability Classification System (MACS). The exclusion criteria consisted of the following: level V in the Gross Motor Function Classification System; and the presence of moderate to severe cognitive and neuropsychological disorders according to the Wechsler Intelligence Scale for Children.

Procedures

The families attended an information session in which the project and steps to be taken in the coming months were explained. After obtaining the informed consent from the parents, we accessed each child's electronic medical records to collect the necessary information about them and their disease process. The data collected were age, gender, diagnosis, surgical interventions, neurological sequelae, use of drugs, arm involvement, dominance, cognitive level and whether they had been and/or were in a radiotherapy and/or chemotherapy programme.

The Data Protection Law (LOPD 3/2018) was always respected, as well as the European regulation (RGPD 2016/679) and rights. Once the necessary data had been collected, 2 chosen assessments were administered to determine the starting point of the patients' ADL performance, as well as the manipulation skills they presented at the start of the project.

We provided the families with the ABILHAND-Kids (AK) questionnaire. At the end of the questionnaire, the parents had to prioritise the five activities with which they felt their child had the most difficulties; these activities

Fig. 1. Intervention representation.

were addressed in the next phase of the project. If there were several activities with similar difficulty, those the parents considered most relevant in their child's environment or those of greatest importance were chosen. The Jebsen-Taylor Hand Function Test (JTHFT) was then administered.

After conducting the initial assessment, we planned the intervention, which lasted 10 weeks and consisted of 40 sessions for each participant: 10 sessions in the occupational therapy department and 30 at home, where the family conducted the same process performed by the occupational therapist in the department. Each of the 5 activities chosen by the family was performed during 2 consecutive weeks, so that the first activity was addressed during the first and second week, the second activity during the third and fourth week, the third activity during the fifth and sixth week, the fourth activity during the seventh and eighth week, and lastly the fifth activity during the ninth and tenth week. Each session lasted from 20 to 30 min. After finishing the intervention, the main variables were reassessed.

Intervention

The intervention we employed was AO training. For this purpose, a healthy boy and girl were recorded performing each of the activities in which the participants encountered difficulties. Each patient could choose whether they wanted to work with the boy's video or the girl's video during their intervention, depending on which gender they identified with more. The video was filmed from various perspectives (in third person in both the frontal and lateral plane and in first person). Figure 1 Intervention representation. shows an image of the videos employed in this preliminary study.

The video shows how the healthy boy or girl performs the complete activity and how they perform it by sequencing it in simpler motor acts. Each participant was given only those videos for the activities in which they encountered difficulties and were not given the videos of activities that were not worked on during the intervention. Each motor act was observed for 3 min. Once all the videos of the various motor acts had been watched, the patients had to perform all the activities observed in the videos without interruption.

The AO training was combined with other Physiotherapy and Occupational Therapy interventions. These are summarised in Table 1. The Physiotherapy interventions consisted of balance and postural control training, improved motor conditioning and strength exercises, as well as the vestibular system training. Two of the patients received one Physiotherapy session per week, another patient 2 sessions, another 3 sessions and finally the last one did not receive Physiotherapy. Regarding Occupational Therapy, three of the patients did not receive any intervention and the remaining two patients received one session per week. The Occupational Therapy intervention was based on manual dexterity training and motor control tasks oriented to ADL.

Outcome Measures

ABILHAND-Kids

The AK scale assesses the perception of manual ability of children with cerebral palsy in performing the ADL determined in the scale. In total, the scale contains 21 activities classified into 4 separate levels: question mark (not applicable), impossible, difficult and easy. For the paediatric population, the questionnaire is answered by the parents, who provide their perception of their child's manual ability difficulty when performing the proposed ADL. The AK scale shows excellent internal consistency (α=0.94) and test-retest reliability (Pearson's r=0.91)[9]. This scale has also shown adequate convergent validity with respect to the MACS test (r=0.88)[10]. Questionnaires that measure the functional abilities of children through their parents have been shown to be important in the evaluation of clinical changes. This is because children present a more dichotomous perception of their own abilities, allowing the measurement of ability but not of daily performance[11,12].

In the present study, the 21 items of the scale were not evaluated. Instead, parents were asked to indicate, among the 21 activities, the five that presented the greatest difficulties for the children, which were the therapeutic target of the subsequent intervention. Therefore, the results are shown in terms of time required to perform the activity, rather than the degree of performance. These activities could coincide among different children and, were the target of the subsequent intervention.

Jebsen-Taylor Hand Function Test

The JTHFT test measures the time it takes the child to perform each task with both the affected and unaffected arm. The objective of the JTFHT is to assess uni-manual hand functions necessary for activities of daily living. The test consists of 7 subtests, performed with both the non-

Table 1. Sample description and sociodemographic characteristics.

Case	Gender	Age	Affected upper limb	Dominance	Current chemotherapy	Pharmacological therapy	Physical therapy	Occupational therapy (out of study)	Disease staging	Grade of motor paralysis and ataxia	Presence of ocular movement disorders
1	Female	10	Right and Left	Right	Cyclophosphamide	Celecoxib Fenofibrate Thalidomide Cytarabine	1 session/week Postural control and balance treatment. Vestibular retraining	No Only AO treatment of the project	Stage IV	Hemiparesis. Severe global ataxia	Strabismus
2	Female	8	Left	Right	No	No	2 sessions/week Global and selective motor treatment. Physical conditioning, strength training	1 session/week Manual dexterity treatment, bimanual activities, task-oriented motor control for daily living tasks	Stage I	Hemiparesis. Mild global ataxia	Strabismus
3	Female	8	Left	Right	No	Valtrex	3 sessions/week Postural control and balance treatment. Vestibular retraining	1 session/week Manual dexterity treatment, bimanual activities, task-oriented motor control for daily living tasks	Stage II	Hemiparesis. Severe global ataxia	Strabismus Nistagmus
4	Male	7	Left	Right	Cyclophosphamide Etoposide	Cytarabine Neupogen Avastin Bevacizumab	No	No Only AO treatment of the project	Stage IV	Hemiparesis. Severe global ataxia	Strabismus
5	Male	11	Left	Right	No	No	1 session/week Global and selective motor treatment. Physical conditioning, strength training. Pain approach	No. Only AO treatment of the project	Stage I	Hemiparesis. No ataxia.	No

AO, action observation

dominant and dominant hand: writing, turning letters, picking up small objects and placing them in a container, stacking chips, stimulated feeding, and moving light and heavy objects[13]. In this study, all items were tested except writing. There is evidence that the JTHFT is a valid assessment tool for children aged 6 to 18 years with brain injury[14]. The JTHFT is reliable in a brief assessment period in children with brain injury and is responsive to changes in a brief period of intensive therapy. The minimal clinically important difference (MCID) is 54.7 s in the affected limb[15].

Data Analysis

We analysed data from the 5 patients using IBM SPSS Statistics ver. 25.0 (IBM Co., Armonk, NY, USA). We employed descriptive statistics to summarise the data of the continuous variables, which are presented as mean ± standard deviation and a 95% confidence interval. We employed Student's t-test to compare the outcomes of the continuous variables, calculating the effect sizes (Cohen *d*) for the outcome variables. According to Cohen's method, the magnitude of the effect was classified as small (0.20-0.49), medium (0.50-0.79), or large (≥0.8). A value of $p < 0.05$ was considered statistically significant[16].

Results

Our sample was composed of 5 patients (3 girls and 2 boys), with a mean age of 8.8 years (range 7-11 years) and a common medical diagnosis of medulloblastoma. After surgery, the patients presented hemiparesis, with predominant involvement of the left arm. The entire sample underwent radiotherapy and chemotherapy. Currently, none of the patients are undergoing radiotherapy, although 40% are still undergoing chemotherapy. In terms of other drugs, 60% of the sample continues with pharmacological therapy (Table 1), and none of the participants were treated with botulinum toxin. In individual terms, Table 2 shows the preintervention and postintervention data.

Case 1

For this patient, the 5 most difficult ADL were buttoning up a shirt, opening a bag of potato crisps, unwrapping a chocolate bar, opening a jam jar and unscrewing a bottle cap. After the treatment, the times for all of the activities were reduced. The most significant time differences were the activities of buttoning up a shirt and unscrewing a bottle cap, which took 56 and 98.2 s less, respectively. Moreover, after administering the AK post-treatment scale, we observed a score increase of 5 points. In terms of the JTHFT results, there was an increase in time with respect to the preintervention results, indicating no improvement in manipulation dexterity.

Case 2

The 5 ADL that the patient had the most difficulty with were buttoning up a shirt, opening a bag of potato crisps, buttoning up the trouser buttons, buttoning up a jacket and unscrewing a bottle cap. The participant managed to reduce the times for all the trained activities during the intervention, with a marked reduction in time spent buttoning up a shirt (37 s) and unscrewing a bottle cap (128.1 s). In the postintervention assessment, the increase in AK score indicated that the performance of the proposed activities had improved (by 4 points). As for the JTHFT results, there was no demonstrated improvement in manual dexterity.

Case 3

The 5 ADL that the patient had the most difficulty with were buttoning up the trouser buttons, sharpening a pencil, putting toothpaste on a toothbrush, filling a glass of water, and unscrewing a bottle cap. The time was also reduced for all activities in which the intervention was performed. There was a marked reduction in the time to button up trouser buttons (25.7 s) and unscrew a bottle cap (48.7 s). The AK results also confirmed that the performance of these activities had improved by 8 points, a result that was the highest in the entire case series. As in the previous cases, the JTHFT results showed no change in manipulation dexterity.

Case 4

The 5 most difficult ADLs for this patient were buttoning up a shirt, opening a bag of potato crisps, buttoning up the trouser buttons, sharpening a pencil and filling a glass of water. In this case, there was a considerable decrease in the time spent on 3 of the 5 activities addressed during the intervention: buttoning up the shirt, buttoning up the trouser buttons and opening a bag of potatoes (improvement of approximately 8, 6 and 1 min, respectively). In the post-intervention assessment on the AK scale, there was a 7-point increase, which confirms that the performance of the addressed activities after the intervention had improved. In terms of the JTHFT results, this is the only participant who showed reduced time spent on the test (approximately 1 min) compared with the initial assessment.

Case 5

The 5 ADLs where the patient presented the most difficulties were buttoning up a shirt, buttoning up the trousers, opening a toothpaste dispenser, sharpening a pencil, and opening a bread bag. The time spent on these tasks improved but to a lesser extent than the other cases. The activities in which the patient managed to reduce the time spent the most were buttoning up a shirt and opening a bread bag (19.5 and 10.9 s, respectively). In terms of the AK results, there were no differences compared with the re-

Table 2. Preintervention and postintervention data.

Measure	Selected AK Activities of Daily Living												AK t	JTHFT
	Button shirt	Potato bag	Trouser button	Button jacket	Unwrap chocolate	Jam jar	Bottler cap	Open tooth paste	Open bread	Remove tip	Pour tooth paste	Fill glass		
Case 1														
Initial	168.0	28.0	-	-	20.1	12.1	116.0	-	-	-	-	-	78	219.1
Middle	140.0	19.3	-	-	15.2	8.7	124.9	-	-	-	-	-		
Final	112.0	10.6	-	-	10.3	5.3	17.8	-	-	-	-	-	84	269.1
Final-Initial difference	-56.0	-17.4			-9.8	-6.8	-98.2						6	50
Case 2														
Initial	104.9	7.6	14.1	15.0	-	-	136.0	-	-	-	-	-	77	170.2
Middle	85.95	7.35	11.55	13.5	-	-	71.95	-	-	-	-	-		
Final	67.0	7.1	9.0	11.7	-	-	7.9	-	-	-	-	-	81	194.9
Final-Initial difference	-37.0	-0.5	-5.1	-3.6			-128.1						4	24.7
Case 3														
Initial	-	-	35.5	-	-	-	90.0	-	-	14.8	28.5	17.9	71	329.7
Middle	-	-	22.65	-	-	-	65.65	-	-	13.4	27.0	17.65		
Final	-	-	9.8	-	-	-	41.3	-	-	12.0	25.5	17.4	79	394.8
Final-Initial difference			-25.7				-48.7			-2.8	-3.0	0.5	8	65.1
Case 4														
Initial	694.0	82.0	359	-	-	-	-	-	-	14.4	-	26.2	65	526.7
Middle	440.5	49.45	189.5	-	-	-	-	-	-	12.5	-	25.15		
Final	187.0	19.9	20.0	-	-	-	-	-	-	9.9	-	24.1	72	464.8
Final-Initial difference	-507.0	-65.1	-339.0							-4.5		-2.1	7	-61.9
Case 5														
Initial	77.0	-	5.8	-	-	-	-	10.3	28.8	13.3	-	-	84	137.6
Middle	67.25	-	5.65	-	-	-	-	9.05	23.3	12.2	-	-		
Final	57.5	-	5.5	-	-	-	-	7.8	17.9	11.1	-	-	84	164.3
Final-Initial difference	-19.5		0.3					-2.5	-10.9	-2.2			0	26.7
Mean±SD														
Initial													75.00±7.24	276.66±157
Final													80.00±4.95	297.58±128.97
Mean difference SD (95%)													5.00±3.16	20.92±49.25
P value													0.024*	0.396

AK, ABILHAND-Kids questionnaire; AK t, ABILHAND-Kids time in seconds to perform the activity; JTHFT, Jebsen Taylor Hand Function Test; SD, standard deviation

Note: *P<0.05

sults of the preintervention assessment. As to the times obtained in the JTHFT, there was an increase compared with the pre-intervention assessment. Regarding adherence, all patients completed all OA training sessions. Adherence was complete in all cases.

Statistical Analysis

Regarding the AK variable, statistically significant pre- and post-intervention differences were found with a large effect size (p=0.024 *d*=-0.80; t=2.04) (Table 2). However, with regard the JTHFT variable, no statistically significant differences were found (p=0.396) (Table 2).

Discussion

The main aim of the present study was to assess the effects of AO training in ADL and manipulation skills in children with acquired brain injury secondary to an oncologic process. Overall, the results of the postintervention AK questionnaire showed an improvement of 5 points, with a statistically significant difference and large effect size. Eighty per cent of the sample showed better results in the total score, with differences between 4 and 8 points. The remaining 20% (1 child) obtained identical results for the pre-intervention and postintervention assessments. After the intervention, all the sub-tasks trained with the AO approach showed better results in terms of execution time. In relation to manual dexterity as measured by the JTHFT, there were no significant changes except in one of the participants.

All 5 participants were administered a therapeutic intervention of 20 h, distributed over 10 weeks. All participants demonstrated significant changes in trained ADL through the AO technique as measured by the AK. The study by Bleyenheuft et al. of a cohort of 80 children with unilateral cerebral palsy undergoing intensive interventions showed (through the AK questionnaire) improvements in all participants, which was greater in magnitude in the younger children (6-12 years) and with MACS levels above II[17]. Although the clinical diagnoses of the 2 studies differed, our participants had MACS levels between I and II, as well as ages between 7 and 11 years. These changes could be explained by the greater neuroplastic capacity at earlier stages of progression and at younger ages.

In addition, our results only showed significant changes in manual dexterity in 1 patient, with no correlations with ADL performance as measured by AK and manual dexterity. The study conducted by Bleyenheuft et al. showed similar results[17]. It is important to stress that the MCID for the JTHFT in children aged 13-19 years is 54.7. Given that our sample's mean age was 8.8 years (7-11 years) we cannot dispute these data. Regardless, the variations in our study participants do not reach these differences in their pretreatment and post-treatment differences, except for one of the participants, whose results exceeded the MCID.

Another important aspect in our intervention is the focus on goals chosen by the children, increasing their motivation with task-oriented training and participation. For Novak et al., task-oriented, goal-directed training and home programs are highly recommended interventions for children with neuromotor impairment due to cerebral palsy[18].

AO training is a sensorimotor neurotraining tool focused on provoking neurophysiological changes at the cortical level, that is, favouring a process of neuroplasticity with respect to the processes related to the planning, adjustment and automation of voluntary movements[7]. In this population, it is important to be able to implement these techniques, known as movement representation methods, to elicit greater neurophysiological activity at the cerebral level. A recently published umbrella review with the statistical aggregation of meta-analytic results showed that movement representation methods such as AO training and motor imagery could elicit an improvement in ADL in a population with neurological conditions[19], which agrees with the findings in this case series study. ADL, as with any task that is amenable to a learning process, can derive benefits from AO training. For example, Cuenca-Martínez et al. found that AO training alone is an effective method for learning manual gestures for at least 4 months after completion of the intervention[20]. There is ample evidence to support the use of movement representation methods to elicit a specific motor learning process[21-23].

The recent study conducted by Buccino et al. showed the efficacy of a 3-week intervention with AO for the rehabilitation of arm motor functions involved in ADL[24]. The sample included children with cerebral palsy aged 5 to 11 years, who when treated showed increased neurophysiological activation of a parietal-premotor circuit for hand-object interactions. In addition, changes were found through neuroimaging in the left and right premotor cortex, left supramarginal gyrus and left superior temporal. Our therapeutic intervention had to be adapted to the contextual conditions and to be able to intervene in a larger number of ADL.

Limitations

This study has several important limitations that need to be considered. First, this is a case series, and all results should be taken with caution due to the small sample size. It is likely that the results could vary significantly with a larger sample. Second, due to the type of disease, the children underwent other medical interventions that might have influenced the results. We collected only the information that was reported, but this should be considered as highly important confounding variables. In addition, 1 child underwent occupational therapy outside the study, which might also influence the results, making them difficult to attribute to the intervention alone. Finally, basic, and instrumental skills were not assessed, only manual dexterity. Future studies should assess the overall ADL for each patient.

Conclusions

Based on the results, it appears that AO training could elicit positive changes with respect to the development of ADL, but there was almost no influence on manual dexterity in the patients diagnosed with acquired brain injury secondary to an oncologic process. Although these conclusions are valid for a series of 5 cases, the results should be taken with great caution.

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