Exercises utilizing the Hybrid Assistive Limb lumbar type to prevent frailty: a randomized controlled trial

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Abstract

Background: Sarcopenia and frailty often worsen in older adults because of declines in activities of daily living and social connections that are associated with chronic diseases and traumatic injuries such as falls and fractures. Exercise intervention for sarcopenia can take more than three months to improve muscle mass, muscle strength, and walking speed. Thus, a specialized intervention system for shorter periods of time is needed. This study aimed to examine the short-term efficacy of an exercise program utilizing the wearable cyborg Hybrid Assistive Limb (HAL) lumbar type on physical function and frailty prevention.

Methods: This randomized, single-blind, parallel-group study involved 79 community-dwelling older adults with physical frailty or locomotive syndrome assigned to an intervention group (40) with the HAL lumbar type exercise program or a control group (39) without the exercise program. The intervention group underwent trunk training (including trunk and hip flexion, standing and sitting from a single sitting position, and squats) and gait training (treadmill and parallel bars) twice a week for 5 weeks while wearing the HAL lumbar type. The 10-m usual and maximum walking speeds, Timed Up and Go test, 5-times chair-standing test, 5-question Geriatric Locomotive Function Scale (GLFS-5), body-fat percentage, and muscle mass were measured before and after the intervention and analyzed using the intention-to-treat method.

Results: The intervention (23% male; mean age, 74.7±4.7 years) and control (21% male; mean age, 75.1±4.1 years) groups did not differ significantly in baseline characteristics. Seventy-seven participants completed the program; two withdrew for personal reasons. The mean difference (standard error) between the groups for the primary outcome (usual walking speed) was 0.35 (0.04) m/s; the time-by-group interaction was significant ($p<0.001$). Secondary outcomes (maximum walking speed, Timed Up and Go test, 5-times chair-standing test, and GLFS-5) were significantly improved in the intervention group. Body composition was unchanged in both groups.

Conclusions: In community residents with physical frailty and locomotive syndrome not requiring nursing care, a 5-week exercise program using the HAL lumbar type is a promising option for frailty prevention, improving physical function and resulting in clinically meaningful improvements in most physical functions over a short time period.

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Keywords: biofeedback, exercise, frailty, Hybrid Assistive Limb, physical function, sarcopenia

Background

Frailty and sarcopenia are considered major public-health challenges [1-3]. In recent years, frailty has been recognized as a multidimensional phenotype that includes physical, psychological, and social frailty [4, 5]. Furthermore, it has been suggested that sarcopenia is a major component of physical frailty. As there has been an increased focus on the optimization of exercise interventions for preventing frailty and sarcopenia in older adults, there have also been growing expectations for the development and implementation of robot-based exercise programs [6-8]. The Hybrid Assistive Limb (HAL) (Cyberdyne, Japan) is the world's first wearable cyborg. It is characterized by its human-machine fusion technology that facilitates movement via bioelectric potential signals, which are movement commands transmitted from the brain and spinal cord to the muscles when the user attempts to move their body, thereby reflecting their will to move [9]. This technology enables the user to learn how to move their body and apply their strength in real time. To date, three types of HALs have been developed: lower-limb, single-joint, and lumbar types. Previous studies with the HAL lower-limb type have reported improved function, even in chronic stages of spinal cord injury [10], stroke [11, 12], cerebral palsy [13, 14], and progressive neuromuscular disease [15].

The HAL lumbar type used in this study was initially developed to reduce caregiver burden [16]; it is more compact and easier to handle than the conventional lower-limb type, and its application to patients is underway. Previous studies have investigated the efficacy of rehabilitation programs for patients with heart failure [17], as well as exercise training for patients with Parkinson's disease [18]. The effects of exercise therapy with the HAL lumbar type have been explored for a wide range of outcomes; these include studies monitoring the worsening of low-back pain and adverse events [7], immediate changes in low-back pain and hip flexibility [8], and cardiopulmonary strain during squatting exercises [19]. Nevertheless, most of these studies have been conducted in symptomatic patients. Confirmation of the efficacy of the HAL lumbar type in preventing frailty would justify its deployment at relevant facilities (e.g., nursing homes) and in the community.

In preparation for this randomized controlled trial (RCT), we conducted a feasibility study among 22 frail and pre-frail community residents (mean age=72.6 years) in 2019. The primary endpoint was the completion rate; the secondary endpoint was the 10-m usual walking speed. The majority of the participants (20 of 22) were able to

complete the 10-week program of 20 exercise sessions; 2 participants withdrew from the study owing to knee and hip pain. No other significant adverse effects occurred during the program. Pre- and post-program comparisons among those who completed the program showed a significant increase in the usual 10-m walking speed, as well as a trend for improvement in exercise self-efficacy. These results indicated the feasibility of an exercise program using the HAL lumbar type for improving walking speed, which is an indicator of physical frailty.

As life expectancy increases among older adults, there is a corresponding need to extend healthy life expectancy and maintain physical, mental, and social health over the life course. Chronic diseases, new illnesses, and traumatic injuries (e.g., fractures caused by falls) occur more frequently with age, and these events can lead to a decline in activities of daily living and social connections [1]. Declines in physical activity and fitness may also be exacerbated by family events. In a meta-analysis of exercise interventions for sarcopenia, the duration of trials that improved muscle mass, muscle strength, and walking speed was 3 months or longer [20]. Therefore, it is important to have an established professional intervention system that can be enacted for short periods of time when needed. This study aimed to examine the short-term efficacy of an exercise program utilizing the wearable cyborg HAL lumbar type on improving physical function and preventing frailty.

Methods

Study design

This study used a randomized, single-blind, parallel-group design. Study participants were assigned by a stratified block randomization method using a computerized random number generation program. Each block was set to four participants per sex, and the participants were randomly assigned to the intervention and waitlist control groups in the order of enrollment (Figure 1). As the intervention program was expected to be effective, a waitlist control group was established for ethical considerations.

Third-party allocation was used to assign study participants, and researchers responsible for data analysis were blinded to group assignment. Outcomes were assessed by staff who administered the exercise program at the facility. As it was difficult to blind measures in this study, program implementation and outcome assessment were assigned to different staff members for each participant to reduce bias to the extent possible. Outcomes were measured before and after the 5-week intervention period.

Participants

We recruited participants via public relations magazines and flyers. This was done with the cooperation of relevant sections of Fujisawa City Hall and Kamakura City Hall in Kanagawa Prefecture, senior citizen facilities, exercise facilities, senior clubs, social welfare councils, and local media. Inclusion criteria were as follows: participation in the Kanagawa Prospective "ME-BYO" Cohort Study[21, 22]; men and women aged 65–85 years; participants able to wear the HAL (standard body size for HAL: height, 140–180 cm; weight, ≤80 kg); cutoff score of ≥6 on the 5-question Geriatric Locomotive Function Scale (GLFS-5) [23, 24] or usual walking speed <1.0 m/s; and participants not certified for long-term care. Participants were excluded if they (1) did not provide informed consent; (2) had difficulty completing the questionnaire; (3) had difficulty communicating in Japanese; (4) had difficulty wearing HAL owing to body-size discrepancies (e.g., in terms of weight, thigh length, lower leg length, or waist width) or major body deformities; (5) were judged by a physician as unsuitable for wearing or using HAL (e.g., owing to the inability to perform standing/walking exercises); (6) were unable to apply electrodes (e.g., due to skin diseases or allergies); (7) were unable to use fall prevention measures in combination; or (8) were deemed unsuitable for the intervention program in view of the physical and psychological burden that they may be subjected to.

The sample size calculation was based on the results of a 10-m usual walking speed by a feasibility study conducted in 2019. We estimated that a sample size of at least 74 participants was required to detect differences between groups, while accounting for 80% power, an effect size of 0.66, and a two-sided $\alpha = 0.05$. The final sample size was set at 80 participants, in anticipation of dropouts during the course of the study and situations where several applicants signed up at the same time.

While a total of 20 exercise sessions were provided during the feasibility study, improvements were apparent after the completion of 10 sessions. Therefore, in this study, the sample size in the 10-times program was calculated to examine the effect of a shorter period of time.

Exercise program utilizing the HAL lumbar type to prevent frailty

The wearable cyborg HAL lumbar type (HAL-FB02, Cyberdyne Inc., Ibaraki, Japan) has two modes. The Cybernic Voluntary Control (CVC) mode provides appropriate motion assistance based on the intensity of biopotential signals generated according to the user's intention to move. This mode assists the user's movements in accordance with their pre-programmed posture. The Cybernic Autonomous Control mode can support the user's weight for reducing

movements caused by trunk flexion as a gravity-compensation algorithm. Biopotential signals emitted from the body are detected via electrodes set on the user's waist. The detected bio-signals are processed by the built-in computer in HAL, and the power unit in the hip joint is operated by adjusting the level and timing of the assist torque according to the user's intention to move, thereby supporting their movement. The CVC mode was used during training with HAL; the assist torque at the hip and lower back was controlled by triggering the bioelectric potential signal generated by the voluntary muscle contraction of the user. At the start of training, the HAL assist level was optimally set to provide good motion support.

Training was conducted twice a week for a total of 10 sessions. The training was conducted to the extent that good automatic movement could be maintained during assisted standing. The program was conducted by a HAL specialist trainer and a physical therapist. An initial assessment of the participants' activities of daily living was conducted prior to the start of the program, which consisted of walking training on a treadmill and parallel bars, as well as training (trunk and hip flexion, standing and sitting from a single sitting position, squats, and lunges), while wearing HAL. The basic flow of each 90-min training session was as follows: (1) vital check, 10-m walk; (2) stretching; (3) warm-up (walking); (4) exercise using the HAL lumbar type; (5) cool down; and (6) 10-m walk. Exercises using the HAL lumbar type were performed for a maximum of three sets with a 30-second rest between sets at a load that allowed 15 repetitions per set for each exercise.

The exercise program consisted of 10 sessions divided into three STEPs: STEP1 (early program), acquisition of movement form; STEP2 (mid-program), appropriate and progressive increase in load; and STEP3 (late program), acquisition of decreased function. In addition, the program disciplines and their application levels were selected according to each participant's level of physical function, such as strength and functional disability (Figure 2,3,4). No specific intervention was provided to the control group.

Outcome measures

The following assessments were conducted before the intervention program, at the end of the program, and 6 months after the program began. The primary outcome was the 10-m usual walking speed (m/s) [25]. The participants walked 10 m at their usual speed and the time required was measured once with a stopwatch after a practice trial; the instruction given to the participants was “walk at your usual walking speed.” Exercises were performed on a flat indoor area. The time was recorded when the toes of either foot crossed the line between the start and end points. The walking

speed of participants who were clearly too fast or too slow compared to their usual walking speed was re-measured. The time required was measured to the nearest 1/100th of a second. The walking speed was calculated by dividing the distance (10 m) by the time required and expressed in m/s.

Secondary outcomes included the following assessments of physical function: 10-m maximum walking speed (m/s) and walking cadence (usual and maximum) (steps/min), Timed Up and Go (TUG) test (s), two-step test (score), 5-times chair-standing test (s), Functional Reach Test (cm), grip strength (kg), Berg Balance Scale (BBS) (score), and GLFS-5 (score). Body composition was evaluated using the following parameters: body mass index (BMI) (kg/m^2), fat (%), and muscle mass (kg).

The 10-m maximum walking speed was assessed by asking the participant to walk for a distance of 10 m at maximum speed and measuring the time required [25]. The instruction was to "walk as fast as possible"; other aspects of this test were identical to those of the 10-m usual walking speed assessment. The walking cadence was determined by dividing the number of steps taken during each of the usual and maximum10-m walk tests by each walking speed (min).

For the TUG test, participants were instructed to get up from the chair, walk a distance of 3 m as quickly as possible, change direction, and return to the chair to sit down [26]; participants were instructed not to run. Two trials were performed, with the shorter time being used for analysis. The time (s) required was measured with a stopwatch.

In the two-step test, the maximum two-step distance (cm) was measured when the participant took two steps forward with maximum effort. This distance was then divided by the participant's height (cm) to obtain the two-step test score [27-29]. The two-step test was performed three times in succession; the first trial was excluded as a practice run, and the average value from the second and third trials was used as the representative value.

The 5-times chair-standing test (s) required participants to stand up from a chair without arms and sit down as quickly as possible. The time required for the participant to perform this action five times was measured using a stopwatch [30].

The Functional Reach Test [31] was performed using a measuring stick. Participants stood upright and held their right arm horizontally, with the left hand placed at the side of the body (basic posture). They were then instructed to extend their right hand as far forward as possible. Two trials were performed with a short break in between, and the highest value obtained was used for the analysis.

Grip strength was measured using a Smedley grip strength meter (TKK5401, Takei Kiki Kogyo Co.). After a short

rest, two maximal effort trials were performed separately for the left and right sides. The average of the higher values on the left and right sides was used for analysis.

The BBS was used to evaluate the participants' ability to balance. It consists of 14 items rated on a 5-point scale (from 0 to 4) and has a maximum score of 56 [32, 33]. The GLFS-5 includes five questions that assess locomotive syndrome severity. A 5-point Likert scale is used, with the total score ranging from 0 to 20. The higher the score, the greater the severity of locomotive syndrome; scores of 6 or more were judged to be positive for locomotive syndrome [23, 24]. BMI was recorded, and body composition (fat [%], muscle mass [kg]) was measured with a body composition measuring device (Inbody430, InBody Co., Ltd.).

Statistical analysis

Unpaired t-tests and χ^2 tests were used to compare participant characteristics between groups before the intervention. Repeated measures two-way analysis of variance was used to determine effect sizes (partial η2), and group-time interactions were examined for all outcomes. Intention-to-treat analysis was used to examine the minimal effect of the program. Specifically, baseline values were inserted for missing values (last observation carried forward approach). All statistical analyses were conducted with IBM SPSS Statistics Ver. 27 (IBM Corp, Tokyo, Japan). The level of statistical significance was set at 5%.

Results

Participant characteristics

Figure 1 shows a flowchart of this RCT. In total, 79 participants were recruited and allocated to intervention and control groups. There were no significant differences in baseline characteristics between the two groups (Table 1). No serious adverse events such as accidents, fractures, hospitalization or death occurred during the program. Of the 79 study participants, 77 completed the program. Two participants (one person each in the intervention and control groups) withdrew from the study owing to personal reasons.

Primary outcome

The mean usual walking speed approximated the frailty criterion (<1.0 m/s) in both groups before the intervention. After the program, the usual walking speed (mean [95% confidence interval]) in the intervention group increased to

1.43 [1.35, 1.51] m/s. The difference in the mean (standard error) change between the intervention and control groups was 0.35 [0.04] m/s; the time-by-group interaction was significant (Table 2).

Secondary outcomes

In terms of physical function, the intervention group exhibited significant improvements in all categories, except for functional reach and grip strength. No changes in body composition were observed in either group (Table 2).

Discussion

This study examined the effects of a 5-week exercise program using the wearable cyborg HAL lumbar type to prevent physical frailty in older adults. Most physical functions improved significantly in the intervention group. The mean difference in usual walking speed (mean [standard error]) was 0.35 [0.04] m/s. The minimum clinically meaningful change in usual walking speed is 0.05 m/s, and a change of 0.10 m/s is considered substantial [34]. Thus, the amount of change in the intervention group was well above the clinically meaningful change. Furthermore, the fact that all participants completed the scheduled twice-weekly exercise sessions (for a total of 10 sessions) without any adverse events reflects the overall safety of the exercise program.

Few investigations of the HAL lumbar type have used rigorous study designs such as RCTs. In a previous RCT, 28 patients with chronic heart failure underwent cardiac rehabilitation therapy (sit-to-stand exercises repeated over 6–10 days) with or without HAL [17]. While the Short Physical Performance Battery and 6-min walking distance were significantly improved in both groups, the knee extensor muscle strength was only improved in the HAL group. The increase in lower extremity muscle strength was not due to muscle hypertrophy but was attributed to neurological factors such as an increased discharge rate of motor units. A study of a 5-times-weekly exercise program conducted among 16 frail older adults (eight each with Parkinson's disease and non-Parkinson's disease) who had experienced gait disturbance showed significant improvements in physical function (as reflected by gait speed, the TUG test, and the chair-standing test) in both groups [18]. Limitations of this previous study included the small sample size and the use of convenience sampling.

To date, studies using the HAL lumbar type have primarily focused on the administration of rehabilitation programs, and the lack of validation of HAL efficacy with high-quality research designs has been a challenge. In the present

study, we were able to clarify the effectiveness of the HAL lumbar type in preventing frailty by conducting an RCT on physically frail older adults who were not certified as nursing care recipients.

All secondary outcomes, with the exception of grip strength, functional reach, and body composition, improved significantly in the present study. In the 5-times chair-standing test used to diagnose Asian Working Group for Sarcopenia 2019 [35], the intervention group's preintervention although the mean value was equivalent to the standard of 12 s or more, it improved to 9.2 (95% confidence interval: 8.4, 10.1) s after the intervention. The difference in change (mean [standard error]) between the intervention and control groups was -1.7 [0.6] s, and the time-by-group interaction was also significant. These results suggest that voluntary performance was improved following the short 5-week program. The immediate improvement in physical function with this short-term intervention may be due to the fact that appropriate instruction in physical movement form, as well as low-impact, high-frequency voluntary exercise with HAL, induced nervous system signals to the muscles; this is supported by the results of previous studies [7, 8, 18].

This study also used GLFS-5 to evaluate leg and back pain. The mean value of GLFS-5 was above the cutoff value for locomotive syndrome (6 points) in both groups before the intervention. After the intervention, the mean [95% confidence interval] for the intervention group was 4.4 [3.3, 5.4] points and below the cutoff value. The difference in change (mean [standard error]) from the control group was -3.3 [0.4] points, and the time-by-group interaction was also significant. In a prior before-and-after comparison study [7], 33 participants with locomotive syndrome underwent training with the HAL lumbar type three times a week for 4 weeks; significant improvements were observed in the Visual Analog Scale for pain. The authors considered that HAL, which can detect nerve and muscle action potentials in the lumbar erector spinae muscles and support the user's movements by adjusting the level and timing of torque, as well as coordinate voluntary joint movement via the user's intention, was able to induce positive feedback on the nerves and muscles [7]. Thus, it is expected that individuals who use HAL would not be affected by flail and locomotive syndrome, which are reversible conditions in the short term. Furthermore, these individuals would likely have increased mobility and less pain, thereby leading to increased self-efficacy in exercise participation and improved engagement in social activities.

A strength of this study was the use of a randomized controlled design. Indeed, no prior RCTs have been conducted on the HAL lumbar type, which has been primarily utilized in rehabilitation programs. Furthermore, this study was

able to demonstrate clinically meaningful improvements in both primary and secondary outcomes in the short period of 5 weeks.

This study had several limitations. First, outcome assessors were not blinded to group allocation. The program implementation and outcome evaluation were assigned to different staff members for each participant to avoid bias as much as possible. Although this approach was adopted due to limited staffing and operational issues with the intervention, the possibility of measurement bias could not be completely ruled out. Second, participants in this study entered the program of their own volition. Therefore, selection bias may have occurred due to the possibility that the participants were more concerned about their own health and physical function than other older adults. Additional work is needed to disseminate the program to prioritized populations, such as older adults who are socially isolated or indifferent to exercise. Third, the exercise program included several exercises that did not use the HAL lumbar type. Therefore, it was not possible to definitively attribute all study results to the effects of the HAL lumbar type. Future studies should take into account specific components of this intervention. In addition, a follow-up study is required to examine the impact of this intervention on ongoing post-intervention activities.

In conclusion, this study showed that an exercise program using the HAL lumbar type was able to improve physical function in community residents with physical frailty or locomotive syndrome, who were not in need of nursing care. Notably, most of the investigated physical functions improved to a clinically meaningful degree within a short period of 5 weeks. The exercise program developed in this study may be a promising option for facilitating the prompt resumption of community activities among frail older adults who do not require transitioning to long-term care.

List of abbreviations

BMI, body mass index

CVC, Cybernic Voluntary Control

HAL, Hybrid Assistive Limb

RCT, randomized controlled trial

TUG, Timed Up and Go

Ethics approval and consent to participate: This study was approved by the Research Ethics Review Committee of the Graduate School of Health Innovation, Kanagawa University of Health and Welfare (Approval No.: Hodai No.

30-008) and was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. All persons gave their informed consent prior to their inclusion in the study. The study protocol was registered in the University Hospital Medical Information Network (UMIN) clinical trial registration system (study ID UMIN000042352).

Consent for publication: Not applicable.

Availability of data and materials: The datasets presented in this article are not readily available because data cannot be shared publicly due to ethical restrictions. Requests to access the datasets should be directed to data described in the manuscript will be made available upon application and approval from the ME-BYO cohort office (contact via the corresponding author) for researchers who meet the criteria for data sharing.

Competing interests: The authors declare that they have no competing interests.

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References

1. Dent E, Martin FC, Bergman H, Woo J, Romero-Ortuno R, Walston JD. Management of frailty: opportunities, challenges, and future directions. Lancet. 2019;394:1376-86.

2. Ofori-Asenso R, Chin KL, Mazidi M, Zomer E, Ilomaki J, Zullo AR, et al. Global incidence of frailty and prefrailty among community-dwelling older adults: A systematic review and meta-analysis.

JAMA Netw Open. 2019;2:e198398.

3. Petermann-Rocha F, Balntzi V, Gray SR, Lara J, Ho FK, Pell JP, et al. Global prevalence of sarcopenia and severe sarcopenia: a systematic review and meta-analysis. J Cachexia Sarcopenia Muscle. 2022;13:86-99.

4. Xue QL, Bandeen-Roche K, Varadhan R, Zhou J, Fried LP. Initial manifestations of frailty criteria and the development of frailty phenotype in the Women's Health and Aging Study II. J Gerontol A Biol Sci Med Sci. 2008;63:984-90.

5. Hoogendijk EO, Afilalo J, Ensrud KE, Kowal P, Onder G, Fried LP. Frailty: implications for clinical practice and public health. Lancet. 2019;394:1365-75.

6. Wall A, Borg J, Palmcrantz S. Clinical application of the hybrid assistive limb (HAL) for gait training-a systematic review. Front Syst Neurosci. 2015;9:48.

7. Miura K, Koda M, Tamaki K, Ishida M, Marushima A, Funayama T, et al. Exercise training using hybrid assistive limb (HAL) lumbar type for locomotive syndrome: a pilot study. BMC Musculoskelet Disord. 2021;22:533.

8. Yasunaga Y, Koizumi R, Toyoda T, Koda M, Mamizuka N, Sankai Y, et al. Biofeedback physical therapy with the hybrid assistive limb (HAL) lumbar type for chronic low back pain: A pilot study. Cureus. 2022;14:e23475.

9. Kawamoto H, Taal S, Niniss H, Hayashi T, Kamibayashi K, Eguchi K, et al. Voluntary motion support control of Robot Suit HAL triggered by bioelectrical signal for hemiplegia. Annu Int Conf IEEE Eng Med Biol Soc. 2010;2010:462-6.

10. Grasmücke D, Zieriacks A, Jansen O, Fisahn C, Sczesny-Kaiser M, Wessling M, et al. Against the odds: what to expect in rehabilitation of chronic spinal cord injury with a neurologically controlled Hybrid Assistive Limb exoskeleton. A subgroup analysis of 55 patients according to age and lesion level. Neurosurg Focus. 2017;42:E15.

11. Kawamoto H, Kamibayashi K, Nakata Y, Yamawaki K, Ariyasu R, Sankai Y, et al. Pilot study of locomotion improvement using hybrid assistive limb in chronic stroke patients. BMC Neurol. 2013;13:141.

12. Yoshimoto T, Shimizu I, Hiroi Y, Kawaki M, Sato D, Nagasawa M. Feasibility and efficacy of high-speed gait training with a voluntary driven exoskeleton robot for gait and balance dysfunction in patients with chronic stroke: nonrandomized pilot study with concurrent control. Int J Rehabil Res. 2015;38:338-43.

13. Mataki Y, Mutsuzaki H, Kamada H, Takeuchi R, Nakagawa S, Yoshikawa K, et al. Effect of the hybrid assistive limb on the gait pattern for cerebral palsy. Medicina (Kaunas). 2020;56:673.

14. Matsuda M, Mataki Y, Mutsuzaki H, Yoshikawa K, Takahashi K, Enomoto K, et al. Immediate effects of a single session of robot-assisted gait training using hybrid assistive limb (HAL) for cerebral palsy. J Phys Ther Sci. 2018;30:207-12.

15. Nakajima T, Sankai Y, Takata S, Kobayashi Y, Ando Y, Nakagawa M, et al. Cybernic treatment with wearable cyborg hybrid assistive limb (HAL) improves ambulatory function in patients with slowly

progressive rare neuromuscular diseases: a multicentre, randomised, controlled crossover trial for efficacy and safety (NCY-3001). Orphanet J Rare Dis. 2021;16:304.

16. Hara H, Sankai Y. Development of HAL for lumbar support. SCIS & ISIS 2010. 2010:416-21.

17. Kato H, Watanabe H, Koike A, Wu L, Hayashi K, Konno H, et al. Effects of cardiac rehabilitation with lumbar-type hybrid assistive limb on muscle strength in patients with chronic heart failure - A randomized controlled trial. Circ J. 2021;86:60-7.

18. Kotani N, Morishita T, Yatsugi A, Fujioka S, Kamada S, Shiota E, et al. Biofeedback core exercise using hybrid assistive limb for physical frailty patients with or without Parkinson's disease. Front Neurol. 2020;11:215.

19. Watanabe H, Koike A, Pak YJ, Wu L, Kubota H, Konno H, et al. Effects of a lumbar-type hybrid assistive limb on cardiopulmonary burden during squat exercise in healthy subjects. J Clin Neurosci. 2019;66:226-30.

20. Yoshimura Y, Wakabayashi H, Yamada M, Kim H, Harada A, Arai H. Interventions for treating sarcopenia: A systematic review and meta-analysis of randomized controlled studies. J Am Med Dir Assoc. 2017;18:553 e1- e16.

21. ME-BYO cohort. Kanagawa Prospective "ME-BYO" Cohort Study Homepage. 2021 [cited 2023 March 1]. Available from: https://www.me-byo-cohort.jp.

22. Nakamura S, Watanabe R, Saito Y, Watanabe K, Chung UI, Narimatsu H. The ME-BYO index: A development and validation project of a novel comprehensive health index. Front Public Health. 2023;11:1142281.

23. Seichi A, Hoshino Y, Doi T, Akai M, Tobimatsu Y, Iwaya T. Development of a screening tool for risk of locomotive syndrome in the elderly: the 25-question Geriatric Locomotive Function Scale. J Orthop Sci. 2012;17:163-72.

24. Kobayashi T, Morimoto T, Shimanoe C, Ono R, Otani K, Mawatari M. Development of a simple screening tool based on the 5-question geriatric locomotive function scale for locomotive syndrome. J Orthop Sci. 2022;27:913-20.

25. Saito Y, Nakamura S, Tanaka A, Watanabe R, Narimatsu H, Chung UI. Evaluation of the validity and reliability of the 10-meter walk test using a smartphone application among Japanese older adults. Front Sports Act Living. 2022;4:904924.

26. Podsiadlo D, Richardson S. The timed "Up & Go": a test of basic functional mobility for frail elderly persons. J Am Geriatr Soc. 1991;39:142-8.

27. Yoshimura N, Muraki S, Oka H, Tanaka S, Ogata T, Kawaguchi H, et al. Association between new indices in the locomotive syndrome risk test and decline in mobility: third survey of the ROAD study. J Orthop Sci. 2015;20:896-905.

28. Muranaga S. Evaluation of the muscular strength of the lower extremities using the standing movement and clinical application. J Showa Med Assoc. 2001;61:362-7. (in Japanese).

29. Muranaga S, Hirano K. Development of a convenient way to predict ability to walk, using a

two-step test. J Showa Med Assoc. 2003;63:301-8. (in Japanese).

30. Bohannon RW, Bubela DJ, Magasi SR, Wang YC, Gershon RC. Sit-to-stand test: performance and determinants across the age-span. Isokinet Exerc Sci. 2010;18:235-40.

31. Duncan PW, Weiner DK, Chandler J, Studenski S. Functional reach: a new clinical measure of balance. J Gerontol. 1990;45:M192-7.

32. Berg KO, Wood-Dauphinee SL, Williams JI, Maki B. Measuring balance in the elderly: validation of an instrument. Can J Public Health. 1992;83:S7-11.

33. Kornetti DL, Fritz SL, Chiu YP, Light KE, Velozo CA. Rating scale analysis of the Berg Balance Scale. Arch Phys Med Rehabil. 2004;85:1128-35.

34. Perera S, Mody SH, Woodman RC, Studenski SA. Meaningful change and responsiveness in common physical performance measures in older adults. J Am Geriatr Soc. 2006;54:743-9.

35. Chen LK, Woo J, Assantachai P, Auyeung TW, Chou MY, Iijima K, et al. Asian Working Group for Sarcopenia: 2019 Consensus update on sarcopenia diagnosis and treatment. J Am Med Dir Assoc. 2020;21:300-7 e2.

Table 1. Baseline characteristics of the study participants

	Intervention group (n = 40)		Control group (n = 39)		p-value
	Mean	SD	Mean	SD	
Age, years	74.7	4.7	75.1	4.1	0.686
Male, n (%)	9	(22.5)	8	(20.5)	0.830
Physical function					
Walking speed: usual (m/s)	1.05	0.23	1.03	0.21	0.806
Walking cadence: usual (steps/min)	109	13.4	107	12.3	0.523
Walking speed: max (m/s)	1.47	0.28	1.47	0.29	0.994
Walking cadence: max (steps/min)	128	17.1	126	14.8	0.584
2-step test (score)	1.21	0.21	1.24	0.22	0.605
Timed Up and Go test (s)	8.3	3.3	8.1	1.7	0.652
5-times chair standing test (s)	11.9	3.8	11.1	2.5	0.247
Functional Reach Test (cm)	29.0	7.1	28.7	6.0	0.863
Grip strength (kg)	23.0	8.6	21.9	6.1	0.508
BBS (score)	53.4	6.6	54.4	2.0	0.366
GLFS-5 (score)	8.5	2.9	8.1	2.4	0.482
Body composition					
BMI (kg/m^2)	22.9	3.1	22.2	3.0	0.290
Fat (%)	29.4	7.7	29.2	5.9	0.885
Muscle mass (kg)	37.5	7.5	36.3	5.5	0.421

SD: standard deviation, BBS: Berg Balance Scale, GLFS-5: 5-question Geriatric Locomotive Function Scale, BMI: body mass index

Table 2. Effects of exercise program using Hybrid Assistive Limb lumbar type

	Baseline	Post-intervention	Between-group difference in change following intervention[a] Mean (standard error)	Time-by-group interaction[b]		
	Mean (95% CI)			F-value	p-value	Partial η^2
Physical function						
Walking speed: usual (m/s)						
Intervention	**1.05 (0.98, 1.12)**	**1.43 (1.35, 1.51)**	**0.35 (0.04)**	**93.63**	**<0.001**	**0.55**
Control	**1.03 (0.96, 1.10)**	**1.06 (0.98, 1.14)**				
Walking cadence: usual (steps/min)						
Intervention	**109 (105, 113)**	**120 (116, 123)**	**9.9 (2.0)**	**24.33**	**<0.001**	**0.24**
Control	**107 (103, 111)**	**108 (105, 112)**				
Walking speed: max (m/s)						
Intervention	**1.47 (1.38, 1.56)**	**1.75 (1.65, 1.85)**	**0.25 (0.04)**	**38.77**	**<0.001**	**0.34**
Control	**1.47 (1.38, 1.56)**	**1.49 (1.39, 1.59)**				
Walking cadence: max (steps/min)						
Intervention	**128 (123, 133)**	**133 (128, 139)**	**6.2 (2.5)**	**6.03**	**0.016**	**0.07**
Control	**126 (121, 132)**	**125 (119, 131)**				
2-step test (score)						
Intervention	**1.21 (1.14, 1.28)**	**1.34 (1.27, 1.40)**	**0.12 (0.02)**	**32.60**	**<0.001**	**0.30**
Control	**1.24 (1.17, 1.31)**	**1.24 (1.17, 1.31)**				
Timed Up and Go test (s)						
Intervention	**8.3 (7.5, 9.2)**	**7.0 (6.2, 7.7)**	**-1.1 (0.3)**	**19.83**	**<0.001**	**0.21**
Control	**8.1 (7.2, 8.9)**	**7.8 (7.1, 8.6)**				
5-times chair-standing test (s)						
Intervention	**11.9 (10.9, 12.9)**	**9.2 (8.4, 10.1)**	**-1.7 (0.6)**	**9.61**	**0.003**	**0.11**
Control	**11.1 (10.0, 12.1)**	**10.1 (9.3, 11.0)**				
Functional Reach Test (cm)						
Intervention	29.0 (26.9, 31.1)	31.9 (29.9, 33.8)	2.0 (1.2)	2.91	0.092	0.04
Control	28.7 (26.7, 30.8)	29.6 (27.6, 31.6)				
Grip strength (kg)						
Intervention	23.0 (20.7, 25.4)	24.1 (21.8, 26.4)	0.5 (0.6)	0.65	0.423	0.01

Control	21.9 (19.5, 24.3)	22.5 (20.1, 24.9)				
BBS (score)						
Intervention	**53.4 (51.8, 54.9)**	**54.5 (52.9, 56.0)**	**0.6 (0.3)**	**4.28**	**0.042**	**0.05**
Control	**54.4 (52.8, 55.9)**	**54.8 (53.3, 56.4)**				
GLFS-5 (score)						
Intervention	**8.5 (7.7, 9.3)**	**4.4 (3.3, 5.4)**	**-3.3 (0.4)**	**87.49**	**<0.001**	**0.53**
Control	**8.1 (7.2, 8.9)**	**7.3 (6.2, 8.3)**				
Body composition						
BMI (kg/m^2)						
Intervention	22.7 (21.8, 23.7)	22.7 (21.7, 23.6)	0.1 (0.1)	0.50	0.484	0.01
Control	22.4 (21.4, 23.3)	22.2 (21.3, 23.1)				
Fat (%)						
Intervention	29.2 (27.0, 31.4)	28.0 (25.7, 30.3)	0.2 (0.4)	0.29	0.595	0.00
Control	29.2 (27.0, 31.4)	27.8 (25.4, 30.1)				
Muscle mass (kg)						
Intervention	37.2 (35.1, 39.3)	37.8 (35.8, 39.9)	-0.1 (0.1)	0.13	0.721	0.00
Control	36.3 (34.2, 38.4)	37.0 (34.9, 39.1)				

BBS: Berg Balance Scale, GLFS-5: 5-question Geriatric Locomotive Function Scale, BMI: body mass index, CI: confidence interval
Boldface indicates statistical significance ($p < 0.05$).
[a] Difference in mean change from baseline to post-intervention between the intervention and control groups.
[b] p-values were generated using repeated-measures analysis of variance.

Figure 1 Study flow of the randomized controlled trial

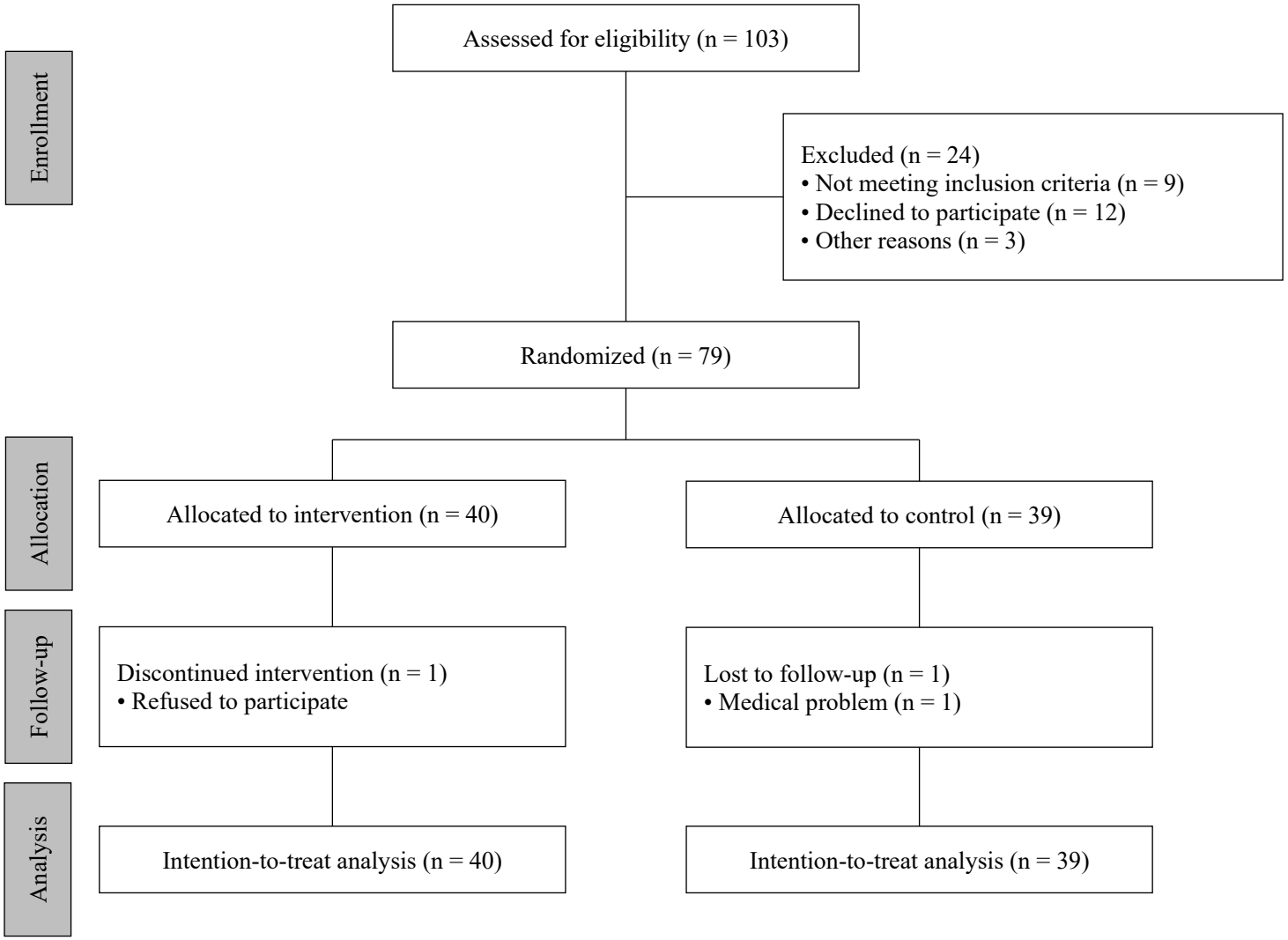
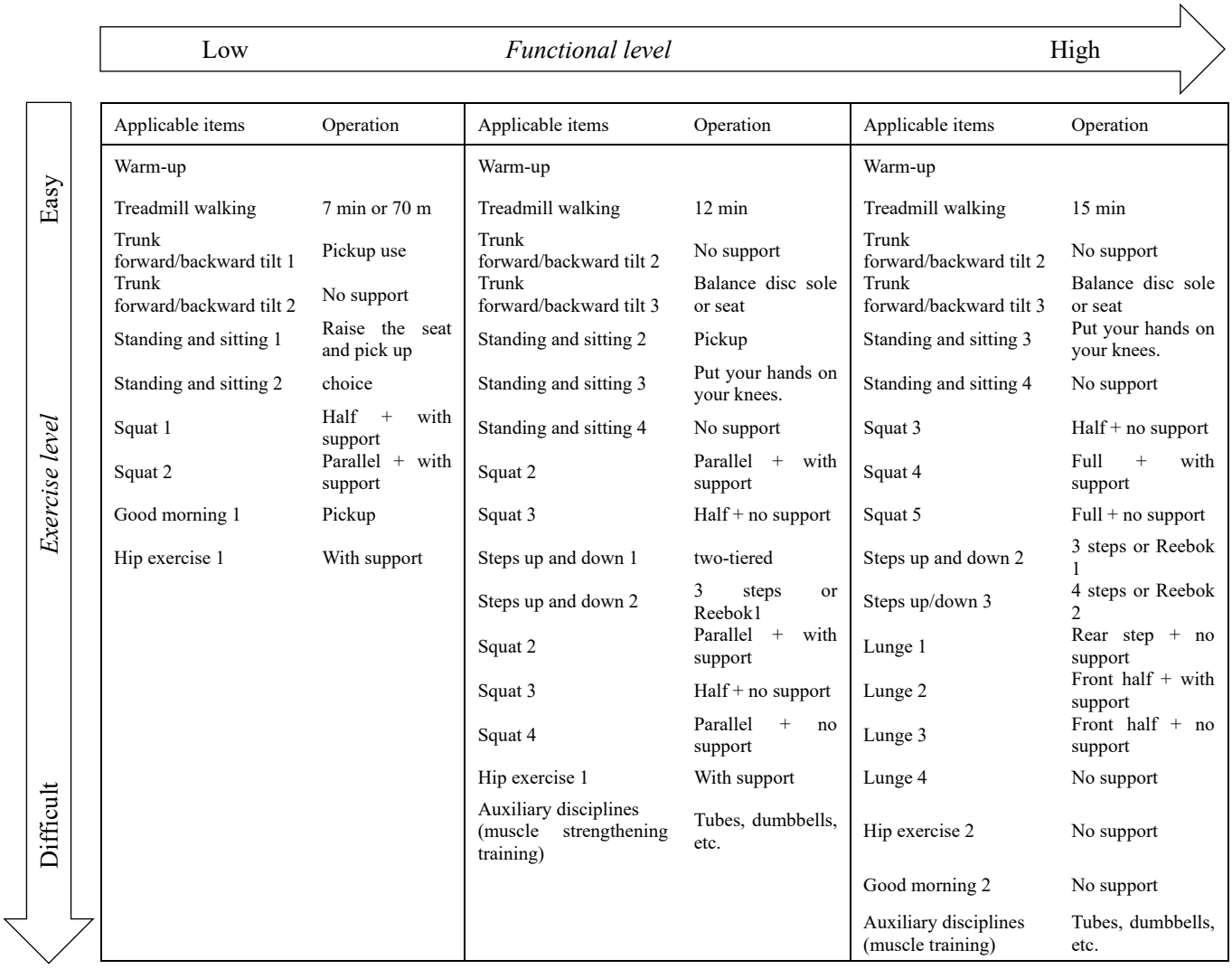


Figure 2 Exercise program utilizing the Hybrid Assistive Limb lumbar type



Applicable items	Operation	Applicable items	Operation	Applicable items	Operation
Warm-up		Warm-up		Warm-up	
Treadmill walking	7 min or 70 m	Treadmill walking	12 min	Treadmill walking	15 min
Trunk forward/backward tilt 1	Pickup use	Trunk forward/backward tilt 2	No support	Trunk forward/backward tilt 2	No support
Trunk forward/backward tilt 2	No support	Trunk forward/backward tilt 3	Balance disc sole or seat	Trunk forward/backward tilt 3	Balance disc sole or seat
Standing and sitting 1	Raise the seat and pick up	Standing and sitting 2	Pickup	Standing and sitting 3	Put your hands on your knees.
Standing and sitting 2	choice	Standing and sitting 3	Put your hands on your knees.	Standing and sitting 4	No support
Squat 1	Half + with support	Standing and sitting 4	No support	Squat 3	Half + no support
Squat 2	Parallel + with support	Squat 2	Parallel + with support	Squat 4	Full + with support
Good morning 1	Pickup	Squat 3	Half + no support	Squat 5	Full + no support
Hip exercise 1	With support	Steps up and down 1	two-tiered	Steps up and down 2	3 steps or Reebok 1
		Steps up and down 2	3 steps or Reebok1	Steps up/down 3	4 steps or Reebok 2
		Squat 2	Parallel + with support	Lunge 1	Rear step + no support
		Squat 3	Half + no support	Lunge 2	Front half + with support
		Squat 4	Parallel + no support	Lunge 3	Front half + no support
		Hip exercise 1	With support	Lunge 4	No support
		Auxiliary disciplines (muscle strengthening training)	Tubes, dumbbells, etc.	Hip exercise 2	No support
				Good morning 2	No support
				Auxiliary disciplines (muscle training)	Tubes, dumbbells, etc.

Figure 3 Trunk forward/backward tilt training with the HAL lumbar type

Figure 4 Squat training with the HAL lumbar type