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The effects of flexi-bar training on muscle strength and physical performance in the older people with dynapenia: protocol of a randomized controlled trial

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Protocol

The effects of flexi-bar training on muscle strength and physical performance in the older people with dynapenia: protocol of a randomized controlled trial

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ABSTRACT

Introduction: Dynapenia is a relative new term, which is used to describe age-related loss of muscle strength. Flexi-bar training is a safe and feasible device for the older people with dynapenia. The objective of this study is to investigate the effects of 4-week flexi-bar training program on muscle strength and physical function in the older people with dynapenia.

Methods and analysis: One hundred and fourteen participants (aged above 65 years old) with age-related muscle loss will be randomly divided into 3 equal groups, namely, flexi-bar group, placebo group and control group to participate a 4-week flexi-bar training program. Assessments will be done at pre-, post-intervention and 4 weeks after training completion including Timed-up-and-go test, five-repetition sit-to-stand and 10-meter walking test. The levels of serum albumin and hemoglobin will be measured at pre- and post-intervention.

Ethics and dissemination: The procedures of this study were reviewed and approved by the Human Ethics Review Board of Wuhan Brain Hospital (General Hospital of the Yangtze River Shipping) on 29th Sep 2020 (L20200013). The findings of this study will be published in peer-reviewed journals and presented at conferences.

Word count: 2144

Trial registration number is ISRCTN 14316668. It was registered on 6th Nov 2020. https://doi.org/10.1186/ISRCTN14316668

Strengths and limitations of this study

- This is the first study to investigate the effects of flexi-bar training on

muscle strength and physical performance in the older population with dynapenia.

- In this study, we will try to find whether 4-week flexi-bar training would influence the level of albumin and hemoglobin, which might explain the effect of flexi-bar training on the muscle strength in the older people with dynapenia.
- The muscle loading might be insufficient for some participants since the flexi-bar is an active induced training device.

Key words: rehabilitation medicine, geriatric medicine, musculoskeletal disorders

INTRODUCTION

Dynapenia is defined as age-related loss of muscle strength, which was proposed by Clark and Manini in 2008.[1] The prevalence of dynapenia was more than 20% in some countries.[2,3] Age-related loss of muscle strength was strongly associated with high risk of falls [4], poor physical performance,[5,6] disability [7] and mortality.[8] The incidence of falls among dynapenic older people was 17.2%.[4] Hasselgren et al. (2011) reported the score of Berg Balance Scale and Physiotherapy Clinical Outcome Variable Scale were significantly correlated with muscle strength in the very old people.[5] Newman et al. (2006) found muscle strength, not muscle mass, was strongly related to mortality in the older people.[8] Some recent studies have found that long-term exercise training program could improve both muscle and functional performance in older people with dynapenia.[9-12]

Flexi-bar is one type of vibration training. It consists of a bar and two weighty rubbers at each end of the bar. Its frequency is 5 Hz.[13] Compared to conventional training, it is portable and feasible for physical training in the older population, especially those with dynapenia. Some previous studies have found long-term flexi-bar had positive effects on muscle mass in young people [14] and physical function in old people.[15,16] It was reported that the thickness of transversus abdominis muscle of young university adults increase 2.4 mm after 6-month (48 times) flexi-bar training program, which was statistically significantly different from the control group (0.9mm).[14] Lee et al. (2018) found the score of BBS increased 3.2, the duration of completion TUG and 10MWT significantly decreased 4.2s and 4.6s, respectively, after 4 weeks flexi-bar training (20 times), in older people with chronic stroke.[15] For muscle strength, although there was no direct evidence, Meliva et al. (2010) recoreded the EMG of biceps brachii, triceps brachii, rectus femoris, and vastus lateralis during

one set of flexi-bar training and concluded that Flexi-bar training could induce a stronger training stimulus on the muscle during submaximal exercise.[13] This findings can give a hint that flexi-bar training might be effective approach to enhance muscle strength with submaximal level.

Regarding to the findings of the previous studies, flexi-bar might be an effective and safe training device for the older people with dynapenia. Considering the limited studied conducted in the population with dynapenia, it is meaningful to examine the effects of flexi-bar on muscle and physical performance in the older people with dynapenia. The objective of this study is to investigate the effects of 4-week flexi-bar training program on muscle strength and physical function in the older people with dynapenia.

METHOSD AND ANALYSIS

Participants

The advertisement will be put on the notice board in the Health Service Centers in General Hospital of the Yangtze River Shipping, Wuhan. Participants aged 65 years or above attending the Health Center will be invited to a screening test of handgrip strength measurement. Men and women with muscle strength less than 26kg and 18kg, respectively, will be diagnosed as dynapenia.[17] Participants with severe heart problem, neuro-degenerative diseases, vestibular disorders, cognitive impairment, severe osteoporosis, visual impairment or mental diseases will be excluded from this study. All participants will give their written consent to the principal investigator (NW) before participating in the study. Only the principal investigator (NW) can access the personal information of the study participants, which will be kept confidentially during and after the study. The procedures were reviewed and approved by the Human Ethics

Review Board of Wuhan Brain Hospital (General Hospital of the Yangtze River Shipping) prior to commencement of the study (#L20200013). The clinical registration number is ISRCTN 14316668 on 6th Nov 2020. https://doi.org/10.1186/ISRCTN14316668

Randomization and blinding

This protocol was designed as a single-blinded randomized controlled trail and adheres to SPIRIT guidelines. The participants will be randomized to flexi-bar group, sham group and control group (no training). Each participants will be given an identification number by the main investigator (NW), who performed the randomization with a computer program (Research Randomizer Form www.randomizer.org/). All training sessions will be conducted under the supervision of a physical therapist, who will be blinded to the randomization. The assessments and data analysis will be performed by a researcher (XXW). Two research assistant (LC and MYLyu) will be responsible for data entry (double data entry). Both of them will be blinded to randomization and intervention.

Patient and public involvement

Patients or members of the public will not be involved in this study. The research design, enrolment, allocation, interventions and assessments will be conducted by the trained researchers and physical therapists.

Interventions

A total of 20 training sessions (5 days/week, 4 weeks) will be conducted in Health Service Centers. Each training session will include 10 sets of 30-second vibration or

sham exercise. One minute of rest period will be given between training set to avoid over exertion of the participants. During training, the flexi-bar group will hold a Flexi-Bar (FLEXI-BAR®; Flexi-Sports, Germany) with shoulder flexed 90° to perform an up-and-down vibration exercise. The sham group will hold the same flexi-bar with no active vibration workout. During the training sessions, the participants will be asked to stand with knee angle of 120°. In order to cater for mission appointments, extra sessions will be arranged to make sure all participants will completer the same number of training sessions. The training sessions will be supervised by a physical therapist, who will be blinded to the randomization. Any adverse event will be reported to the Human Ethics Review Board of Wuhan Brain Hospital (General Hospital of the Yangtze River Shipping). The control group will receive no additional exercise training during the study. All participants will be asked to keep their lifestyle as usual.

Outcome variables

The assessments, including handgrip muscle strength, five-repetition sit-to-stand test (5STS), 10-meter walking test (10MWT) and timed-up-and-go test (TUG) will be conducted at baseline, post-intervention (one day after training completion) and 4 weeks after training completion to investigate the effects of flexi-bar training on physical performance in the older people with dynapenia. The levels of serum albumin and hemoglobin will be examined at baseline and post-intervention (one day after training completion) to explore the possible mechanisms of flexi-bar training on muscle strength. The study plan for recruitment, interventions, assessment for the participants are summarized in Table 1.

Table 1 Timetable of activities planned during the study.

	STUDY PERIOD					
	Enrolment	Allocation	Post-allocation			Close-out
TIMEPOINT	*Day 0*		*week 0*	*Week 4*	*Week 8*	*After Week 8*
ENROLMENT:						
Eligibility screen	X					
Informed consent	X					
Randomization	X					
Allocation	X					
INTERVENTIONS:						
Flexi-bar group			←	—	→	
Sham group			←	—	→	
Control group			←	—	→	
ASSESSMENTS:						
Five-repetition sit-to-stand test			X	X	X	
10-meter walking test			X	X	X	
Timed-up-and-go test			X	X	X	
serum albumin			X	X	X	
hemoglobin			X	X		

Maximum muscle strength of dominant side was measured by hand-held dynamometry (kg; CAMRY® Model EH101). Participants were asked to stand straight with arms close to the body and the elbow flexed at 90°. Participants were instructed to squeeze the dynamometer as hard as possible. The maximum value of three trails will

be used for analyses.

The timed-up and go test (TUG) was recommended as a suitable assessment for balance and physical function in the older people with low muscle strength.[18] Participants performed this test with their regular footwear. They stand up from an armchair, walk a distance of 3 meters, turn and walk back to the chair, and sit down with their normal pace without help from another person. The average time of two trials will be used in the data analysis.

The five-repetition sit-to-stand test (5STS) is a reliable and valid assessment for physical function.[18] The participant sat on a chair of 43-47cm high with back against the chair, arms crossed on the chest, feet comfortably placed on the floor. When the tester said“start”, the participant would rise from the chair to assume a full standing position and return to a sitting position for five times without rest in between. The time taken to complete the test will be recorded and the average time of two tests will be calculated.

10-meter walking test will be assessed at self-preferred and maximum walking speed. It is used as a golden tool to evaluate the mobility in the older people.[18] The time was measured only for the middle 6 meters. Walking aid was allowed in this test. The average walking speed of three trials was used in the data analysis.

The levels of serum albumin and hemoglobin will be measured in complete blood count. Blood will be collected from the antecubital vein with participants seated after a 12-hour fasting period. After collection, tubes containing ethylenediamine tetra-aceticacid plus samples will be centrifuged at 3.000 g for 15 min and plasma aliquots

stored at -70ºC until analysis.

Sample size calculation

Until now, there was no study examined the long-term effects of Flexi-bar training in the older people with dynapenia. Thus, this study adopted an effect size of 0.27 to estimate the sample size, which was reported in a previous study investigating the effects of 12-week power training program on TUG in the older people with dynapenia [10]. Since this study involved two groups and three times of assessments, the sample size for each group was calculated as 30 with a power of 0.8 and α value of 0.05. In consideration of 20% dropout rate, the total sample size was 114.

Patient and public involvement

Patients or members of the public will not be involved in this study. The research design, enrolment, allocation, interventions and assessments will be conducted by the trained researchers.

Data analysis

To compare the baseline characteristics of the three groups, one-way ANOVA (for data with normal distribution) or Kruskal-Wallis test (for data with non-normal distribution) will be conducted. Two-way repeated measures ANOVA (time × group) or Friedman test will be used to explore the effect of Flexi-bar training on muscle strength and physical performance in the people with dynapenia. The last observation carried forward of an intention-to-treat analysis will be used for data analysis. Descriptive analyses will be reported as means ± standard deviations. SPSS 20.0 (SPSS Inc., Chicago, Illinois, USA) will be used for statistical analysis. Significance level will

be set at $p < 0.05$, unless otherwise state.

DISCUSSION

To our knowledge, it is the first study to investigate the effects of flexi-bar training on muscle strength and physical performance in the older people with dynapenia. Two previous studies had investigated the effects of flexi-bar training physical performance in the old people.[15,16] They had reported that the performance in TUG and 10MWT were improved after long-term flexi-bar training.[15] However, there was no placebo group in their studies. Thus, it is premature to draw a conclusion from this two studies.

Some previous studies had pointed that the older people with lower muscles strength would have lower levels of albumin and hemoglobin.[19-21] One population-based cross-sectional study reported serum albumin and hemoglobin was positively associated with muscle strength and balance, but negatively with IADL in the community dwelling aged 55 and above.[19]

The strengths of this study are as below: first, this is the first study to investigate the effects of flexi-bar training on muscle strength and physical performance in the older population with dynapenia. In this study, we will try to find whether 4-week flexi-bar training would influence the level of albumin and hemoglobin, which might explain the effect of flexi-bar training on the muscle strength in the older people with dynapenia. Second, there will be a placebo group in this study, which can rule out the effect of static squatting. The limitations of this study are as below: First, the muscle loading might be insufficient for some participants since the flexi-bar is an active induced training device. However, the participant in this study will be the older people with dynapenia at different phase. Thus, unified muscle loading might not

suitable for our participants. Second, the training will conduct 5 times per week for 4 weeks, which might be too intensive to induce high drop-out rate.

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CONTRIBUTORS

NW made substantial contributions to conception and design. XXW, MYL and LC will collect and analyze data. The manuscript was drafted by NW.

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ERHICS APPROVAL

The Human Ethics Review Board of Wuhan Brain Hospital (General Hospital of the Yangtze River Shipping) (#L20200013).

CONFLICTS OF INTEREST

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

DISSEMINATIONS

The findings of this study will be published in peer-viewed journals and presented in conferences. Meanwhile, the results will be disseminated to the study participants.

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SPIRIT
STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	_____1_____
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	_____2_____
	2b	All items from the World Health Organization Trial Registration Data Set	_____/_____
Protocol version	3	Date and version identifier	_____2_____
Funding	4	Sources and types of financial, material, and other support	_____11_____
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	_____1_____
	5b	Name and contact information for the trial sponsor	_____1_____
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	_____11_____
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	_____/_____

Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	3-4
	6b	Explanation for choice of comparators	/
Objectives	7	Specific objectives or hypotheses	4
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	6
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	5
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	5-6
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	5-6
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	/
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	6
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	7
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	7-8
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	8

Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	10
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	5
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	6
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	6
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	6
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	5
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	5
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	7-10
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	/

Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	6
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	10
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	/
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	10
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	/
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	/
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	7
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	/
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	6
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	/

Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	6
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	/
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	6
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	12
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	12
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	/
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	12
	31b	Authorship eligibility guidelines and any intended use of professional writers	/
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	/
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	/
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	/

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

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Keywords:	REHABILITATION MEDICINE, GERIATRIC MEDICINE, Musculoskeletal disorders < ORTHOPAEDIC & TRAUMA SURGERY

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Protocol

The effects of flexi-bar training on muscle strength and physical performance in the older people with dynapenia: protocol of a randomized controlled trial

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ABSTRACT

Introduction: Dynapenia is a relative new term, which is used to describe the age-related loss of muscle strength. Flexi-bar training is a safe and feasible device for the older people with dynapenia. This study aims to investigate the effects of a 12-week flexi-bar training program on muscle strength and physical function in the older people with dynapenia.

Methods and analysis: One hundred and fourteen participants (aged above 65 years) with age-related muscle loss will be randomly divided into three equal groups, namely, flexi-bar, placebo and control to participate in a 12-week flexi-bar training program. The primary outcomes will be measured at pre-, post-intervention and 12 weeks after training completion including Timed-up-and-go test, five-repetition sit-to-stand and 10-meter walking test. The levels of serum albumin and hemoglobin will be measured as the secondary outcomes at pre- and post-intervention.

Ethics and dissemination: The procedures of this study were reviewed and approved by the Human Ethics Review Board of Wuhan Brain Hospital (General Hospital of the Yangtze River Shipping) on 29th Sep 2020 (L20200013). The findings of this study will be published in peer-reviewed journals and presented at conferences.

Word count: 2268

Trial registration number is ISRCTN 14316668. It was registered on 6th Nov 2020. https://doi.org/10.1186/ISRCTN14316668

Strengths and limitations of this study

- This study is the first parallel randomized controlled trial for this topic,

and a placebo group is added in this study design.

- This study, including 12-week flexi-bar training and 12-week follow-up, is sufficient to examine the effects of flexi-bar on older people with dynapenia.
- The first limitation of this study might be the unified muscle loading.
- The second limitation would be the single-blinded design.

Key words: rehabilitation medicine, geriatric medicine, musculoskeletal disorders

INTRODUCTION

Dynapenia is defined as age-related loss of muscle strength, which was proposed by Clark and Manini in 2008.[1] The prevalence of dynapenia was more than 20% in some countries.[2,3] The mechanisms of dynapenia are unclear to date. The likely contributors to dynapenia could be age-related neuromuscular impairments.[4] Age-related loss of muscle strength was strongly associated with high risk of falls, [5] poor physical performance,[6,7] disability [8] and mortality.[9] Moreover, a few previous studies had found that low muscle strength was related to a low level of serum albumin and hemoglobin. [10,11] Long-term exercise training program was proved to be an effective approach to improve both muscle and functional performance in older people with dynapenia.[12-15]

Flexi-bar is a type of vibration training. It consists of a bar and two weighty rubbers at each end of the bar. [16] Compared to conventional training, it is portable and feasible for physical training in the older population, particularly those with dynapenia. Some previous studies have found long-term flexi-bar having positive effects on muscle mass in young people [17] and physical function in older people.[18,19] It was reported that the thickness of transversus abdominis muscle of young university adults increased 2.4 mm after a 6-month (48 times) flexi-bar training program, which was statistically significantly different from the control group (0.9mm).[17] Lee et al. (2018) found that the score of Berg Balance Scale (BBS) increased 3.2, and the duration of completion of Timed-up-and-go test (TUG) and 10-meter walking test (10MWT) significantly decreased 4.2s and 4.6s, respectively, after 4 weeks of flexi-bar training (20 times) in older people with chronic stroke.[19] Although there was no direct evidence for muscle strength, Meliva et al. (2010) recorded the electromuography of biceps brachii, triceps brachii, rectus femoris, and

vastus lateralis during one set of flexi-bar training and concluded that flexi-bar training could induce a stronger training stimulus on the muscle during submaximal exercise.[16] These findings indicate that flexi-bar training might be an effective approach to enhance muscle strength at the submaximal level.

Regarding to the findings of the previous studies, flexi-bar might be an effective and safe training device for the older people with dynapenia. Considering the limited studies conducted in the population with dynapenia, it is meaningful to examine the effects of flexi-bar on muscle and physical performance in the older people with dynapenia. Thus, the objective of this study is to investigate the effects of a 12-week flexi-bar training program on muscle strength and physical function in the older people with dynapenia.

METHODS AND ANALYSIS

Participants

The advertisement will be put on the notice board in the Health Service Centers in General Hospital of the Yangtze River Shipping, Wuhan. Participants aged 65 years or above attending the Health Center will be invited to a screening test of handgrip strength measurement. Men and women with muscle strength less than 26kg and 18kg, respectively, will be diagnosed as dynapenia.[20] Participants with severe heart problem, neuro-degenerative diseases, vestibular disorders, cognitive impairment, severe osteoporosis, visual impairment or mental diseases will be excluded from this study. All participants will give their written consent to the principal investigator (NW) before participating in the study. Only the principal investigator (NW) can access the personal information of the study participants, which will be kept confidentially during and after the study. The procedures were reviewed and approved by the Human Ethics

Review Board of Wuhan Brain Hospital (General Hospital of the Yangtze River Shipping) before the commencement of the study (#L20200013). The clinical registration number is ISRCTN 14316668 on 6th Nov 2020. https://doi.org/10.1186/ISRCTN14316668

Randomization and blinding

This protocol was designed as a single-blinded randomized controlled trail, adhering to Standard Protocol Items: Recommendations for Interventional Trials guidelines. The participants will be randomized to flexi-bar, placebo and control groups (no training). Each participants will be given an identification number by the main investigator (NW), who will perform the randomization using a computer program (Research Randomizer Form www.randomizer.org/). All training sessions will be conducted under the supervision of a physical therapist, who will be blinded to the randomization. The assessments and data analysis will be performed by a researcher (XXW). Two research assistant (LC and MYLyu) will be responsible for data entry (double data entry). Both of them will be blinded to randomization and intervention.

Patient and public involvement

Patients or members of the public will not be involved in this study. The research design, enrolment, allocation, interventions and assessments will be conducted by the trained researchers and physical therapists.

Interventions

A total of 36 training sessions (3 times/week, 12 weeks) will be conducted at Health Service Centers. Each training session will include 10 sets of 30-second

vibration or sham exercises. One minute of rest period will be given between training set to avoid over-exertion of the participants. During training, the flexi-bar group will hold a flexi-Bar (FLEXI-BAR®; Flexi-Sports, Germany) with the shoulder flexed 90° to perform an up-and-down vibration exercise. The participants will be instructed to active the flexi-bar at individual highest frequency. The placebo group will hold the same flexi-bar with no active vibration workout. During the training sessions, the participants will be asked to stand with a knee angle of 120°. [21] To cater to mission appointments, extra sessions will be arranged to make sure all participants will completer the same number of training sessions. The training sessions will be supervised by a physical therapist, who will be blinded to the randomization. Any adverse event will be reported to the Human Ethics Review Board of Wuhan Brain Hospital (General Hospital of the Yangtze River Shipping) and the intervention will be discontinued for the particular participant. The control group will receive no additional exercise training during the study. All participants will be asked to maintain their normal lifestyle during the training and follow-up period.

Outcome variables

The primary outcomes, including handgrip muscle strength, five-repetition sit-to-stand test (5STS), 10-meter walking test (10MWT) and timed-up-and-go test (TUG) will be measured at baseline, post-intervention (1 day after training completion) and 12 weeks after training completion to investigate the effects of flexi-bar training on physical performance in the older people with dynapenia. The levels of serum albumin and hemoglobin will be examined as the secondary outcomes at baseline and post-

intervention (1 day after training completion) to explore the possible mechanisms of flexi-bar training on muscle strength. To promote the retention, all assessments will be free and transportation fee will be reimbursed. The study plan for recruitment, interventions, and assessment for the participants is summarized in Table 1.

	STUDY PERIOD					
	Enrolment	Allocation	Post-allocation			Close-out
TIMEPOINT	*Day 0*		*week 0*	*Week 12*	*Week 24*	*After Week 24*
ENROLMENT:						
Eligibility screen	X					
Informed consent	X					
Randomization	X					
Allocation	X					
INTERVENTIONS:						
Flexi-bar group			←	—		
Sham group			←	—		
Control group			←	—		
ASSESSMENTS:						
Five-repetition sit-to-stand test			X	X	X	
10-meter walking test			X	X	X	
Timed-up-and-go test			X	X	X	
serum albumin			X	X	X	
hemoglobin			X	X		

Table 1 Timetable of activities planned during the study.

The maximum muscle strength of dominant side will be measured using hand-held dynamometry (kg; CAMRY® Model EH101). Participants will be instructed to stand straight with arms close to the body and the elbow flexed at 90°. Participants will be then asked to squeeze the dynamometer as hard as possible. The maximum value of three trials will be used for analyses.

The TUG was recommended as a suitable assessment for balance and physical function in the older people with low muscle strength.[21] Participants performed this test with their regular footwear. They will stand up from an armchair, walk a distance of 3 meters, turn and walk back to the chair, and sit down with their normal pace without help from another person. The average time of two trials will be used in the data analysis.

The 5STS is a reliable and valid assessment for physical function in the older people. [21] The participant will sit on a chair with a height of 43-47cm with back against the chair, arms crossed on the chest, feet comfortably placed on the floor. When the tester will say “start”, the participant will rise from the chair to assume a full standing position and return to a sitting position for five times without rest in between. The time taken to complete the test will be recorded and the average time of two tests will be calculated.

The 10MWT will be assessed at self-preferred and maximum walking speed. It is used as a golden tool to evaluate the mobility in the older people. [21] The time will be measured only for the middle 6 meters. Walking aid is allowed in this test. The average walking speed of three trials will be in the data analysis.

The levels of serum albumin and hemoglobin will be measured in complete blood

count. Blood will be collected from the antecubital vein with participants seated after a 12-hour fasting period. After collection, tubes containing ethylenediamine tetra-aceticacid plus samples will be centrifuged at 3.000 g for 15 min and plasma aliquots stored at -70ºC until analysis.

Sample size calculation

To date, no study has examined the long-term effects of flexi-bar training in the older people with dynapenia. Thus, this study adopted an effect size of 0.27 to estimate the sample size, as reported in a previous study investigating the effects of 12-week power training program on TUG in the older people with dynapenia [13]. Since this study involved two factors (two groups and three times of assessments), the sample size was calculated to be 30 for each group with a power of 0.8 and α value of 0.05 using the software (GPower 3.1). In consideration of 20% dropout rate, the total sample size was 114.

Patient and public involvement

Patients or members of the public will not be involved in this study. The research design, enrolment, allocation, interventions and assessments will be conducted by the trained researchers.

Data analysis

To compare the baseline characteristics of the three groups, one-way analysis of variance (ANOVA) (for data with normal distribution) or Kruskal-Wallis test (for data with non-normal distribution) will be conducted. Two-way repeated-measures ANOVA (time × group) or Friedman test will be used to explore the effect of flexi-bar

training on muscle strength and physical performance in the people with dynapenia. The last observation carried forward of an intention-to-treat analysis will be used for data analysis. Descriptive analyses will be reported as means ± standard deviations. SPSS 20.0 (SPSS Inc., Chicago, Illinois, USA) will be used for statistical analysis. The significance level will be set at $p < 0.05$, unless stated otherwise.

Ethics and dissemination

The procedures of this study were reviewed and approved by the Human Ethics Review Board of Wuhan Brain Hospital (General Hospital of the Yangtze River Shipping) on 29th Sep 2020 (L20200013). The findings of this study will be published in peer-reviewed journals and presented at conferences. Meanwhile, the results will be disseminated to the study participants.

DISCUSSION

To the best of our knowledge, this is the first study to investigate the effects of flexi-bar training on muscle strength and physical performance in the older people with dynapenia. Two previous studies had investigated the effects of flexi-bar training physical performance in the older population.[18,19] They had reported that the performance in TUG and 10MWT were improved after long-term flexi-bar training.[18] However, there was no placebo group in their studies. Thus, it is premature to draw a conclusion from these two studies.

Some previous studies had pointed that the older people with lower muscles strength would have lower levels of albumin and hemoglobin.[22-24] One population-based cross-sectional study reported serum albumin and hemoglobin to be positively

associated with muscle strength and balance; however, negatively with instrumental activities of daily living in the community-dwelling population aged 55 years and above.[22]

The strengths of this study are as follows: First, this is the first study to investigate the effects of flexi-bar training on muscle strength and physical performance in the older population with dynapenia. In this study, we will attempt to determine whether a 12-week flexi-bar training program would influence the level of albumin and hemoglobin, which might explain the effect of flexi-bar training on the muscle strength in the older people with dynapenia. Second, there will be a placebo group in this study, which can rule out the effect of static squatting.

The limitations of this study are as follows: First, the muscle loading might not be unified since the flexi-bar is an individually active induced training device. However, the physical therapist will ask the participants to try their best to active the flexi-bar during training. If participants do not try their best, the flexi-bar will stop vibrating. In this case, the therapist will remind the participants to active the flexi-bar more intensively. Considering the participants in our study might be at a different level of health condition, it is better and safe to training them with individual efforts. Thus, unified muscle loading might not be suitable for our participants. Second, due to practical consideration, this study is designed as a single-blinded randomized controlled trial, and not double-blinded.

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CONTRIBUTORS

NW made substantial contributions to conception and design. XXW, MYL and LC will collect and analyze data. The manuscript was drafted by NW.

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ERHICS APPROVAL

The Human Ethics Review Board of Wuhan Brain Hospital (General Hospital of the Yangtze River Shipping) (#L20200013).

CONFLICTS OF INTEREST

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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SPIRIT

STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	2
	2b	All items from the World Health Organization Trial Registration Data Set	2 registration website
Protocol version	3	Date and version identifier	2
Funding	4	Sources and types of financial, material, and other support	11
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1
	5b	Name and contact information for the trial sponsor	1
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	11
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	13

Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	3-4
	6b	Explanation for choice of comparators	7
Objectives	7	Specific objectives or hypotheses	4
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	6
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	5
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	5-6
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	5-6
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	7
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	8
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	7
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	7-8
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	8

Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	10
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	5
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	6
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	6
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	6
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	5
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	5
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	7-10
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	8

Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	6
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	10
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	/
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	10
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	the study period is relatively short
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	No interim analyses
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	7
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	no auditing
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	6
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	/

Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	6
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	/
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	6
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	12
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	12
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	/
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	12
	31b	Authorship eligibility guidelines and any intended use of professional writers	13
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	6
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	The form is in Chinese, added as supplemental material
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	/

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated.

BMJ Open

The effects of flexi-bar training on muscle strength and physical performance in older people with dynapenia: the protocol of a randomised controlled trial

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Secondary Subject Heading:	Geriatric medicine
Keywords:	REHABILITATION MEDICINE, GERIATRIC MEDICINE, Musculoskeletal disorders < ORTHOPAEDIC & TRAUMA SURGERY

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Protocol

The effects of flexi-bar training on muscle strength and physical performance in older people with dynapenia: the protocol of a randomised controlled trial

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ABSTRACT

Introduction: Dynapenia is a new term that is used to describe the age-related loss of muscle strength. Flexi-bar training is a safe and feasible device for older people with dynapenia. This study will investigate the effects of a 12-week flexi-bar training programme on muscle strength and physical function in older people with dynapenia.

Methods and analysis: A total of 114 participants (aged more than 65 years) with age-related muscle loss will participate in a 12-week flexi-bar training programme. The participants will be randomly divided into three groups, namely flexi-bar, placebo, and control, with equal number of participants in each group. The assessments will be conducted at pre-, post-intervention, and 12 weeks after training completion. The primary outcome is Timed-up-and-go test. The secondary outcomes are five-repetition sit-to-stand, 10-metre walking test, handgrip strength, as well as the serum albumin and haemoglobin levels.

Ethics and dissemination: The procedures of this study were reviewed and approved by the Human Ethics Review Board of Wuhan Brain Hospital (General Hospital of the Yangtze River Shipping) on 29 Sep 2020 (L20200013). The findings of this study will be published in peer-reviewed journals and presented at conferences.

Word count: 2247

The trial was registered on 6 Nov 2020. The trial registration number is ISRCTN 14316668 (https://doi.org/10.1186/ISRCTN14316668).

Strengths and limitations of this study

- This study is the first parallel randomised controlled trial on the effects of

a 12-week flexi-bar training programme on muscle strength and physical function in older people with dynapenia, and the study design involves a placebo group.

- This study, comprising 12-week flexi-bar training and 12-week follow-up, can accurately examine the effects of flexi-bar on older people with dynapenia.
- The first limitation of this study is that the muscle loading of each participant will not be uniform.
- The second limitation is that the sample size may be insufficient for the secondary outcome variables.
- The third limitation is the single-blinded design.

Key words: rehabilitation medicine, geriatric medicine, musculoskeletal disorders

INTRODUCTION

Dynapenia is the age-related loss of muscle strength and was defined by Clark and Manini in 2008.[1] The prevalence of dynapenia is more than 20% in some countries.[2,3] The mechanisms of dynapenia remain unclear; however, age-related biological factors, unhealthy lifestyle, and mental-health variables have been identified as the possible factors contributing to dynapenia.[4,5] Age-related loss of muscle strength is strongly associated with a high risk of falls,[6] poor physical performance,[7,8] disability,[9] and mortality.[10] Moreover, a few studies have reported that low muscle strength is related to a low level of serum albumin and haemoglobin.[11,12] Long-term exercise training programme has been proved to be an effective approach to improve both muscle and functional performance in older people with dynapenia.[13-16]

Flexi-bar is a type of vibration device, and it consists of a bar, with two weighty rubbers at each end of the bar.[17] Some studies have reported that long-term flexi-bar training has positive effects on the muscle mass,[18,19] muscle strength,[20] and physical performance.[21,22] A study reported that the thickness of the transversus abdominis muscle of young university adults increases to 2.4 mm after a 6-month (48 times) flexi-bar training programme.[18] In another study, the overweight adults with a 12-week flexi-bar training programme exhibited a significant increase in handgrip strength, which was significantly different from that of the control group.[20] In a study on the physical performance by Lee et al. (2018), older people with chronic stroke exhibited significant improvement in the score of Berg Balance Scale (BBS), the duration of completion of Timed-up-and-go test (TUG), and 10-metre walking test (10MWT) after 4 weeks of flexi-bar training (20 times).[21] Moreover, the flexi-bar training could induce a strong stimulus on the muscle during submaximal

exercise,[17,23] which could be the indirect evidence for supporting the positive effect of flexi-bar training on muscle strength. These findings suggest that flexi-bar training might be an effective approach to enhance muscle strength and physical performance at the submaximal level.

According to the findings of the previous studies, flexi-bar might be an effective and safe training device for older people with dynapenia. Considering the inadequacy of the number of studies conducted in the population with dynapenia, examining the effects of flexi-bar training on the muscle and physical performance in older people with dynapenia seems meaningful. The present study aims to investigate the effects of a 12-week flexi-bar training programme on muscle strength and physical function in older people with dynapenia.

METHODS AND ANALYSIS

Participants

The advertisement will be put on the notice board in the Health Service Centres in General Hospital of the Yangtze River Shipping, Wuhan. Participants aged 65 years or more attending the Health Centre will be invited to a screening test of handgrip strength measurement. Men and women with muscle strength less than 26 kg and 18 kg, respectively, and diagnosed as having dynapenia will be included.[24] Participants with severe heart diseases, neuro-degenerative diseases, vestibular disorders, cognitive impairment, severe osteoporosis, visual impairment, or mental diseases will be excluded from this study. All participants will provide their written consent to the principal investigator (NW) before participating in the study. Only the principal investigator (NW) will be able to access the personal information of the study participants, and the information will be kept confidential during and after the study.

The procedures have been reviewed and approved by the Human Ethics Review Board of Wuhan Brain Hospital (General Hospital of the Yangtze River Shipping; #L20200013). The trial was registered on 6 Nov 2020, and the clinical registration number is ISRCTN 14316668 (https://doi.org/10.1186/ISRCTN14316668).

Randomisation and blinding

This protocol was designed as a single-blinded randomised controlled trail in accordance with the Standard Protocol Items: Recommendations for Interventional Trials guidelines. The participants will be randomised into flexi-bar, placebo, and control groups (no training). Each participant will be provided an identification number by the main investigator (NW), who will perform the randomisation using a computer programme (Research Randomizer Form; www.randomizer.org/). All training sessions will be conducted under the supervision of a physical therapist, who will be blinded to the randomisation. The assessments and data analysis will be performed by a researcher (XXW). Two research assistants (LC and MYLyu) will be responsible for data entry (double data entry), and both of them will be blinded to randomisation and intervention.

Interventions

A total of 36 training sessions (3 times/week, 12 weeks) will be conducted at Health Service Centres. Each training session will include 10 sets of 30-second vibration or sham exercises. One minute of rest period will be given between training sets to avoid over-exertion of the participants. During training, the flexi-bar group will hold a flexi-Bar (FLEXI-BAR®; Flexi-Sports, Germany), with the shoulder flexed at 90°, to perform an up-and-down vibration exercise. The participants will be instructed

	STUDY PERIOD			
	Enrolm	Allocation	Post-allocation	Close-out

to activate the flexi-bar at the highest individual frequency. The placebo group will hold the same flexi-bar with no active vibration workout. During the training sessions, the participants will be asked to stand with a knee angle of 120°.[25] To cater for missing appointments, extra sessions will be arranged to ensure that all the participants complete the equal number of training sessions. The training sessions will be supervised by a physical therapist, who will be blinded to the randomisation. Any adverse event will be reported to the Human Ethics Review Board of Wuhan Brain Hospital (General Hospital of the Yangtze River Shipping), and the intervention will be discontinued for the participant reporting adverse events. The control group will receive no additional exercise training during the study period. All the participants will be asked to maintain their normal lifestyle during the training and follow-up period.

Outcome variables

The primary outcome is TUG, whereas the secondary outcomes are handgrip muscle strength, five-repetition sit-to-stand test (5STS), 10-metre walking test (10MWT), as well as the serum albumin and haemoglobin levels. Both primary and secondary outcomes will be measured at baseline, post-intervention (1 day after training completion), and 12 weeks after training completion. To promote the retention, all the assessments will be provided free of cost, and transportation fee will be reimbursed. The study plan for recruitment, interventions, and assessment for participants is summarized in Table 1.

	ent				
TIMEPOINT	***Day 0***	***week 0***	***Week 12***	***Week 24***	***After Week 24***
ENROLMENT:					
Eligibility screen	X				
Informed consent	X				
Randomisation	X				
Allocation	X				
INTERVENTIONS					
Flexi-bar group		←	—	→	
Sham group		←	—	→	
Control group		←	—	→	
ASSESSMENTS:					
Timed-up-and-go test		X	X	X	
10-metre walking test		X	X	X	
Five-repetition sit-to-stand test		X	X	X	
Handgrip strength		X	X	X	
Serum albumin		X	X	X	
Haemoglobin		X	X	X	

Table 1 Timetable of activities planned during the study

The TUG was recommended as a suitable assessment for balance and physical function in older people with low muscle function.[25] The participants will perform this test with their regular footwear. They will stand up from an armchair, walk a distance of 3 metres, turn and walk back to the chair, and sit down with their normal pace without taking help from another person. The average time of the two trials will

be used for data analysis.

The 5STS is a reliable and valid assessment for physical function in older people.[25] The participant will sit on a chair of 43–47-cm height, with back against the chair, arms crossed on the chest, and feet comfortably placed on the floor. When the tester will say 'start', the participant will rise from the chair to assume a full standing position and return to a sitting position, and this action will be repeated five times without rest in between. The time taken to complete the test will be recorded, and the average time of the two tests will be calculated.

The 10MWT will be assessed at a self-preferred and maximum walking speed. It is used as a golden tool to evaluate the mobility in the older people.[25] The time will be measured only for the middle 6 metres. Walking aid is allowed in this test. The average walking speed of three trials will be for the data analysis.

The handgrip strength of the dominant side will be measured using a hand-held dynamometer (kg; CAMRY® Model EH101). Participants will be instructed to stand straight, with arms close to the body and the elbow flexed at 90°. The participants will then be asked to squeeze the dynamometer as hard as possible. The maximum value of the three trials will be used for analyses.

The serum albumin and haemoglobin levels will be measured. Blood will be collected from the antecubital vein, with participants seated after a 12-h fasting period. After collection, the tubes containing ethylenediamine tetra-aceticacid and samples will be centrifuged at 3.000 g for 15 min, and plasma aliquots will be stored at −70ºC until analysis.

Sample size calculation

To date, no study has examined the long-term effects of flexi-bar training in older people with dynapenia. Thus, this study adopted an effect size of 0.27 to estimate the sample size, as reported in a previous study investigating the effects of 12-week power training programme on TUG in older people with dynapenia.[14] Since this study involved two factors (two groups and three times of assessments), the sample size calculated using a software (GPower 3.1) was 30 for each group, with a power of 0.8 and an α value of 0.05. Considering a 20% dropout rate, the total sample size will be 114.

Patient and public involvement

Patients or members of the public will not be involved in this study. The research design, enrolment, allocation, interventions, and assessments will be conducted by trained researchers.

Data analysis

To compare the baseline characteristics of the three groups, one-way analysis of variance (ANOVA) (for data with normal distribution) or Kruskal–Wallis test (for data with non-normal distribution) will be conducted. Two-way repeated-measures ANOVA (time × group) or Friedman test will be used to explore the effect of flexi-bar training. The last observation, carried forward of an intention-to-treat analysis, will be used for data analysis. Descriptive analyses will be reported as means ± standard deviations. SPSS 20.0 (SPSS Inc., Chicago, Illinois, USA) will be used for statistical analyses. The significance level will be set at $p < 0.05$, unless stated otherwise.

Ethics and dissemination

The procedures of this study were reviewed and approved by the Human Ethics Review Board of Wuhan Brain Hospital (General Hospital of the Yangtze River Shipping) on 29 Sep 2020 (L20200013). The findings of this study will be published in peer-reviewed journals and presented at conferences. Meanwhile, the results will be disseminated to the study participants.

DISCUSSION

To the best of our knowledge, this study is the first to investigate the effects of flexi-bar training on muscle strength and physical performance in older people with dynapenia. Two studies have investigated the effects of flexi-bar training on the physical performance in the older population.[21,22] The authors reported that the performance in TUG and 10MWT was improved after long-term flexi-bar training.[21] However, these studies had no placebo group. Thus, drawing a conclusion from these two studies is inappropriate.

Some studies have indicated that older people with low muscles strength exhibit low levels of albumin and haemoglobin.[26-28] One population-based cross-sectional study reported that serum albumin and haemoglobin levels are associated positively with muscle strength and balance but negatively with instrumental activities of daily living in the community-dwelling population aged 55 years and more.[26]

This study has some strengths. First, this study is the first to investigate the effects of flexi-bar training on muscle strength and physical performance in older population with dynapenia. In this study, we will attempt to determine whether a 12-week flexi-

bar training programme would influence the level of albumin and haemoglobin, which might explain the effect of flexi-bar training on the muscle strength in older people with dynapenia. Second, this study will involve a placebo group, which can rule out the effect of static squatting.

The study will have some limitations. First, the muscle loading might not be unified since the flexi-bar is an individually active induced training device. However, the physical therapist will ask the participants to try their best to activate the flexi-bar during training. If participants do not try their best, the flexi-bar will stop vibrating. In this case, the therapist will remind the participants to activate the flexi-bar more intensively. Considering that the participants in our study might be at a different level of health condition, training them with individual efforts is an effective and safe approach. Thus, uniform muscle loading might not be suitable for our participants. Second, the sample size might be insufficient for assessing the secondary outcomes. In this protocol, the sample size will be calculated according to the effect size of the primary outcome. However, whether the sample size is adequate for each secondary outcome remains uncertain. Third, due to practical consideration, this study is designed as a single-blinded randomised controlled trial and not as a double-blinded trial.

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CONTRIBUTORS

NW made substantial contributions to conception and design. XXW, MYL, and

LC will collect and analyse data. The manuscript was drafted by NW.

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ERHICS APPROVAL

The Human Ethics Review Board of Wuhan Brain Hospital (General Hospital of the Yangtze River Shipping) (#L20200013).

CONFLICTS OF INTEREST

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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SPIRIT
STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	2
	2b	All items from the World Health Organization Trial Registration Data Set	2 registration website
Protocol version	3	Date and version identifier	2
Funding	4	Sources and types of financial, material, and other support	13
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1
	5b	Name and contact information for the trial sponsor	1
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	13
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	13

Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4-5
	6b	Explanation for choice of comparators	7
Objectives	7	Specific objectives or hypotheses	5
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	6
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	5
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	5-6
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	5-6
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	7
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	7
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	7
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	7-9
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	8

Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	10
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	5
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	6
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	6
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	6
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	6
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	6
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	7-11
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	7&10

Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	6
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	10
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	/
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	10
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	the study period is relatively short
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	No interim analyses
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	7
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	no auditing
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	6
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	/

Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	5
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	/
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	5
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	13
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	6
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	/
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	11
	31b	Authorship eligibility guidelines and any intended use of professional writers	13
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	11
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	The form is in Chinese, added as supplemental material
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	/

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated.