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Effectiveness of the self-fatigue assessment in guiding early postoperative ambulation in gynecologic oncology patients: study protocol for a randomized controlled trial

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ABSTRACT

Introduction Enhanced recovery after surgery guidelines strongly recommends that patients be in early postoperative ambulation within 24 h. This study aims to assess the effectiveness and safety of the self-fatigue assessment method to guide patients' early postoperative ambulation.

Methods and analysis This is a single-center, randomized, open, parallel-controlled trial. Five hundred fifty-two patients who meet the inclusion criteria for gynecologic oncology surgery are randomly assigned in a 1:1 ratio to either a self-fatigue assessment group (study group) or a fixed activity distance assessment group (control group). The fixed activity distance group adopts a fixed early postoperative ambulation distance to guide the patient's activity, while the self-fatigue assessment group uses the Borg Exercise Scale to assess the patient's fatigue and stops activity when the fatigue level reaches 5-6. The primary outcome measure is the time to first postoperative exhaust. Secondary outcome measures are the time to first bowel movement, the incidence of moderate to severe bloating, the incidence of bowel obstruction or Venous thromboembolism, the incidence of adverse events (nausea, vomiting, dizziness), patient satisfaction, sleep quality scores, patient compliance with activities, hospital costs, and days in hospital.

Ethics and dissemination This study was approved by the Independent Ethics Committee of Xiangyang Central Hospital affiliated with Hubei University of Arts and Sciences and registered with the China Clinical Trials Registry in May 2021. The results of the trial will be disseminated through open access peer-reviewed journals and abstracts will be submitted to relevant national and international conferences.

Trial registration number: CTR2100046035, date: 02 May 2021.

Keywords gynecologic oncology, early ambulation, self-fatigue assessment, fixed activity distance assessment, study protocol

Strengths and limitations of this study

► The results from this randomized clinical trial will provide new and high-quality evidence to support early postoperative ambulation in gynecologic oncology patients.

► All interventions will be instructor-led, patients in both groups are to be assisted to get out of bed on the first 24 h after surgery, decreasing the risk of adverse events.

► One limitation is that the trial is not a double-blind, placebo-controlled trial and implemented in only one hospital.

► Another limitation is that the trial is implemented in only one hospital in Chinese subjects, which may limit its generalisability.

INTRODUCTION

Gynecologic tumor surgery is a large and complex surgery consisting of such procedures as expanded radical surgery for malignant tumors and resection for benign tumors. Such surgeries are often characterized by substantial surgical invasions and surgical complications, which lead to slow postoperative recovery, prolonged hospitalization, and increased medical costs, thus increasing the physical, psychological, and economic burden on patients.[1]

Reducing surgical complications in gynecologic oncology and promoting early patient recovery are important clinical issues that need to be addressed. The current global quality improvement initiative for surgery is Enhanced Recovery After Surgery (ERAS), which aims to improve perioperative care, shorten hospital stays, reduce surgical stress, reduce complications and accelerate recovery.[2] It provides both clinical improvement [3] and cost benefits to the healthcare system.[4]

ERAS guidelines for gynecologic oncology surgery encourage patients to have early postoperative ambulation within 24 h.[2] Having early mobilization can significantly shorten patients' anal venting time, promote patients' gastrointestinal motility, reduce the risk of pulmonary infection and thrombosis, and accelerate organism recovery. Advocacy of early mobilization has been increasingly used as an effective intervention in the concept of rapid rehabilitation surgery.

However, although ERAS guidelines on gynecologic oncology strongly recommend that patients be in early postoperative ambulation within 24 h, ERAS has not yet given specific strategies for guiding patient activity.[2] Currently, a few studies have evaluated patient strategies for early postoperative ambulation, mainly around patients after thoracoscopic lobectomy,[5-6] laparoscopic hepatectomy,[7-8] prostate cancer,[9] and gastric cancer.[10-11] However, all of these studies adopted a fixed daily activity distance to guide postoperative patients, a strategy that undoubtedly did not specifically consider differences in patient fitness, disease severity, and comorbidities, and in particular, did not take into account patient fatigue and acceptability.

We hypothesized that a strategy based on self-fatigue assessment rather than a fixed activity distance to guide early postoperative activity would be easy, individualized, safe, and have better early recovery outcomes as well as compliance, but would need to be supported by high-quality studies. Therefore, this study aims to investigate the effectiveness and safety of a self-fatigue-based assessment to guide early postoperative activity in patients with gynecologic oncology.

METHODS AND ANALYSIS

Study design

This study is a randomized, open parallel controlled study that consists of a screening period of approximately 2-3 days, an intervention period of approximately 2-7 days, and a follow-up period of several days. The study is being conducted between 01/06/2021 and 30/05/2022 at Xiangyang Central Hospital, Affiliated Hospital of Hubei University of Arts and Science. **Figure 1** shows the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) diagram.[30] The SPIRIT checklist is provided in **Appendix I**.

Inclusion criteria

Included in this study are subjects meeting the following inclusion criteria: female, aged ≥18 years, undergoing gynecologic oncologic surgery (both open and lumpectomy), with normal preoperative limb

movement, stable surgical condition, ability to get out of bed, and who voluntarily participated and signed an informed consent form.

Exclusion criteria

Excluded from the study are those meeting any one of the following exclusion criteria: (1) patients undergoing emergency gynecological abdominal surgery; (2) those with mental illness; (3) those with poorly controlled hypertension and poorly controlled diabetes; (4) those with severe hepatic or renal insufficiency; (5) those with the cardiac function of grade 3 or higher, concerning New York Heart Association (NYHA) for cardiac function diagnosis classification criteria;[12] (6) those with confirmed lower extremity venous thrombosis; (7) those with elective surgical stroke within 6 months; (8) those having inpatient day surgery; (9) those with a prior history of intestinal obstruction or those at high risk for intestinal obstruction; (10) those with re-operation within the last 1 month; (11) those who are pregnant or breastfeeding; (12) those with a history of alcohol or drug abuse within the last 12 months; (13) preoperative patients with persistent fever.

Participant recruitment

All patients with gynecologic oncology who have been admitted to the gynecology department at Xiangyang Central Hospital and meet the eligibility criteria are invited to participate in this study, and potential participants are then asked to have a face-to-face conversation with the professional coordinator to discuss the study and the eligibility criteria. After obtaining the informed consent of eligible and interested patients, information on basic patient demographic characteristics (e.g., age, gender, educational background, marital status, type of disease, etc.) is collected and patients are randomized into two groups to receive different interventions.

Informed consent

The general study process is explained to participants at the time of participant recruitment before the start of the study. Participants are informed that participation in the trial is completely voluntary and that they can withdraw from the trial at any time. If they withdraw midway through the study, the data collected about the participant will not be deleted and will be used in the final analysis. Written informed consent is obtained from each participant before they receive any interventions related to the study.

Randomization and allocation concealment

In this study, block randomization is used to generate a sufficient number of random sequence numbers using the statistical program SAS 9.4 PROC PLAN, which were then randomly divided into 2 groups according to a 1:1 ratio before the intervention; the group status was sealed in an opaque envelope and assigned a random number based on a random code. The researcher opened the corresponding numbered envelopes to obtain group status according to the order in which the subjects entered the group. An explicit blinded design would be difficult to implement and of little value to the investigator and patients due to the different strategies for quantifying the two activities and the objectification of the main observations. Therefore, an open study was used in this investigation.

Interventions

Subjects who pass the initial screening are reassessed at the end of the procedure, and those confirmed eligible are formally randomly assigned in a 1:1 ratio to two groups: (1) study group: self-fatigue

assessment group, and (2) control group: fixed activity distance assessment group. Patients in both groups are to be assisted to get out of bed on the first 24 h after surgery, with 15-20 minutes of preparation time before each mobilization, and assisted to walk after completion of the activity assessment by the investigator.If subjects don't meet the intervention volume during each activity intervention, their activity compliance and influencing factors will be assessed. Once adverse events occur during the intervention, the trained nurses will take appropriate nursing actions to mitigate.

Prepare for getting out of bed and moving around

Patients are fed fluids 4-6 hours after surgery, and fully awake patients are instructed to prepare for early mobilization 30-60 minutes after feeding. Patients are maintained in a sitting position for 15-20 min before getting out of bed and instructed to do rehabilitation exercises and ankle pump exercises in bed.

Pain status is assessed based on an inpatient pain dynamic assessment record form: the score ranges from no pain to extreme pain, with the lowest score of 0 and the highest score of 10, for a total of 10 grades. Pain scores 1-3 are classified as mild pain, 4-6 as moderate pain, and ≥ 7 as severe pain. To improve adherence to intervention protocols, patients using an analgesia pump receive an increase in the pre-activity dose; patients not using an analgesia pump receive rectal diclofenac suppositories 30 minutes before getting out of bed or are given 50 mg of Flurbiprofen intravenously 15 minutes before the ambulation. Patients are discharged from bed according to the three "30 seconds" principle and start to mobilize after no discomfort, **see Appendix II**.

Study group: self-fatigue intervention

Postoperative fatigue is assessed by The Borg Rating of Perceived Exertion (RPE) Scale.[14] The RPE is a widely used psychophysiological assessment tool for assessing subjective perception during exercise, ranging from "not feeling breathless or fatigued at all" to "extremely breathless or fatigued" on a scale of 0 for the lowest level and 10 for the highest level. Patients are instructed to perform the activity until the self-fatigue assessment reaches levels 5-6, intervening and assessing every 24 hours until the primary outcome occurs. When using the fatigue assessment intervention, patients are required to wear an electronic bracelet throughout to record the distance (in meters) of early postoperative mobilization, though this is not the focus for this group.

Control group: fixed activity distance intervention

The fixed activity distance group uses an electronic bracelet (brand: Huawei Honor 5i) to record their postoperative mobilization distance (in meters). Patients are instructed to mobilize about 1000-1200 m for the first 24 hours postoperatively[13] for about 1-2 hours; thereafter, the daily activity distance is increased by 500 m on top of the previous day's ambulation distance for 1-2 hours until the primary outcome occurs. When assessed using a fixed activity distance, patients are assessed for fatigue at the end of each intervention using the Borg Exercise Scale. There is no mandatory requirement for fatigue status in this group.

Data collection

Data collection is conducted by trained nursing assessors who assess and collect data from patients during the screening and baseline, intervention period, follow-up period, and close-out.

Enrolment and baseline (V_1, V_2)

Patients are screened upon admission based on inclusion-exclusion criteria, and subjects who meet the screening criteria provide basic demographic characteristics information (e.g., age, gender, educational background, marital status, type of disease, etc.). When the patient is further screened at the end of the procedure for their confirmation of inclusion-exclusion criteria, they are enrolled and their vital signs (pulse, respiratory rate, temperature, and blood pressure) are measured by the study nurse and assessed using a modified version of the Morse Scale used to measure the risk of falling out of bed in adults, including 10 items with a score ranging from 0-20. The Caprini Risk Assessment Scale is used to assess the occurrence of venous thromboembolism (VTE). This helpful risk quantification tool[15] can effectively screen high-risk patients for VTE [16]. The Caprini Risk Assessment Scale includes 39 risk factors (17 risk factors were assigned 1 point, 7 risk factors were assigned 2 points, 10 risk factors were assigned 3 points and 5 risk factors were assigned 5 points). Caprini scores were 0-1 for low-risk VTE, 2 for medium-risk VTE, 3-4 for high-risk VTE, and ≥5 for very high-risk VTE.

Intervention (V_2-V_x)

During the intervention period, one activity intervention is completed within each 24 h cycle, with the study nurse asking the patient if they had anal venting before each intervention. The patient's vital signs (pulse, respiratory rate, temperature, and blood pressure) are assessed after the intervention and the following indicators:

Bloating is assessed during each visit cycle, and moderate and severe cases are recorded. Bloating is classified into 4 grades: (1) no bloating; (2) mild: abdominal distension is elevated and slightly higher than the chest, percussion is a low-pitched drum sound, bowel sounds may be diminished, slightly hyperactive or normal, mild abdominal distension may be present; (3) moderate: the abdomen is elevated and significantly higher than the chest with some tension, percussion is a mid-pitched drum sound with increased and pronounced range and intensity, bowel sounds are mostly diminished, and there is significant conscious bloating that interferes with eating or another metabolism; (4) severe: the whole abdomen is bulging in a spherical shape, hard and uncomfortable when pressed, without rebound pain, the percussion is a high-pitched drum sound and may appear as a metallic percussion, without any change in position bowel sounds are markedly diminished or non-existent, and there are obvious gastrointestinal reactions. To assess the possibility of intestinal obstruction during each visit, if highly suspected, an abdominal radiograph should be used.

The Pittsburgh sleep quality index (PSQI) scale is used to assess the sleep quality of patients during each interview period. The scale had high reliability and validity [17, 18]; the scale is composed of 19 self-rated items and 5 other items, where the 19th self-rated entry and 5 other-rated entries are not involved in scoring, and the 18 self-rated entries form a total of 7 components, each component is scored on a scale of 0-3. The cumulative component score is the total PSQI score, ranging from 0-2l, with higher scores indicating poorer sleep quality.

The occurrence of adverse events such as nausea, vomiting, and vertigo during each visiting period is investigated and the outcome recorded.

Subjects' activity compliance is assessed by the degree to which they meet the intervention volume after each activity intervention.

Follow up (V_x)

If the patient appears to exhibit anal exhaust, the intervention period is over. The exact time when the patient experienced the first anal venting (hours) is determined. The patient's vital signs at the end of the intervention period are assessed, total compliance with activities throughout the intervention period is calculated, the incidence of bowel obstruction and the moderate and worst degree of abdominal distension is calculated, and the mean sleep quality score and the incidence of adverse patient reactions are calculated.

Close-out (V_{x+1})

After the intervention, follow-up continues until discharge from the hospital, at which time information on the hospitalization costs and days of hospitalization, the degree of bloating, the occurrence of intestinal obstruction, the sleep quality score, the satisfaction with the early mobility instructions, and other relevant information is collected. The registration, intervention, assessment, and access schedules of participants are shown in **Table 1**.

Table 1 Study plan detailing the procedures

	Study Period				
	Enrolment	**Allocation**	**Post-allocation**	**Follow up**	**Close-out**
Visit	V_1	V_2	.....	V_x	V_{x+1}
Timepoint	Hospitalization	End of surgery	1 intervention in every 24 h	When the primary outcome occurs	Discharge
Enrolment:					
Informed consent	×				
Eligibility screen	×	×			
Demographics	×				
Allocation		×			
Intervention:					
Self-fatigue assessment			→		
Fixed activity distance assessment			→		
Assessments:					
vital signs	×	×	×	×	×
Risk of falls	×	×			
First exhaust time			×	×	
Moderate to severe bloating			×	×	×
Intestinal obstruction			×	×	×
Venous thromboembolism		×			×
Pain score		×			
Adverse reactions			×	×	

(nausea, vomiting, dizziness)					
Sleep quality score	×		×	×	×
Hospitalization costs					×
Length of hospitalization					×
Activity compliance			×	×	
Patient satisfaction					×

Outcome measures

The primary and secondary outcomes are shown in **Table 2**.

Table 2 Primary and secondary outcomes

	Outcome measure
Primary outcome	
To compare the effect of early bedtime activity in the self-fatigue assessment group with that in the fixed activity distance group on the time to first post-operative exhaustion in gynecological oncology patients.	Time from the end of the procedure to the patient's first venting (h).
Secondary outcomes	
To compare the effects of early bed activity in the self-fatigue assessment group with those in the fixed activity distance group on the time to the first bowel movement, the incidence of moderate to severe bloating, the incidence of bowel obstruction or Venous thromboembolism, the incidence of adverse effects (nausea, vomiting, dizziness), patient satisfaction, mean sleep quality score, patient compliance with activities, and hospital costs and days of hospitalization in gynecologic oncology patients.	1. Time from the end of the procedure to the patient's first bowel movement (h). 2. Incidence of post-activity adverse reactions (nausea, vomiting, dizziness) = number of patients in each group with post-activity adverse reactions (nausea, vomiting, dizziness) / total number of patients in the group × 100%. 3. Incidence of moderate to severe abdominal distention after patient activity = number of patients in each group with moderate to severe abdominal distention after intervention activity/total number of patients in that group x 100%. 4. Incidence of post-activity bowel obstruction or Venous thromboembolism in patients = number of post-activity bowel obstruction or Venous thromboembolism in each group/total number of patients in that group × 100%. 5. Patient satisfaction rate with bed mobility instruction = number of patients in each group satisfied with early bed mobility instruction/total number of patients in that group x 100%. 6. Mean post-activity sleep quality score for patients. 7.Patient compliance with activity = number of patients in each group who met the standard for early postoperative bed activity/total number of patients in the group x 100%. 8. The average cost of hospitalization and the average number of days in the hospital for each group of patients.
Safety outcome	
Evaluating the safety of two activity	Incidence of adverse events/serious adverse events.

strategies	Vital characteristics (including data on the pulse, respiration, temperature, blood pressure, etc.).

Quality control

Before the trial, all staff will be required to attend a series of training courses. These courses will ensure that relevant personnel is fully aware of the study protocol and standard operating procedures for the study. To maintain the high quality of the clinical trial, the Xiangyang Central Hospital Clinical Research Centre will regularly monitor study documents, informed consent forms, Case Report Forms (CRFs), serious adverse events, and data records.

Data management

The CRFs and adverse event forms will be completed first and then electronically entered into the electronic data capture (EDC) system by two independent investigators as the first level of control to ensure data accuracy. The second level of data integrity will include data monitoring and validation, which will occur at regular intervals throughout the study. The original CRFs and all other forms (including consent forms) will be kept securely at the Clinical Research Center of Xiangyang Central Hospital, Hubei College of Arts and Sciences for 5 years after the last paper or study report is published.

The safety of this study will be monitored by the Data and Safety Monitoring Board (DSMB) of the Clinical Assessment Center at Xiangyang Central Hospital, Hubei College of Arts and Sciences, which is composed of independent clinical experts and statisticians. The DSMB is independent of competing interests and study sites and will review the performance and safety of the trial every month.

Criteria for discontinuation of the assigned intervention for a given participant include serious complications or a serious adverse event, if any, as described previously. The DSMB will make the final decision to terminate the trial.

The final trial dataset will be maintained by Xiangyang Central Hospital. The data management staff of the Xiangyang Central Hospital clinical assessment center will have access to the complete, anonymized final dataset. Access to the final dataset or identifiable data by others will require written request approval by the DSMB of the Xiangyang Central Hospital clinical assessment center and all investigators.

Patients and public involvement

Patients and the public are not involved in the design or conduct of the study or the outcome measures, and no attempt will be made to assess the burden of the intervention on the patients themselves.

Sample size estimate

The sample size is determined based on the results of a literature review and pre-trial,[19-20] and 552 patients will be included in this study. This sample size is based on the following statistical considerations: the primary outcome hypothesis was that patients with gynecologic oncology were non-inferior to patients with self-fatigue assessment in early postoperative ambulation in terms of time to first postoperative exhaust compared to patients with fixed activity distance assessment. Based on the literature review and pre-trial studies, a conservative estimate of the standard deviation (SD) of the change in postoperative time to first anal venting was 8 h, with a non-inferiority cut-off of 2 h. At a bilateral 0.05 alpha level and 20% dropout rate, 552 patients with a 1:1 allocation rate (276 patients per group) would provide at least 85% validity to detect at least 2 h difference in change in time to first postoperative anal venting.

Statistical analysis

All data will be analyzed by statisticians using SAS 9.4 (SAS Institute, Cary, NC, USA) at the Xiangyang Central Hospital clinical research center. Baseline assessments will be performed before randomization to groups and include patient gender and age, type of disease, vital signs (pulse, respiratory rate, temperature, and blood pressure), fall risk level, ability to perform activities of daily living, the primary outcome (Anal venting), and secondary outcomes (complications, adverse effects, degree of bloating, sleep quality score, activity compliance, cost of hospitalization and the length of hospitalization). All patients randomly assigned to each group will be included in the analysis, and data analysis will be performed using a 5% two-sided significance test.

The primary analysis population will be based on the Full Analysis Set (FAS) of data and all analyses will be based on the intention-to-treat principle (ITT) using the last observation carried forward principle. Missing values will be filled by multiple imputations (MI). Continuous variables that conform to a normal distribution are expressed as means ± standard deviations (SDs) and compared by independent samples t-test. For variables that do not conform to a normal distribution, data will be expressed as median (25%-75%) and compared using a non-parametric test. Categorical variables will be expressed as numbers (%) and analyzed using the chi-square test or Fisher's exact test. Descriptive statistics will be used to detail baseline participant demographics and general patient status characteristics such as gender, age, disease type, vital signs, fall risk rating, and ability to perform activities of daily living. A chi-square test will be used to compare the differences in time to first anal venting, complications, adverse events, degree of bloating, sleep quality score, activity compliance, cost

of hospitalization, the length of hospitalization, and incidence of adverse events between the two groups.

ETHICS AND DISSEMINATION

The trial was approved by the Independent Ethics Committee of Xiangyang Central Hospital affiliated with Hubei University of Arts and Sciences (Project No. 2021C12) and registered with the China Clinical Trials Registry (https://register.clinicaltrials.gov/, Registration No. CTR2100046035, Registration Date: 02/05/2021). The results of the trial will be submitted to peer-reviewed journals and abstracts will be submitted to relevant national and international conferences.

Signed and dated informed consent will be provided by each subject before the conduct of the study. This study is strictly confidential concerning patient information and no public information will reveal the identity of the subjects.

DISCUSSION

ERAS guidelines strongly recommend that patients achieve early ambulation within 24 h after surgery,[3,21] but these recommendations lack in-depth research on strategies to guide early mobilization. Early postoperative ambulation can promote gastrointestinal recovery, but it is not possible to determine the level of activity required for gastrointestinal recovery, which can lead to over-or under-activity and complications in postoperative recovery. In a survey on the demand for postoperative ambulation health education for patients undergoing abdominal surgery, 47.07% of patients wanted to know "how to arrange the amount of early ambulation ",[22] which shows that patients have a greater demand for precise activity guidance after surgery.

The main factors influencing early postoperative ambulation in patients undergoing abdominal surgery are patient incisional pain,[23-25] postoperative fatigue, upright intolerance,[26-27] demographic factors,[28] and psychosocial factors. Some studies[5,29] quantified only the distance and duration of activity and did not consider individual differences in surgical patients in terms of age, complications, and postoperative fatigue. Therefore, a good early activity guidance strategy should be based on the patient's actual situation to guide early bed activity. Assessing the amount of early mobilization based on self-fatigue adequately takes into account individual patient differences and appears to be more effective than simply assessing the distance and duration of early bed activity for patients. However, to our knowledge, no studies are examining the validity and safety of assessing patients' early postoperative bed activity based on self-fatigue, and its benefits need to be further confirmed by standardized, transparent, and well-conducted randomized clinical trials.

This study is the first randomized controlled trial of early postoperative mobilization strategy guidance for gynecologic oncology patients to investigate the effectiveness and safety of early postoperative mobilization in inpatients undergoing gynecologic oncology surgery based on self-fatigue assessment relative to those based on fixed activity distance assessment, and it may provide support for early postoperative mobilization strategy guidance for patients undergoing gynecologic oncology surgery.

Trial status

The first participant was enrolled in June 2021. and the study is expected to end in June 2022.

Author contributions XJH is the principal investigator of this study and refined the protocol. QD, BC, and SYX wrote the manuscript and contributed to the design of the study. QD will recruit the patients and conduct the trial. HH, XMQ, and TTK will supervise the trial. BC, the medical statistician for the study, will contribute to the statistical design and analysis of data. All authors have revised the protocol critically for important intellectual content and approved the final manuscript.

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Disclaimer Sponsors of the study had no involvement in the collection, analysis, and interpretation of data or the writing of the manuscript.

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval The study protocol has been approved by the Independent Ethics Committee of Xiangyang Central Hospital affiliated with Hubei University of Arts and Sciences (permission number: 2021C12) (May 2021).

Provenance and peer review Not commissioned; externally peer-reviewed

Data sharing statement The submitted manuscript is a study protocol that includes no primary data now. Further information unaddressed can be obtained from the corresponding author by the contact methods provided in the manuscript.

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Figures legends

Figure 1 Flowchart of the trial design, based on the SPIRIT 2013.

Appendix I SPIRIT-Checklist

Appendix II Exercising steps before getting out of bed

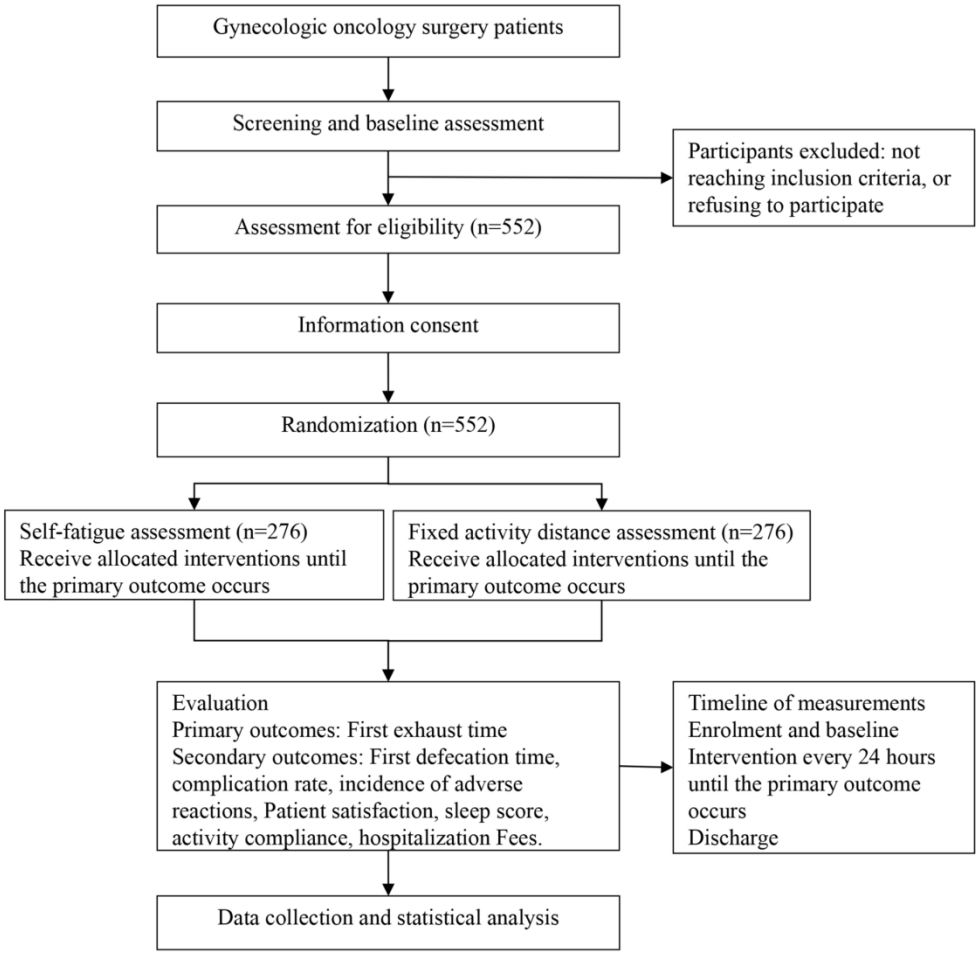

Figure 1 Flowchart of the trial design, based on the SPIRIT 2013.

173x167mm (300 x 300 DPI)

Appendix I 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	None
Protocol version	3	Date and version identifier	None
Funding	4	Sources and types of financial, material, and other support	12
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	12
	5b	Name and contact information for the trial sponsor	None
	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	12
	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)	None
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
	6b	Explanation for choice of comparators	3

Objectives	7	Specific objectives or hypotheses	3
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)	3
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	3
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)	3-4
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	4-5
	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)	4-5
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	5
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	5
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)	7-8
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	9-10
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	4

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	4
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	4
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	4
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	4
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	None

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	5-7
	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	None
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	9

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)	None
	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	9
	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	9
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	5
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	9
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	11
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)	None
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	11

	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	None
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	11
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	None
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	None
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	12
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	None
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	None

*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.

Appendix II: Exercising steps before getting out of bed

1. Rehabilitation exercises: alternate all exercises left and right, train three groups per day.

(1) Upper limb flexion for hands clenched fist relaxation exercises 20-30 times / group.

(2) Upper limb elevation, elbow flexion and extension, fist clenching and upper limb flattening exercises 5-10 times / group.

(3) Lower limb flexion, single foot stirrups and lower limb flattening exercises 5-10 times / group.

(4) Lower limb elevation, knee bending and lower limb flattening exercises 5-10 times / group.

2. Ankle pump exercises: extension and flexion around the ring for 1 group, eight groups per hour, eight times a day.

(1) Dorsal foot extension and flexion action: the patient lies or sits on the bed, the lower limb is extended, the thigh is relaxed, slowly hooks the toe and tries his best to make the toe face himself, keep it for 10-20 seconds at the maximum.

(2) Ankle loop: The patient lies or sits on the bed with the lower limbs extended and the thighs relaxed, making a 360-degree loop with the ankle joint as the center, practicing clockwise and counterclockwise for 10 seconds each.

3. The three "30 seconds" principle:

(1) Lie in bed and spend thirty seconds moving your hands and feet.

(2) Get up slowly, sit for 30 seconds and move your hands and feet.

(3) Get out of bed and stand up for thirty seconds and start walking.

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Effectiveness of the self-fatigue assessment in guiding early postoperative ambulation in gynecologic oncology patients: study protocol for a randomized controlled trial

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Primary Subject Heading:	Surgery
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Effectiveness of the self-fatigue assessment in guiding early postoperative ambulation in gynecologic oncology patients: study protocol for a randomized controlled trial

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ABSTRACT

Introduction Enhanced recovery after surgery guidelines strongly recommends that patients be in early postoperative ambulation within 24 h. This study aims to assess the effectiveness and safety of the self-fatigue assessment method to guide patients' early postoperative ambulation.

Methods and analysis This is a single-center, randomized, open, parallel-controlled trial. Five hundred fifty-two patients who meet the inclusion criteria for gynecologic oncology surgery are randomly assigned in a 1:1 ratio to either a self-fatigue assessment group (study group) or a fixed activity distance assessment group (control group). The fixed activity distance group adopts a fixed early postoperative ambulation distance to guide the patient's activity, while the self-fatigue assessment group uses the Borg Exercise Scale to assess the patient's fatigue and stops activity when the fatigue level reaches 5-6. The primary outcome measure is the time to first postoperative flatus. Secondary outcome measures are the time to first bowel movement, the incidence of moderate to severe bloating, the incidence of bowel obstruction or Venous thromboembolism, the incidence of adverse events (nausea, vomiting, dizziness), patient satisfaction, sleep quality scores, patient compliance with activities, hospital costs, and days in hospital.

Ethics and dissemination This study was approved by the Independent Ethics Committee of Xiangyang Central Hospital affiliated with Hubei University of Arts and Sciences and registered with the China Clinical Trials Registry in May 2021. The results of the trial will be disseminated through open access peer-reviewed journals and abstracts will be submitted to relevant national and international conferences.

Trial registration number: CTR2100046035, date: 02 May 2021.

Keywords gynecologic oncology, early ambulation, self-fatigue assessment, fixed activity distance assessment, study protocol

Strengths and limitations of this study

► The results from this randomized clinical trial will provide new and high-quality evidence to support early postoperative ambulation in gynecologic oncology patients.

► All interventions will be instructor-led, patients in both groups are to be assisted to get out of bed on the first 24 h after surgery, with the aim of decreasing the risk of adverse events.

► One limitation is that the trial is not a double-blind, placebo-controlled trial and implemented in only one hospital, which may limit its generalisability.

► The first flatus status and some secondary outcomes are self-reported by the patient**,** which may lead to recall or report bias.

INTRODUCTION

Gynecologic tumor surgery is a large and complex surgery consisting of such procedures as expanded radical surgery for malignant tumors and resection for benign tumors. Such surgeries are often characterized by substantial surgical invasions and surgical complications, which lead to slow postoperative recovery, prolonged hospitalization, and increased medical costs, thus increasing the physical, psychological, and economic burden on patients.[1]

Reducing surgical complications in gynecologic oncology and promoting early patient recovery are important clinical issues that need to be addressed. The current global quality improvement initiative for surgery is Enhanced Recovery After Surgery (ERAS), which aims to improve perioperative care, shorten hospital stays, reduce surgical stress, reduce complications and accelerate recovery.[2] It provides both clinical improvement [3] and cost benefits to the healthcare system.[4]

ERAS guidelines for gynecologic oncology surgery encourage patients to have early postoperative ambulation within 24 h.[2] Having early mobilization can significantly shorten patients' anal flatus time, promote patients' gastrointestinal motility, reduce the risk of pulmonary infection and thrombosis, and accelerate organism recovery. Advocacy of early mobilization has been increasingly used as an effective intervention in the concept of rapid rehabilitation surgery.

However, although ERAS guidelines on gynecologic oncology strongly recommend that patients be in early postoperative ambulation within 24 h, early ambulation following surgery is substantially impacted by pain management pre and post surgery, [5] postoperative fatigue, upright intolerance, [6-7] as well as the Body Mass Index (BMI). Therefore, ERAS has not yet explicit recommendations for directing and quantifying patient activity.[2] Currently, a few studies have evaluated patient strategies for early postoperative ambulation, mainly around patients after thoracoscopic lobectomy,[8-9] laparoscopic hepatectomy,[10-11] prostate cancer,[12] and gastric cancer.[13-14] However, all of these studies adopted a fixed daily activity distance to guide postoperative patients, a strategy that undoubtedly did not specifically consider differences in patient fitness, disease severity, and comorbidities, and in particular, did not take into account patient fatigue and acceptability.

We hypothesized that a strategy based on self-fatigue assessment rather than a fixed activity distance to guide early postoperative activity would be easy, individualized, safe, and have better early recovery outcomes as well as compliance, but would need to be supported by high-quality studies. Therefore, this study aims to investigate the effectiveness and safety of a self-fatigue-based assessment to guide early postoperative activity in patients with gynecologic oncology.

METHODS AND ANALYSIS

Study design

This study is a randomized, open parallel controlled study that consists of a screening period of approximately 2-3 days, an intervention period of approximately 2-7 days, and a follow-up period of several days. The study is being conducted between 01/06/2021 and 30/05/2022 at Xiangyang Central Hospital, Affiliated Hospital of Hubei University of Arts and Science. **Figure 1** shows the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) diagram.[15] The SPIRIT checklist is provided in **Appendix I**.

Inclusion criteria

Included in this study are subjects meeting the following inclusion criteria: female with no cognition impairment, aged ≥18 years, 18.5 ≤ BMI ≤ 24.9, undergoing gynecologic oncologic elective surgery (open/laparoscopic), with normal preoperative limb movement, stable surgical condition, ability to get out of bed, American Society of Anesthesiologists (ASA) Physical Status Classification I-III, and who voluntarily participated and signed an informed consent form.

Exclusion criteria

Excluded from the study are those meeting any one of the following exclusion criteria: (1) those with delirium after surgery; (3) those with the cardiac function of grade 3 or higher, which referring to New York Heart Association (NYHA) for cardiac function diagnosis classification criteria;[16] (4) perioperative patients with confirmed lower extremity venous thrombosis; (5) those with re-operation within the last 1 month; (6) those who are pregnant or breastfeeding; (7) perioperative patients with persistent fever and temperature is 38.5 or higher.

Participant recruitment

All patients with gynecologic oncology who have been admitted to the gynecology department at Xiangyang Central Hospital and meet the eligibility criteria are invited to participate in this study, and potential participants are then asked to have a face-to-face interview with the professional coordinator to discuss the study and the eligibility criteria. After obtaining the informed consent of eligible and interested patients, information on basic patient demographic characteristics (e.g., age, gender, educational background, marital status, type of disease, etc.) is collected, and patients are randomized into two groups to receive different interventions.

Informed consent

The general study process is explained to participants at the time of participant recruitment before the start of the study. Participants are informed that participation in the trial is completely voluntary and that they can withdraw from the trial at any time. If they withdraw midway through the study, the data collected about the participant will not be deleted and will be used in the final analysis. Written informed consent is obtained from each participant before they receive any interventions related to the study.

Randomization and allocation concealment

In this study, block randomization is used to generate a sufficient number of random sequence numbers using the statistical program SAS 9.4 PROC PLAN, which were then randomly divided into 2 groups according to a 1:1 ratio before the intervention; the group status was sealed in an opaque envelope and assigned a random number based on a random code. The researcher opened the corresponding numbered envelopes to obtain group status according to the order in which the subjects entered the group. An explicit blinded design would be difficult to implement and of little value to the investigator and patients due to the different strategies for quantifying the two activities and the objectification of the main observations. Therefore, an open study was used in this investigation.

Interventions

Subjects who pass the initial screening are reassessed at the end of the procedure, and those confirmed eligible are formally randomly assigned in a 1:1 ratio to two groups: (1) study group: self-fatigue assessment group, and (2) control group: fixed activity distance assessment group. Patients in both groups are to be assisted to get out of bed on the first 24 h after surgery, with 15-20 minutes of preparation time before each mobilization, and assisted to walk after completion of the activity assessment by the investigator.If subjects don't meet the intervention volume during each activity intervention, their activity compliance and influencing factors will be assessed. Once adverse events occur during the intervention, the trained nurses will take appropriate nursing actions to mitigate.

Prepare for getting out of bed and moving around

Patients are fed fluids 4-6 hours after surgery, and fully awake patients are instructed to prepare for early mobilization 30-60 minutes after feeding. Patients are maintained in a sitting position for 15-20 min before getting out of bed and instructed to do rehabilitation exercises and ankle pump exercises in bed.

Our pain management philosophy revolves around setting appropriate patient-centred expectations. Pain status is assessed based on an inpatient pain dynamic assessment record form: the score ranges from no pain to extreme pain, with the lowest score of 0 and the highest score of 10, for a total of 10 grades. Pain scores 1-3 are classified as mild pain, 4-6 as

moderate pain, and ≥ 7 as severe pain. To improve adherence to intervention protocols, patients using an analgesia pump (including hydromorphone, sufentanil, and flurbiprofen ester) will receive a double dose of analgesia in the pre-activity; patients not using an analgesia pump will receive rectal diclofenac suppositories 30 minutes before getting out of bed or are given 50 mg of flurbiprofen intravenously 15 minutes before ambulation. Patients are freed from bed according to the three "30 second" principles and start to mobilize after no discomfort, **see Appendix II**.

Study group: self-fatigue intervention

Postoperative fatigue is assessed by the modified 0–10 category ratio Borg Rating of Perceived Exertion (RPE) Scale.[17] The RPE is a widely used psychophysiological assessment tool for assessing subjective perception during exercise, the end points of the scale were anchored such that zero represented "no discomfort at all" and 10 represented "the most intense discomfort [they] have every experienced or could ever imagine experiencing.. Patients are instructed to perform the activity until the self-fatigue assessment reaches levels 5-6 (intense discomfort, tiredness, and slightly difficult to continue walking), intervening and assessing every 24 hours until the primary outcome occurs. To ensure the reliability of the assessment and to help build the patient's confidence, all key members of the patient's social support network, (the 'family', attending physician, and nurses) are invited for the patient's psychological intervention, and encourage early ambulation. When using the fatigue assessment intervention, patients are required to wear an electronic bracelet throughout to record the distance (in meters) of early postoperative mobilization, though this is not the focus for this group.

Control group: fixed activity distance intervention

The fixed activity distance group uses an electronic bracelet (brand: Huawei Honor 5i) to

record their postoperative mobilization distance (in meters). Patients are instructed to mobilize about 1000-1200 m for the first 24 hours postoperatively[18] for about 1-2 hours; thereafter, the daily activity distance is increased by 500 m on top of the previous day's ambulation distance for 1-2 hours until the primary outcome occurs. When assessed using a fixed activity distance, patients are assessed for fatigue at the end of each intervention using the Borg Exercise Scale. There is no mandatory requirement for fatigue status in this group.

Data collection

Data collection is conducted by trained nursing assessors who assess and collect data from patients during the screening and baseline, intervention period, follow-up period, and close-out.

Enrolment and baseline (V_1, V_2)

Patients are screened upon admission based on inclusion-exclusion criteria, and subjects who meet the screening criteria provide basic demographic characteristics information (e.g., age, gender, educational background, marital status, type of disease, etc.). When the patient is further screened at the end of the procedure for their confirmation of inclusion-exclusion criteria, they are enrolled and their vital signs (pulse, respiratory rate, temperature, and blood pressure) are measured by the study nurse and assessed using a modified version of the Morse Scale used to measure the risk of falling out of bed in adults, including 10 items with a score ranging from 0-20. The Caprini Risk Assessment Scale is used to assess the occurrence of venous thromboembolism (VTE). This helpful risk quantification tool[19] can effectively screen high-risk patients for VTE. [20] The Caprini Risk Assessment Scale includes 39 risk factors (17 risk factors were assigned 1 point, 7 risk factors were assigned 2 points, 10 risk factors were assigned 3 points and 5 risk factors were assigned 5 points). Caprini scores were 0-1 for low-risk VTE, 2 for medium-risk VTE, 3-4 for high-risk VTE, and ≥5 for very high-risk VTE.

Intervention (V_2-V_x)

During the intervention period, one activity intervention is completed within each 24 h cycle, with the study nurse asking the patient if they had anal flatus before each intervention. The patient's vital signs (pulse, respiratory rate, temperature, and blood pressure) are assessed after the intervention and the following indicators:

Bloating is assessed during each visit cycle, and moderate and severe cases are recorded. Bloating is classified into 4 grades: (1) no bloating; (2) mild: abdominal distension is elevated and slightly higher than the chest, percussion is a low-pitched drum sound, bowel sounds may be diminished, slightly hyperactive or normal, mild abdominal distension may be present; (3) moderate: the abdomen is elevated and significantly higher than the chest with some tension, percussion is a mid-pitched drum sound with increased and pronounced range and intensity, bowel sounds are mostly diminished, and there is significant conscious bloating that interferes with eating or another metabolism; (4) severe: the whole abdomen is bulging in a spherical shape, hard and uncomfortable when pressed, without rebound pain, the percussion is a high-pitched drum sound and may appear as a metallic percussion, without any change in position bowel sounds are markedly diminished or non-existent, and there are obvious gastrointestinal reactions. To assess the possibility of intestinal obstruction during each visit, if highly suspected, an abdominal radiograph should be used.

The Pittsburgh sleep quality index (PSQI) scale is used to assess the sleep quality of patients during each interview period. The scale had high reliability and validity; [21-22] the scale is composed of 19 self-rated items and 5 other items, where the 19th self-rated entry and 5 other-rated entries are not involved in scoring, and the 18 self-rated entries form a total of 7 components, each component is scored on a scale of 0-3. The cumulative component score is the total PSQI score, ranging from 0-21, with higher scores indicating poorer sleep quality.

The occurrence of adverse events such as nausea, vomiting, and vertigo during each visiting period is investigated and the outcome recorded.

Subjects' activity compliance is assessed by the degree to which they meet the intervention volume after each activity intervention.

Follow up (V_x)

If the patient appears to exhibit anal flatus, the intervention period is over. The exact time when the patient experienced the first anal flatus (hours) is determined. The patient's vital signs at the end of the intervention period are assessed, total compliance with activities throughout the intervention period is calculated, the incidence of bowel obstruction and the moderate and worst degree of abdominal distension is calculated, and the mean sleep quality score and the incidence of adverse patient reactions are calculated.

Close-out (V_{x+1})

After the intervention, follow-up continues until discharge from the hospital, at which time information on the hospitalization costs and days of hospitalization, the degree of bloating, the occurrence of intestinal obstruction, the sleep quality score, the satisfaction with the early mobility instructions, and other relevant information is collected. The registration, intervention, assessment, and access schedules of participants are shown in **Table 1**.

Table 1 Study plan detailing the procedures

	Study Period				
	Enrolment	**Allocation**	**Post-allocation**	**Follow up**	**Close-out**
Visit	V_1	V_2	.....	V_x	V_{x+1}
Timepoint	Hospitalization	End of surgery	1 intervention in every 24 h	When the primary outcome occurs	Discharge
Enrolment:					
Informed consent	×				

Eligibility screen	×	×			
Demographics	×				
Allocation		×			
Intervention:					
Self-fatigue assessment			→		
Fixed activity distance assessment			→		
Assessments:					
vital signs	×	×	×	×	×
Risk of falls	×	×			
First exhaust flatus time			×	×	
Moderate to severe bloating			×	×	×
Intestinal obstruction			×	×	×
Venous thromboembolism		×			×
Pain score		×			
Adverse reactions (nausea, vomiting, dizziness)			×	×	
Sleep quality score	×		×	×	×
Hospitalization costs					×
Length of hospitalization					×
Activity compliance			×	×	
Patient satisfaction					×

Outcome measures

The primary and secondary outcomes are shown in **Table 2**.

Table 2 Primary and secondary outcomes

	Outcome measure
Primary outcome	
To compare the effect of early bedtime activity in the self-fatigue assessment group with that in the fixed activity distance group on the time to first post-operative flatus in gynecological oncology patients.	Time from the end of the procedure to the patient's first flatus (h).
Secondary outcomes	
To compare the effects of early bed activity in the self-fatigue assessment group with those in the fixed activity distance group on the time to the first bowel movement,	1. Time from the end of the procedure to the patient's first bowel movement (h). 2. Incidence of post-activity adverse reactions (nausea, vomiting, dizziness) = number of patients in each group with post-activity adverse

the incidence of moderate to severe bloating, the incidence of bowel obstruction or Venous thromboembolism, the incidence of adverse effects (nausea, vomiting, dizziness), patient satisfaction, mean sleep quality score, patient compliance with activities, and hospital costs and days of hospitalization in gynecologic oncology patients.	reactions (nausea, vomiting, dizziness) / total number of patients in the group × 100%. 3. Incidence of moderate to severe abdominal distention after patient activity = number of patients in each group with moderate to severe abdominal distention after intervention activity/total number of patients in that group x 100%. 4. Incidence of post-activity bowel obstruction or Venous thromboembolism in patients = number of post-activity bowel obstruction or Venous thromboembolism in each group/total number of patients in that group × 100%. 5. Patient satisfaction rate with bed mobility instruction = number of patients in each group satisfied with early bed mobility instruction/total number of patients in that group x 100%. 6. Mean post-activity sleep quality score for patients. 7.Patient compliance with activity = number of patients in each group who met the standard for early postoperative bed activity/total number of patients in the group x 100%. 8. The average cost of hospitalization and the average number of days in the hospital for each group of patients.
Safety outcome	
Evaluating the safety of two activity strategies	Incidence of adverse events/serious adverse events. Vital characteristics (including data on the pulse, respiration, temperature, blood pressure, etc.).

Quality control

Before the trial, all staff will be required to attend a series of training courses. These courses will ensure that relevant personnel is fully aware of the study protocol and standard operating procedures for the study. To maintain the high quality of the clinical trial, the Xiangyang Central Hospital Clinical Research Centre will regularly monitor study documents, informed consent forms, Case Report Forms (CRFs), serious adverse events, and data records.

Data management

The CRFs and adverse event forms will be completed first and then electronically entered into the

electronic data capture (EDC) system by two independent investigators as the first level of control to ensure data accuracy. The second level of data integrity will include data monitoring and validation, which will occur at regular intervals throughout the study. The original CRFs and all other forms (including consent forms) will be kept securely at the Clinical Research Center of Xiangyang Central Hospital, Hubei College of Arts and Sciences for 5 years after the last paper or study report is published.

The safety of this study will be monitored by the Data and Safety Monitoring Board (DSMB) of the Clinical Assessment Center at Xiangyang Central Hospital, Hubei College of Arts and Sciences, which is composed of independent clinical experts and statisticians. The DSMB is independent of competing interests and study sites and will review the performance and safety of the trial every month.

Criteria for discontinuation of the assigned intervention for a given participant include serious complications or a serious adverse event, if any, as described previously. The DSMB will make the final decision to terminate the trial.

The final trial dataset will be maintained by Xiangyang Central Hospital. The data management staff of the Xiangyang Central Hospital clinical assessment center will have access to the complete, anonymized final dataset. Access to the final dataset or identifiable data by others will require written request approval by the DSMB of the Xiangyang Central Hospital clinical assessment center and all investigators.

Patients and public involvement

Patients and the public are not involved in the design or conduct of the study or the outcome measures, and no attempt will be made to assess the burden of the intervention on the patients themselves.

Sample size estimate

The sample size is determined based on the results of a literature review and pre-trial,[23-24] and 552 patients will be included in this study. This sample size is based on the following statistical considerations: the primary outcome hypothesis was that patients with gynecologic oncology were non-inferior to patients with self-fatigue assessment in early postoperative ambulation in terms of time to first postoperative flatus compared to patients with fixed activity distance assessment. Based on the literature review and pre-trial studies, a conservative estimate of the standard deviation (SD) of the change in postoperative time to first anal flatus was 8 h, with a non-inferiority cut-off of 2 h. At a bilateral 0.05 alpha level and 20% dropout rate, 552 patients with a 1:1 allocation rate (276 patients per group) would provide at least 85% validity to detect at least 2 h difference in change in time to first postoperative anal flatus.

Statistical analysis

All data will be analyzed by statisticians using SAS 9.4 (SAS Institute, Cary, NC, USA) at the Xiangyang Central Hospital clinical research center. Baseline assessments will be performed before randomization to groups and include patient gender and age, type of disease, vital signs (pulse, respiratory rate, temperature, and blood pressure), fall risk level, ability to perform activities of daily living, the primary outcome (time to first flatus), and secondary outcomes (complications, adverse effects, degree of bloating, sleep quality score, activity compliance, cost of hospitalization and the length of hospitalization). All patients randomly assigned to each group will be included in the analysis, and data analysis will be performed using a 5% two-sided significance test.

The primary analysis population will be based on the Full Analysis Set (FAS) of data and all analyses will be based on the intention-to-treat principle (ITT) using the last observation carried forward principle. Missing values will be filled by multiple imputations (MI). Continuous variables that conform to a normal distribution are expressed as means ± standard deviations (SDs) and compared by independent samples t-test. For variables that do not conform to a normal distribution, data will be expressed as median (25%-75%) and compared using a non-parametric test. Categorical variables will be expressed as numbers (%) and analyzed using the chi-square test or Fisher's exact test. Descriptive statistics will be used to detail baseline participant demographics and general patient status characteristics such as gender, age, disease type, vital signs, fall risk rating, and ability to perform

activities of daily living. A chi-square test will be used to compare the differences in time to first anal flatus, complications, adverse events, degree of bloating, sleep quality score, activity compliance, cost of hospitalization, the length of hospitalization, and incidence of adverse events between the two groups.

ETHICS AND DISSEMINATION

The trial was approved by the Independent Ethics Committee of Xiangyang Central Hospital affiliated with Hubei University of Arts and Sciences (Project No. 2021C12) and registered with the China Clinical Trials Registry (http://www.chictr.org.cn/index.aspx, Registration No. CTR2100046035, Registration Date: 02/05/2021). The results of the trial will be submitted to peer-reviewed journals and abstracts will be submitted to relevant national and international conferences.

Signed and dated informed consent will be provided by each subject before the conduct of the study. This study is strictly confidential concerning patient information and no public information will reveal the identity of the subjects.

DISCUSSION

ERAS guidelines strongly recommend that patients achieve early ambulation within 24 h after surgery,[3,25] but these recommendations lack in-depth research on strategies to guide early mobilization. Early postoperative ambulation can promote gastrointestinal recovery, but it is not possible to determine the level of activity required for gastrointestinal recovery, which can lead to over-or under-activity and complications in postoperative recovery. In a survey on the demand for postoperative ambulation health education for patients undergoing abdominal surgery, 47.07% of patients wanted to know "how to arrange the amount of early ambulation ",[26] which shows that patients have a greater demand for precise activity guidance after surgery.

The main factors influencing early postoperative ambulation in patients undergoing abdominal surgery are patient incisional pain,[27-29] postoperative fatigue, upright intolerance,[6-7] demographic factors,[30] and psychosocial factors. Some studies[6,31] quantified only the distance and duration of activity and did not consider individual differences in surgical patients in terms of age, complications, and postoperative fatigue. Therefore, a good early activity guidance strategy should be based on the patient's actual situation to guide early bed activity. Assessing the amount of early mobilization based on self-fatigue adequately takes into account individual patient differences and appears to be more effective than simply assessing the distance and duration of early bed activity for patients. However, to our knowledge, no studies are examining the validity and safety of assessing patients' early postoperative bed activity based on self-fatigue, and its benefits need to be further confirmed by standardized, transparent, and well-conducted randomized clinical trials.

This study is the first randomized controlled trial of early postoperative mobilization strategy guidance for gynecologic oncology patients to investigate the effectiveness and safety of early postoperative mobilization in inpatients undergoing gynecologic oncology surgery based on self-fatigue assessment relative to those based on fixed activity distance assessment, and it may provide support for early postoperative mobilization strategy guidance for patients undergoing gynecologic oncology surgery.

Trial status

The first participant was enrolled in June 2021. and the study is expected to end in June 2022.

Author contributions XJH is the principal investigator of this study and refined the protocol. QD, BC, and SYX wrote the manuscript and contributed to the design of the study. QD will recruit the patients and conduct the trial. HH, XMQ, and TTK will supervise the trial. BC, the medical statistician for the study, will contribute to the statistical design and analysis of data. All authors have revised the protocol critically for important intellectual content and approved the final manuscript.

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Disclaimer Sponsors of the study had no involvement in the collection, analysis, and interpretation of data or the writing of the manuscript.

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval The study protocol has been approved by the Independent Ethics Committee of Xiangyang Central Hospital affiliated with Hubei University of Arts and Sciences (permission number: 2021C12) (May 2021).

Provenance and peer review Not commissioned; externally peer-reviewed

Data sharing statement The submitted manuscript is a study protocol that includes no primary data now. Further information unaddressed can be obtained from the corresponding author by the contact methods provided in the manuscript.

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Figures legends

Figure 1 Flowchart of the trial design, based on the SPIRIT 2013.

Appendix I SPIRIT-Checklist

Appendix II Exercising steps before getting out of bed

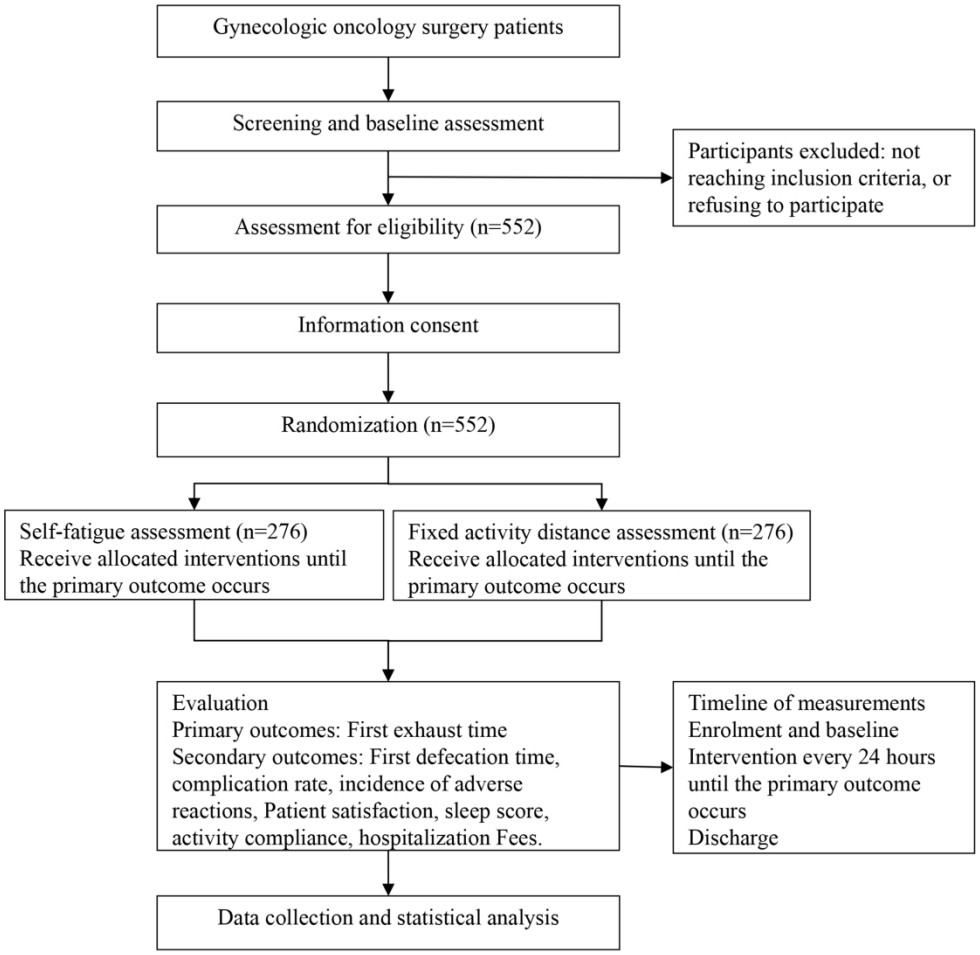

Figure 1 Flowchart of the trial design, based on the SPIRIT 2013.

Appendix I 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	None
Protocol version	3	Date and version identifier	None
Funding	4	Sources and types of financial, material, and other support	12
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	12
	5b	Name and contact information for the trial sponsor	None
	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	12
	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)	None
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
	6b	Explanation for choice of comparators	3

Objectives	7	Specific objectives or hypotheses	3
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)	3
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	3
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)	3-4
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	4-5
	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)	4-5
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	5
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	5
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)	7-8
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	9-10
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	4

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	4
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	4
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	4
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	4
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	None

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	5-7
	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	None
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	9

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)	None
	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	9
	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	9
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	5
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	9
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	11
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)	None
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	11

	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	None
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	11
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	None
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	None
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	12
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	None
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	None

*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.

Appendix II: Exercising steps before getting out of bed

1. Rehabilitation exercises: alternate all exercises left and right, train three groups per day.

(1) Upper limb flexion for hands clenched fist relaxation exercises 20-30 times / group.

(2) Upper limb elevation, elbow flexion and extension, fist clenching and upper limb flattening exercises 5-10 times / group.

(3) Lower limb flexion, single foot stirrups and lower limb flattening exercises 5-10 times / group.

(4) Lower limb elevation, knee bending and lower limb flattening exercises 5-10 times / group.

2. Ankle pump exercises: extension and flexion around the ring for 1 group, eight groups per hour, eight times a day.

(1) Dorsal foot extension and flexion action: the patient lies or sits on the bed, the lower limb is extended, the thigh is relaxed, slowly hooks the toe and tries his best to make the toe face himself, keep it for 10-20 seconds at the maximum.

(2) Ankle loop: The patient lies or sits on the bed with the lower limbs extended and the thighs relaxed, making a 360-degree loop with the ankle joint as the center, practicing clockwise and counterclockwise for 10 seconds each.

3. The three "30 seconds" principle:

(1) Lie in bed and spend thirty seconds moving your hands and feet.

(2) Get up slowly, sit for 30 seconds and move your hands and feet.

(3) Get out of bed and stand up for thirty seconds and start walking.

BMJ Open

Effectiveness of the self-fatigue assessment in guiding early postoperative ambulation in gynecologic oncology patients: study protocol for a randomized controlled trial

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Primary Subject Heading:	Surgery
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Keywords:	Protocols & guidelines < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Gynaecological oncology < ONCOLOGY, Adult surgery < SURGERY

Effectiveness of the self-fatigue assessment in guiding early postoperative ambulation in gynecologic oncology patients: study protocol for a randomized controlled trial

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ABSTRACT

Introduction Enhanced recovery after surgery guidelines strongly recommends that patients be in early postoperative ambulation within 24 h. This study aims to assess the effectiveness and safety of the self-fatigue assessment method to guide patients' early postoperative ambulation.

Methods and analysis This is a single-center, randomized, open, parallel-controlled trial. Five hundred fifty-two patients who meet the inclusion criteria for gynecologic oncology surgery are randomly assigned in a 1:1 ratio to either a self-fatigue assessment group (study group) or a fixed activity distance assessment group (control group). The fixed activity distance group adopts a fixed early postoperative ambulation distance to guide the patient's activity, while the self-fatigue assessment group uses the Borg Exercise Scale to assess the patient's fatigue and stops activity when the fatigue level reaches 5-6. The primary outcome measure is the time to first postoperative flatus. Secondary outcome measures are the time to first bowel movement, the incidence of moderate to severe bloating, the incidence of bowel obstruction or Venous thromboembolism, the incidence of adverse events (nausea, vomiting, dizziness), patient satisfaction, sleep quality scores, patient compliance with activities, hospital costs, and days in hospital.

Ethics and dissemination This study was approved by the Independent Ethics Committee of Xiangyang Central Hospital affiliated with Hubei University of Arts and Sciences and registered with the China Clinical Trials Registry in May 2021. The results of the trial will be disseminated through open access peer-reviewed journals and abstracts will be submitted to relevant national and international conferences.

Trial registration number: CTR2100046035, date: 02 May 2021.

Keywords gynecologic oncology, early ambulation, self-fatigue assessment, fixed activity distance assessment, study protocol

Strengths and limitations of this study

► All interventions will be instructor-led, patients in both groups are to be assisted to get out of bed on the first 24 h after surgery, with the aim of decreasing the risk of adverse events.

► One limitation is that the trial is not a double-blind, placebo-controlled trial and implemented in only one hospital, which may limit its generalisability.

► The first flatus status and some secondary outcomes are self-reported by the patient**,** which may lead to recall or report bias.

INTRODUCTION

Gynecologic tumor surgery is a large and complex surgery consisting of such procedures as expanded radical surgery for malignant tumors and resection for benign tumors. Such surgeries are often characterized by substantial surgical invasions and surgical complications, which lead to slow postoperative recovery, prolonged hospitalization, and increased medical costs, thus increasing the physical, psychological, and economic burden on patients.[1]

Reducing surgical complications in gynecologic oncology and promoting early patient recovery are important clinical issues that need to be addressed. The current global quality improvement initiative for surgery is Enhanced Recovery After Surgery (ERAS), which aims to improve perioperative care, shorten hospital stays, reduce surgical stress, reduce complications and accelerate recovery.[2] It provides both clinical improvement [3] and cost benefits to the healthcare system.[4]

ERAS guidelines for gynecologic oncology surgery encourage patients to have early postoperative ambulation within 24 h.[2] Having early mobilization can significantly shorten patients' anal flatus time, promote patients' gastrointestinal motility, reduce the risk of pulmonary infection and thrombosis, and accelerate organism recovery. Advocacy of early mobilization has been increasingly used as an effective intervention in the concept of rapid rehabilitation surgery.

However, although ERAS guidelines on gynecologic oncology strongly recommend that patients be in early postoperative ambulation within 24 h, early ambulation following surgery is substantially impacted by pain management pre and post surgery, [5] postoperative fatigue, as well as orthostatic intolerance. [6-7] Therefore, ERAS has not yet explicit recommendations for directing and quantifying patient activity.[2] Currently, a few studies have evaluated patient strategies for early postoperative ambulation, mainly around patients after thoracoscopic lobectomy,[8-9] laparoscopic hepatectomy,[10-11] prostate cancer,[12] and gastric cancer.[13-14] However, all of these studies adopted a fixed daily activity distance to guide postoperative patients, a strategy that undoubtedly did not specifically consider differences in patient fitness, disease severity, and comorbidities, and in particular, did not take into account patient fatigue and acceptability.

We hypothesized that a strategy based on self-fatigue assessment rather than a fixed activity distance to guide early postoperative activity would be easy, individualized, safe, and have better early recovery outcomes as well as compliance, but would need to be supported by high-quality studies. Therefore, this study aims to investigate the effectiveness and safety of a self-fatigue-based assessment to guide early postoperative activity in patients with gynecologic oncology.

METHODS AND ANALYSIS

Study design

This study is a randomized, open parallel controlled study that consists of a screening period of approximately 2-3 days, an intervention period of approximately 2-7 days, and a follow-up period of several days. The study is being conducted between 01/06/2021 and 30/05/2022 at Xiangyang Central Hospital, Affiliated Hospital of Hubei University of Arts and Science. **Figure 1** shows the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) diagram.[15] The SPIRIT checklist is provided in **Appendix I**.

Inclusion criteria

Included in this study are subjects meeting the following inclusion criteria: female with no cognition impairment, aged ≥18 years, 18.5 ≤ BMI ≤ 24.9, undergoing gynecologic oncologic elective surgery (open/laparoscopic), with normal preoperative limb movement, stable surgical condition, ability to get out of bed, American Society of Anesthesiologists (ASA) Physical Status Classification I-III, and who voluntarily participated and signed an informed consent form.

Exclusion criteria

Excluded from the study are those meeting any one of the following exclusion criteria: (1) those with delirium after surgery; (3) those with the cardiac function of grade 3 or higher, which referring to New York Heart Association (NYHA) for cardiac function diagnosis classification criteria;[16] (4) perioperative patients with confirmed lower extremity venous thrombosis; (5) those with re-operation within the last 1 month; (6) those who are pregnant or breastfeeding; (7) perioperative patients with persistent fever and temperature is 38.5 or higher.

Participant recruitment

All patients with gynecologic oncology who have been admitted to the gynecology department at Xiangyang Central Hospital and meet the eligibility criteria are invited to participate in this study, and potential participants are then asked to have a face-to-face interview with the professional coordinator to discuss the study and the eligibility criteria. After obtaining the informed consent of eligible and interested patients, information on basic patient demographic characteristics (e.g., age, gender, educational background, marital status, type of disease, etc.) is collected, and patients are randomized into two groups to receive different interventions.

Informed consent

The general study process is explained to participants at the time of participant recruitment before the start of the study. Participants are informed that participation in the trial is completely voluntary and that they can withdraw from the trial at any time. If they withdraw midway through the study, the data collected about the participant will not be deleted and will be used in the final analysis. Written informed consent is obtained from each participant before they receive any interventions related to the study.

Randomization and allocation concealment

In this study, block randomization is used to generate a sufficient number of random sequence numbers using the statistical program SAS 9.4 PROC PLAN, which were then randomly divided into 2 groups according to a 1:1 ratio before the intervention; the group status was sealed in an opaque envelope and assigned a random number based on a random code. The researcher opened the corresponding numbered envelopes to obtain group status according to the order in which the subjects entered the group. An explicit blinded design would be difficult to implement and of little value to the investigator and patients due to the different strategies for quantifying the two activities and the objectification of the main observations. Therefore, an open study was used in this investigation.

Interventions

Subjects who pass the initial screening are reassessed at the end of the procedure, and those confirmed eligible are formally randomly assigned in a 1:1 ratio to two groups: (1) study group: self-fatigue assessment group, and (2) control group: fixed activity distance assessment group. Patients in both groups are to be assisted to get out of bed on the first 24 h after surgery, with 15-20 minutes of preparation time before each mobilization, and assisted to walk after completion of the activity assessment by the investigator.If subjects don't meet the intervention volume during each activity intervention, their activity compliance and influencing factors will be assessed. Once adverse events occur during the intervention, the trained nurses will take appropriate nursing actions to mitigate.

Prepare for getting out of bed and moving around

Patients are fed fluids 4-6 hours after surgery, and fully awake patients are instructed to prepare for early mobilization 30-60 minutes after feeding. Patients are maintained in a sitting position for 15-20 min before getting out of bed and instructed to do rehabilitation exercises and ankle pump exercises in bed.

Our pain management philosophy revolves around setting appropriate patient-centred expectations. Pain status is assessed based on an inpatient pain dynamic assessment record form: the score ranges from no pain to extreme pain, with the lowest score of 0 and the highest score of 10, for a total of 10 grades. Pain scores 1-3 are classified as mild pain, 4-6 as

moderate pain, and ≥ 7 as severe pain. To improve adherence to intervention protocols, patients using an analgesia pump (including hydromorphone, sufentanil, and flurbiprofen ester) will receive a double dose of analgesia in the pre-activity; patients not using an analgesia pump will receive rectal diclofenac suppositories 30 minutes before getting out of bed or are given 50 mg of flurbiprofen intravenously 15 minutes before ambulation. Patients are freed from bed according to the three "30 second" principles and start to mobilize after no discomfort, **see Appendix II**.

Study group: self-fatigue intervention

Postoperative fatigue is assessed by the modified 0–10 category ratio Borg Rating of Perceived Exertion (RPE) Scale.[17] The RPE is a widely used psychophysiological assessment tool for assessing subjective perception during exercise, the end points of the scale were anchored such that zero represented "no discomfort at all" and 10 represented "the most intense discomfort [they] have every experienced or could ever imagine experiencing.. Patients are instructed to perform the activity until the self-fatigue assessment reaches levels 5-6 (intense discomfort, tiredness, and slightly difficult to continue walking), intervening and assessing every 24 hours until the primary outcome occurs. To ensure the reliability of the assessment and to help build the patient's confidence, all key members of the patient's social support network, (the 'family', attending physician, and nurses) are invited for the patient's psychological intervention, and encourage early ambulation. When using the fatigue assessment intervention, patients are required to wear an electronic bracelet throughout to record the distance (in meters) of early postoperative mobilization, though this is not the focus for this group.

Control group: fixed activity distance intervention

The fixed activity distance group uses an electronic bracelet (brand: Huawei Honor 5i) to

record their postoperative mobilization distance (in meters). Patients are instructed to mobilize about 1000-1200 m for the first 24 hours postoperatively[18] for about 1-2 hours; thereafter, the daily activity distance is increased by 500 m on top of the previous day's ambulation distance for 1-2 hours until the primary outcome occurs. When assessed using a fixed activity distance, patients are assessed for fatigue at the end of each intervention using the Borg Exercise Scale. There is no mandatory requirement for fatigue status in this group.

Data collection

Data collection is conducted by trained nursing assessors who assess and collect data from patients during the screening and baseline, intervention period, follow-up period, and close-out.

Enrolment and baseline (V_1, V_2)

Patients are screened upon admission based on inclusion-exclusion criteria, and subjects who meet the screening criteria provide basic demographic characteristics information (e.g., age, gender, educational background, marital status, type of disease, etc.). When the patient is further screened at the end of the procedure for their confirmation of inclusion-exclusion criteria, they are enrolled and their vital signs (pulse, respiratory rate, temperature, and blood pressure) are measured by the study nurse and assessed using a modified version of the Morse Scale used to measure the risk of falling out of bed in adults, including 10 items with a score ranging from 0-20. The Caprini Risk Assessment Scale is used to assess the occurrence of venous thromboembolism (VTE). This helpful risk quantification tool[19] can effectively screen high-risk patients for VTE. [20] The Caprini Risk Assessment Scale includes 39 risk factors (17 risk factors were assigned 1 point, 7 risk factors were assigned 2 points, 10 risk factors were assigned 3 points and 5 risk factors were assigned 5 points). Caprini scores were 0-1 for low-risk VTE, 2 for medium-risk VTE, 3-4 for high-risk VTE, and ≥5 for very high-risk VTE.

Intervention (V_2-V_x)

During the intervention period, one activity intervention is completed within each 24 h cycle, with the study nurse asking the patient if they had anal flatus before each intervention. The patient's vital signs (pulse, respiratory rate, temperature, and blood pressure) are assessed after the intervention and the following indicators:

Bloating is assessed during each visit cycle, and moderate and severe cases are recorded. Bloating is classified into 4 grades: (1) no bloating; (2) mild: abdominal distension is elevated and slightly higher than the chest, percussion is a low-pitched drum sound, bowel sounds may be diminished, slightly hyperactive or normal, mild abdominal distension may be present; (3) moderate: the abdomen is elevated and significantly higher than the chest with some tension, percussion is a mid-pitched drum sound with increased and pronounced range and intensity, bowel sounds are mostly diminished, and there is significant conscious bloating that interferes with eating or another metabolism; (4) severe: the whole abdomen is bulging in a spherical shape, hard and uncomfortable when pressed, without rebound pain, the percussion is a high-pitched drum sound and may appear as a metallic percussion, without any change in position bowel sounds are markedly diminished or non-existent, and there are obvious gastrointestinal reactions. To assess the possibility of intestinal obstruction during each visit, if highly suspected, an abdominal radiograph should be used.

The Pittsburgh sleep quality index (PSQI) scale is used to assess the sleep quality of patients during each interview period. The scale had high reliability and validity; [21-22] the scale is composed of 19 self-rated items and 5 other items, where the 19th self-rated entry and 5 other-rated entries are not involved in scoring, and the 18 self-rated entries form a total of 7 components, each component is scored on a scale of 0-3. The cumulative component score is the total PSQI score, ranging from 0-21, with higher scores indicating poorer sleep quality.

The occurrence of adverse events such as nausea, vomiting, and vertigo during each visiting period is investigated and the outcome recorded.

Subjects' activity compliance is assessed by the degree to which they meet the intervention volume after each activity intervention.

Follow up (V_x)

If the patient appears to exhibit anal flatus, the intervention period is over. The exact time when the patient experienced the first anal flatus (hours) is determined. The patient's vital signs at the end of the intervention period are assessed, total compliance with activities throughout the intervention period is calculated, the incidence of bowel obstruction and the moderate and worst degree of abdominal distension is calculated, and the mean sleep quality score and the incidence of adverse patient reactions are calculated.

Close-out (V_{x+1})

After the intervention, follow-up continues until discharge from the hospital, at which time information on the hospitalization costs and days of hospitalization, the degree of bloating, the occurrence of intestinal obstruction, the sleep quality score, the satisfaction with the early mobility instructions, and other relevant information is collected. The registration, intervention, assessment, and access schedules of participants are shown in **Table 1**.

Table 1 Study plan detailing the procedures

	Study Period				
	Enrolment	**Allocation**	**Post-allocation**	**Follow up**	**Close-out**
Visit	V_1	V_2	.....	V_x	V_{x+1}
Timepoint	Hospitalization	End of surgery	1 intervention in every 24 h	When the primary outcome occurs	Discharge
Enrolment:					
Informed consent	×				

Eligibility screen	×	×			
Demographics	×				
Allocation		×			
Intervention:					
Self-fatigue assessment			→		
Fixed activity distance assessment			→		
Assessments:					
vital signs	×	×	×	×	×
Risk of falls	×	×			
First exhaust flatus time			×	×	
Moderate to severe bloating			×	×	×
Intestinal obstruction			×	×	×
Venous thromboembolism		×			×
Pain score		×			
Adverse reactions (nausea, vomiting, dizziness)			×	×	
Sleep quality score	×		×	×	×
Hospitalization costs					×
Length of hospitalization					×
Activity compliance			×	×	
Patient satisfaction					×

Outcome measures

The primary and secondary outcomes are shown in **Table 2**.

Table 2 Primary and secondary outcomes

	Outcome measure
Primary outcome	
To compare the effect of early bedtime activity in the self-fatigue assessment group with that in the fixed activity distance group on the time to first post-operative flatus in gynecological oncology patients.	Time from the end of the procedure to the patient's first flatus (h).
Secondary outcomes	
To compare the effects of early bed activity in the self-fatigue assessment group with those in the fixed activity distance group on the time to the first bowel movement,	1. Time from the end of the procedure to the patient's first bowel movement (h). 2. Incidence of post-activity adverse reactions (nausea, vomiting, dizziness) = number of patients in each group with post-activity adverse

the incidence of moderate to severe bloating, the incidence of bowel obstruction or Venous thromboembolism, the incidence of adverse effects (nausea, vomiting, dizziness), patient satisfaction, mean sleep quality score, patient compliance with activities, and hospital costs and days of hospitalization in gynecologic oncology patients.	reactions (nausea, vomiting, dizziness) / total number of patients in the group × 100%. 3. Incidence of moderate to severe abdominal distention after patient activity = number of patients in each group with moderate to severe abdominal distention after intervention activity/total number of patients in that group x 100%. 4. Incidence of post-activity bowel obstruction or Venous thromboembolism in patients = number of post-activity bowel obstruction or Venous thromboembolism in each group/total number of patients in that group × 100%. 5. Patient satisfaction rate with bed mobility instruction = number of patients in each group satisfied with early bed mobility instruction/total number of patients in that group x 100%. 6. Mean post-activity sleep quality score for patients. 7.Patient compliance with activity = number of patients in each group who met the standard for early postoperative bed activity/total number of patients in the group x 100%. 8. The average cost of hospitalization and the average number of days in the hospital for each group of patients.
Safety outcome	
Evaluating the safety of two activity strategies	Incidence of adverse events/serious adverse events. Vital characteristics (including data on the pulse, respiration, temperature, blood pressure, etc.).

Quality control

Before the trial, all staff will be required to attend a series of training courses. These courses will ensure that relevant personnel is fully aware of the study protocol and standard operating procedures for the study. To maintain the high quality of the clinical trial, the Xiangyang Central Hospital Clinical Research Centre will regularly monitor study documents, informed consent forms, Case Report Forms (CRFs), serious adverse events, and data records.

Data management

The CRFs and adverse event forms will be completed first and then electronically entered into the electronic data capture (EDC) system by two independent investigators as the first level of control to ensure data accuracy. The second level of data integrity will include data monitoring and validation, which will occur at regular intervals throughout the study. The original CRFs and all other forms (including consent forms) will be kept securely at the Clinical Research Center of Xiangyang Central Hospital, Hubei College of Arts and Sciences for 5 years after the last paper or study report is published.

The safety of this study will be monitored by the Data and Safety Monitoring Board (DSMB) of the Clinical Assessment Center at Xiangyang Central Hospital, Hubei College of Arts and Sciences, which is composed of independent clinical experts and statisticians. The DSMB is independent of competing interests and study sites and will review the performance and safety of the trial every month.

Criteria for discontinuation of the assigned intervention for a given participant include serious complications or a serious adverse event, if any, as described previously. The DSMB will make the final decision to terminate the trial.

The final trial dataset will be maintained by Xiangyang Central Hospital. The data management staff of the Xiangyang Central Hospital clinical assessment center will have access to the complete, anonymized final dataset. Access to the final dataset or identifiable data by others will require written request approval by the DSMB of the Xiangyang Central Hospital clinical assessment center and all investigators.

Patients and public involvement

Patients and the public are not involved in the design or conduct of the study or the outcome measures, and no attempt will be made to assess the burden of the intervention on the patients themselves.

Sample size estimate

The sample size is determined based on the results of a literature review and pre-trial,[23-24] and 552 patients will be included in this study. This sample size is based on the following statistical considerations: the primary outcome hypothesis was that patients with gynecologic oncology were non-inferior to patients with self-fatigue assessment in early postoperative ambulation in terms of time to first postoperative flatus compared to patients with fixed activity distance assessment. Based on the literature review and pre-trial studies, a conservative estimate of the standard deviation (SD) of the change in postoperative time to first anal flatus was 8 h, with a non-inferiority cut-off of 2 h. At a bilateral 0.05 alpha level and 20% dropout rate, 552 patients with a 1:1 allocation rate (276 patients per group) would provide at least 85% validity to detect at least 2 h difference in change in time to first postoperative anal flatus.

Statistical analysis

All data will be analyzed by statisticians using SAS 9.4 (SAS Institute, Cary, NC, USA) at the Xiangyang Central Hospital clinical research center. Baseline assessments will be performed before randomization to groups and include patient gender and age, type of disease, vital signs (pulse, respiratory rate, temperature, and blood pressure), fall risk level, ability to perform activities of daily living, the primary outcome (time to first flatus), and secondary outcomes (complications, adverse effects, degree of bloating, sleep quality score, activity compliance, cost of hospitalization and the length of hospitalization). All patients randomly assigned to each group will be included in the analysis, and data analysis will be performed using a 5% two-sided significance test.

The primary analysis population will be based on the Full Analysis Set (FAS) of data and all analyses will be based on the intention-to-treat principle (ITT) using the last observation carried forward principle. Missing values will be filled by multiple imputations (MI). Continuous variables that conform to a normal distribution are expressed as means ± standard deviations (SDs) and compared by independent samples t-test. For variables that do not conform to a normal distribution, data will be expressed as median (25%-75%) and compared using a non-parametric test. Categorical variables will be expressed as numbers (%) and analyzed using the chi-square test or Fisher's exact test. Descriptive statistics will be used to detail baseline participant demographics and general patient status characteristics such as gender, age, disease type, vital signs, fall risk rating, and ability to perform

activities of daily living. A chi-square test will be used to compare the differences in time to first anal flatus, complications, adverse events, degree of bloating, sleep quality score, activity compliance, cost of hospitalization, the length of hospitalization, and incidence of adverse events between the two groups. Stratified analysis based patients with or without opioid usage and open/laparoscopic will be performed.

ETHICS AND DISSEMINATION

The trial was approved by the Independent Ethics Committee of Xiangyang Central Hospital affiliated with Hubei University of Arts and Sciences (Project No. 2021C12) and registered with the China Clinical Trials Registry (http://www.chictr.org.cn/index.aspx, Registration No. CTR2100046035, Registration Date: 02/05/2021). The results of the trial will be submitted to peer-reviewed journals and abstracts will be submitted to relevant national and international conferences.

Signed and dated informed consent will be provided by each subject before the conduct of the study. This study is strictly confidential concerning patient information and no public information will reveal the identity of the subjects.

DISCUSSION

ERAS guidelines strongly recommend that patients achieve early ambulation within 24 h after surgery,[3,25] but these recommendations lack in-depth research on strategies to guide early mobilization. Early postoperative ambulation can promote gastrointestinal recovery, but it is not possible to determine the level of activity required for gastrointestinal recovery, which can lead to over-or under-activity and complications in postoperative recovery. In a survey on the demand for postoperative ambulation health education for patients undergoing abdominal surgery, 47.07% of patients wanted to know "how to arrange the amount of early ambulation ",[26] which shows that patients have a greater demand for precise activity guidance after surgery.

The main factors influencing early postoperative ambulation in patients undergoing abdominal surgery are patient incisional pain,[27-29] postoperative fatigue, orthostatic intolerance,[6-7,30] demographic factors,[31] and psychosocial factors. Some studies[6,32] quantified only the distance and duration of activity and did not consider individual differences in surgical patients in terms of age, complications, and postoperative fatigue. Therefore, a good early activity guidance strategy should be based on the patient's actual situation to guide early bed activity. Assessing the amount of early mobilization based on self-fatigue adequately takes into account individual patient differences and appears to be more effective than simply assessing the distance and duration of early bed activity for patients. However, to our knowledge, no studies are examining the validity and safety of assessing patients' early postoperative bed activity based on self-fatigue, and its benefits need to be further confirmed by standardized, transparent, and well-conducted randomized clinical trials.

This study is the first randomized controlled trial of early postoperative mobilization strategy guidance for gynecologic oncology patients to investigate the effectiveness and safety of early postoperative mobilization in inpatients undergoing gynecologic oncology surgery based on self-fatigue assessment relative to those based on fixed activity distance assessment, and it may provide support for early postoperative mobilization strategy guidance for patients undergoing gynecologic oncology surgery, the results of the study may also contribute/influence the patient screening to surgery (in/out patient) and the development of pain management in outpatient surgery.

Trial status

The first participant was enrolled in June 2021. and the study is expected to end in June 2022.

Author contributions XJH is the principal investigator of this study and refined the protocol. QD, BC, and SYX wrote the manuscript and contributed to the design of the study. QD will recruit the patients and conduct the trial. HH, XMQ, and TTK will supervise the trial. BC, the medical statistician for the study, will contribute to the statistical design and analysis of data. All authors have revised the protocol critically for important intellectual content and approved the final manuscript.

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Disclaimer Sponsors of the study had no involvement in the collection, analysis, and interpretation of data or the writing of the manuscript.

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval The study protocol has been approved by the Independent Ethics Committee of Xiangyang Central Hospital affiliated with Hubei University of Arts and Sciences (permission number: 2021C12) (May 2021).

Provenance and peer review Not commissioned; externally peer-reviewed

Data sharing statement The submitted manuscript is a study protocol that includes no primary data now. Further information unaddressed can be obtained from the corresponding author by the contact methods provided in the manuscript.

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Figures legends

Figure 1 Flowchart of the trial design, based on the SPIRIT 2013.

Appendix I SPIRIT-Checklist

Appendix II Exercising steps before getting out of bed

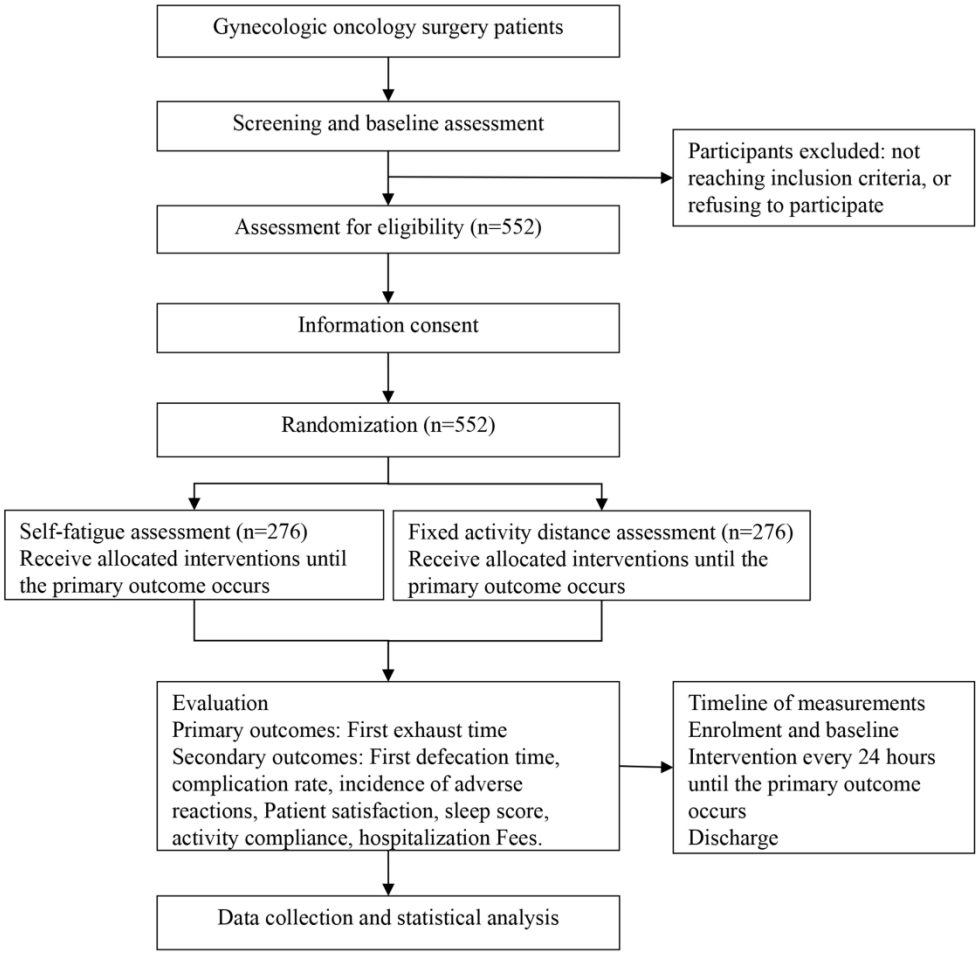

Figure 1 Flowchart of the trial design, based on the SPIRIT 2013.

Appendix I 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	None
Protocol version	3	Date and version identifier	None
Funding	4	Sources and types of financial, material, and other support	12
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	12
	5b	Name and contact information for the trial sponsor	None
	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	12
	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)	None
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
	6b	Explanation for choice of comparators	3

Objectives	7	Specific objectives or hypotheses	3
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)	3
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	3
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)	3-4
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	4-5
	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)	4-5
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	5
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	5
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)	7-8
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	9-10
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	4

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	4
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	4
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	4
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	4
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	None

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	5-7
	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	None
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	9

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)	None
	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	9
	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	9
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	5
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	9
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	11
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)	None
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	11

	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	None
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	11
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	None
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	None
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	12
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	None
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	None

*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.

Appendix II: Exercising steps before getting out of bed

1. Rehabilitation exercises: alternate all exercises left and right, train three groups per day.

(1) Upper limb flexion for hands clenched fist relaxation exercises 20-30 times / group.

(2) Upper limb elevation, elbow flexion and extension, fist clenching and upper limb flattening exercises 5-10 times / group.

(3) Lower limb flexion, single foot stirrups and lower limb flattening exercises 5-10 times / group.

(4) Lower limb elevation, knee bending and lower limb flattening exercises 5-10 times / group.

2. Ankle pump exercises: extension and flexion around the ring for 1 group, eight groups per hour, eight times a day.

(1) Dorsal foot extension and flexion action: the patient lies or sits on the bed, the lower limb is extended, the thigh is relaxed, slowly hooks the toe and tries his best to make the toe face himself, keep it for 10-20 seconds at the maximum.

(2) Ankle loop: The patient lies or sits on the bed with the lower limbs extended and the thighs relaxed, making a 360-degree loop with the ankle joint as the center, practicing clockwise and counterclockwise for 10 seconds each.

3. The three "30 seconds" principle:

(1) Lie in bed and spend thirty seconds moving your hands and feet.

(2) Get up slowly, sit for 30 seconds and move your hands and feet.

(3) Get out of bed and stand up for thirty seconds and start walking.