The First Affiliated Hospital of Kunming Medical University

Clinical Research Protocol

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Department	Department of Orthopaedics
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Contents

Protocol Synopsis....4
Principal Investigator Information....6
Abbreviations....7
1. Clinical Background....8
1.1 Epidemiology of Degenerative Lumbar Disorders....8
1.2 Challenges Associated with Surgery....8
1.3 Development of Enhanced Recovery After Surgery....8
1.4 Use of Probiotic Preparations in Surgery....9
1.5 Problems Encountered in Our Department....9
2. Study Objectives....9
3. Study Plan....9
3.1 Feasibility Assessment....9
3.1.1 Research Team and Technical Feasibility....9
3.1.2 Feasibility of Participant Recruitment....10
3.1.3 Feasibility of the Timeline and Funding....10
3.2 Overall Study Design....10
3.2.1 Randomization and Blinding....10
3.2.2 Study Endpoints and Outcome Measures....11
3.3 Study Population....11
3.3.1 Participant Age Range....11
3.3.2 Inclusion Criteria....11
3.3.3 Exclusion Criteria....12
3.3.4 Participant Withdrawal and Loss to Follow-up....12
3.3.5 Retention and Handling of Participants in the Analysis....12
4. Study Procedures....12
4.1 Informed Consent and Enrollment....14
4.2 Participant Identification Numbers....14
4.3 Data Sources and Data Collection....14
4.4 Criteria for Study Termination or Suspension....15
4.5 Bias Control and Management of Protocol Deviations....15
4.5.1 Measures to Prevent Bias....15

4.5.2 Monitoring and Management of Deviations..... 15
4.5.3 Protocol Amendment Process..... 15
4.6 Adverse Event Monitoring and Management..... 15
4.6.1 Definition and Classification of Adverse Events..... 15
4.6.2 Adverse Event Monitoring and Reporting..... 16
4.6.3 Management of Adverse Events..... 16
4.6.4 Potential Adverse Events and Management Measures..... 16
5. Statistical Methods..... 16
5.1 General Principles..... 16
5.2 Sample Size Estimation..... 17
5.3 Statistical Analysis Set..... 17
5.4 Handling of Missing Data and Outliers..... 17
5.5 Analysis of Outcome Measures..... 17
5.5.1 Primary Endpoint Analysis..... 17
5.5.2 Secondary Endpoint Analysis..... 17
5.6 Safety Analysis..... 18
6. Ethics..... 18
6.1 Ethical Requirements..... 18
6.2 Informed Consent..... 18
6.3 Privacy of Personal Data..... 19
7. Study Management..... 19
7.1 Quality Control and Quality Assurance..... 19
7.1.1 Quality Control Procedures..... 19
7.1.2 Training..... 20
7.2 Protocol Changes..... 20
7.3 Data Recording and Document Retention..... 20
8. Investigator Responsibilities..... 20
9. Confidentiality and Publication of Study Results..... 21
10. Final Report..... 21
11. Conflict of Interest Statement..... 21
References..... 22

Protocol Synopsis

Study Title	Perioperative Nutritional Management in Patients Undergoing Open Posterior Lumbar Surgery: A Comparative Study of the Clinical Efficacy of No Intervention, Nutritional Support, and Nutritional Support Combined with Probiotics
Study Overview	This study compares the effects of three strategies on postoperative recovery in patients undergoing open posterior lumbar fusion: routine perioperative management, optimized nutritional management, and optimized nutritional management combined with probiotics. Postoperative length of stay (LOS) is the sole primary endpoint. Other recovery measures, complications, scale scores, anthropometric measurements, and laboratory parameters are secondary endpoints.
Study Objectives	To evaluate the effect of optimized perioperative nutritional management on postoperative LOS and inform perioperative nutritional management in this department. The study will also explore the clinical effects of adding probiotics to the same nutritional management regimen.
Study Design	A single-center, prospective, three-arm, parallel-group, open-label randomized controlled trial with blinded outcome assessors. The study will begin after ethics approval and continue for approximately 10 months. Ninety patients will be allocated in a 1:1:1 ratio to the control group, intervention group A, or intervention group B, with 30 patients per group.
Total Enrollment	90 patients, with 30 patients per group.
Inclusion Criteria	(1) Aged at least 18 years and younger than 75 years; diagnosed with a noninfectious lumbar disorder and scheduled for elective open posterior lumbar fusion in this department. (2) No marked abnormalities in recent dietary intake and no recent use of probiotic preparations. (3) Surgery under general anesthesia, with fusion involving 1–3 levels. (4) Voluntary participation and provision of written informed consent.
Exclusion Criteria	(1) Chronic kidney disease, a history of malignancy, or infectious diseases such as pulmonary or spinal infection. (2) Impaired immune function, immunodeficiency, or use of immunosuppressive medication for a medical condition. (3) Preoperative malnutrition or hypoalbuminemia (serum albumin <35 g/L). (4) High bleeding risk, such as coagulation abnormalities, preoperative anemia, severe cardiac, hepatic, or renal dysfunction, or recent use of antiplatelet or anticoagulant medication. (5) Lower-extremity deep vein thrombosis at admission. (6) Intolerance or allergy to the medications or nutritional supplements used in this study. (7) A disease causing severe impairment of digestion or absorption. (8) Poorly controlled diabetes mellitus or hypertension. (9) Emergency surgery. (10) Any other condition that, in the investigator's judgment, prevents the patient from meeting study requirements.

Study Interventions	The control group will receive routine perioperative management. Group A will receive oral nutritional supplements (ONS) prepared by the hospital's Department of Nutrition and perioperative carbohydrate loading, alongside optimized diet and feeding timing. Group B will receive the same management as group A plus Jinshuangqi (Bifidobacterium and Lactobacillus triple viable bacteria tablets), 2 g per dose, three times daily. See Section 4 for details.
Statistical and Endpoint Summary	The primary endpoint is postoperative LOS, measured in days. The day of surgery is day 0, and the first postoperative day is day 1. LOS is recorded through actual discharge from the index hospitalization and calculated as the actual discharge date minus the surgery date. Only the actual discharge date is recorded; the date on which discharge criteria are met is not separately recorded. The primary comparisons are group A versus the control group and group B versus the control group. After Bonferroni correction, the two-sided α is 0.025 for each comparison. The comparison of group B versus group A is exploratory. The sample size is 90 patients, with 30 per group. All randomized patients will be analyzed in their originally assigned groups. Secondary endpoints and safety measures will be analyzed as specified in Sections 3.2.2 and 5. All patients will be followed until 1 month after surgery.
Study Duration	Approximately 10 months, starting after ethics approval.
Duration of Participant Involvement	From enrollment until 1 month after surgery; LOS is recorded through actual discharge from the index hospitalization.
Study Institution and Site	Department of Orthopaedics, The First Affiliated Hospital of Kunming Medical University

Principal Investigator Information

Names, Qualifications, and Contact Details of the Principal Investigators

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Abbreviations

Abbreviation	Full Term
ERAS	Enhanced Recovery After Surgery
PLIF	Posterior Lumbar Interbody Fusion
RCT	Randomized Controlled Trial
MNA	Mini Nutritional Assessment
VAS	Visual Analog Scale for Pain
JOA	Japanese Orthopaedic Association Low Back Pain Score
NRS 2002	Nutritional Risk Screening 2002
CHI	Creatinine Height Index
CONUT	Controlling Nutritional Status
PNI	Prognostic Nutritional Index
GCP	Good Clinical Practice
ICMJE	International Committee of Medical Journal Editors
CRF	Case Report Form
eCRF	Electronic Case Report Form

1. Clinical Background

1.1 Epidemiology of Degenerative Lumbar Disorders

Population aging in China continues to increase. According to the Statistical Communiqué of the People's Republic of China on the 2023 National Economic and Social Development, published by the National Bureau of Statistics in 2024, 296.97 million people were aged 60 years or older at the end of 2023, accounting for 21.1% of the population. Of these, 216.76 million were aged 65 years or older, accounting for 15.4% of the population [1]. As the older population grows, perioperative management needs among patients with degenerative lumbar disorders and those undergoing related surgery are becoming increasingly prominent.

Degenerative lumbar disorders are common in middle-aged and older adults. They mainly include lumbar spondylolisthesis, disc herniation, and spinal stenosis, which cause acute or chronic low back pain and impaired motor function [2]. Chronic low back pain is the leading cause of disability worldwide. It substantially reduces quality of life and imposes additional economic burdens on families and society [3]. A community survey of 4,000 people in Hong Kong, China, found a prevalence of spondylolisthesis of 19.1% in older men and 25.0% in older women. Prevalence increased with age in both sexes [4]. The incidence of disc degeneration and spinal stenosis also increases with age [5,6]. For patients with failed conservative treatment or progressive neurological dysfunction, open posterior lumbar fusion provides direct decompression, stabilization of spinal alignment, and restoration of disc height. It has become an important treatment for relieving intractable pain, improving neurological function, and enhancing quality of life.

1.2 Challenges Associated with Surgery

Surgery can induce inflammatory and stress responses, accompanied by increased protein catabolism and negative nitrogen balance. The extent depends on surgical trauma and the patient's preoperative condition [7]. Orthopaedic inpatients may be at nutritional risk or malnourished and require systematic perioperative assessment [8,9]. Previous studies suggest that malnutrition or hypoalbuminemia is associated with infection, wound complications, and impaired recovery after joint and spine surgery [10,11]. Laboratory parameters such as albumin are also affected by inflammation, blood loss, and fluid balance. They cannot independently establish a diagnosis of malnutrition or demonstrate the effectiveness of a nutritional intervention. Patients undergoing open posterior lumbar fusion often have comorbidities. Surgical trauma, blood loss, bed rest, and analgesic use may jointly affect gastrointestinal function and recovery.

1.3 Development of Enhanced Recovery After Surgery

Enhanced recovery after surgery (ERAS) promotes postoperative recovery through patient education, nutritional management, pain management, infection prevention, thromboprophylaxis, and early mobilization [12–16]. Studies of perioperative nutritional management in orthopaedics suggest that nutritional assessment, dietary counseling, and oral nutritional supplementation may improve some recovery measures. However, patient populations, interventions, and outcome definitions vary across studies [17–22]. A 2024 systematic review of joint arthroplasty suggested that dietitian-led perioperative interventions may improve outcomes such as LOS. These results require interpretation in light of differences in populations and interventions and cannot be directly equated with benefits in lumbar fusion patients [23]. A survey of spine surgeons published in the same year found that standardized nutritional optimization pathways remain lacking in clinical practice. Implementation is affected by resources, workflows, and patient adherence [24]. Specific management strategies therefore need evaluation in the context of lumbar surgery, rather than assuming that all nutritional measures have equivalent effects [25].

1.4 Use of Probiotic Preparations in Surgery

Probiotics are live microorganisms that may benefit host health when administered in adequate amounts. Their potential effects involve the intestinal barrier, microbial interactions, and immune responses [26]. Previous surgical studies and systematic reviews suggest that some probiotic or synbiotic regimens may reduce infectious or gastrointestinal complications. However, the evidence mainly comes from specific populations undergoing trauma or gastrointestinal surgery, with inconsistent species, doses, and administration schedules [27–29]. Oral nutritional supplementation and probiotics are different interventions. Effects observed in studies of nutritional supplementation alone cannot be treated as evidence for probiotics [19,30]. Whether adding probiotics provides additional clinical benefit beyond the same nutritional management regimen in open posterior lumbar fusion requires specific evaluation. This study will not collect data on gut microbiota composition or function. It therefore does not aim to verify microbiota changes or their mechanisms.

1.5 Problems Encountered in Our Department

In clinical practice, patients undergoing open posterior lumbar fusion in our department may experience delayed passage of flatus and stool, abdominal distension, constipation, nausea, or vomiting. Evidence on postoperative ileus following spine surgery suggests associations with perioperative fluid and electrolyte disturbances, multilevel surgery, anesthesia, and analgesia. Incidence estimates for ileus cannot be used interchangeably with those for general gastrointestinal symptoms [31]. A retrospective survey of 204 patients who underwent open posterior lumbar fusion in our department from November 2023 to March 2024 found constipation in 65 patients (31.9%), vomiting in 23 (11.3%), and diarrhea in 4 (2.0%). These data identify the clinical problem motivating this study; they do not constitute evidence of efficacy for this randomized trial. The department already has routine pathways for antibiotic prophylaxis, analgesia, thromboprophylaxis, and tranexamic acid use, but nutritional management requires further optimization. The control group will follow the routine dietary management pathway used at the time of study initiation. The intervention groups will receive a combined strategy incorporating ONS, carbohydrate loading, and optimized feeding timing.

Accordingly, this study will evaluate the clinical effects of three perioperative management strategies. Comparisons of group A or group B with the control group reflect the effects of the complete management strategy. The exploratory comparison of group B versus group A will evaluate differences after adding probiotics. Effects of the combined strategy will not be attributed to any single component.

2. Study Objectives

(1) To evaluate optimized nutritional management, with or without probiotics, versus routine management, using postoperative LOS as the sole primary endpoint.

(2) To compare secondary endpoints, including gastrointestinal recovery, postoperative recovery, scale scores, anthropometric measurements, laboratory parameters, and complications, to inform departmental management pathways.

(3) To explore the clinical effects of adding probiotics to the same optimized nutritional management regimen, without inferring unmeasured microbiota changes or mechanisms of action.

3. Study Plan

3.1 Feasibility Assessment

3.1.1 Research Team and Technical Feasibility

The study will be conducted jointly by orthopaedic clinicians, physicians from the Department of Nutrition, designated nurses, and research staff. Appropriately licensed physicians will be responsible for

clinical care and safety assessments. Physicians from the Department of Nutrition will help develop nutritional regimens. Data collectors will perform assessments and maintain records according to standardized requirements. Before study initiation, training will cover eligibility criteria, random allocation, intervention delivery, outcome measurement, informed consent, and data management.

3.1.2 Feasibility of Participant Recruitment

Participants will be recruited from the Department of Orthopaedics at The First Affiliated Hospital of Kunming Medical University. A survey identified 204 patients who underwent open posterior lumbar surgery in this department from November 2023 to March 2024, indicating a substantial eligible population and sufficient surgical volume. Detailed explanations of informed consent and patient education will help improve participation. At least 90 participants are expected to be recruited within the planned study period, meeting the sample size requirement.

3.1.3 Feasibility of the Timeline and Funding

The study will begin after ethics approval and continue for approximately 10 months. Nutritional preparations used in the study will be paid for from the research budget. Participants will not be charged additional costs for these preparations because of their randomized allocation. The study will use results from routine clinical examinations and will not require additional study-specific tests. Study-related expenditure will follow research funding and hospital management requirements.

3.2 Overall Study Design

This is a single-center, prospective, three-arm, parallel-group randomized controlled trial. Ninety patients aged 18 to <75 years who are scheduled for elective open posterior lumbar fusion involving 1–3 levels will be enrolled. They will be allocated in a 1:1:1 ratio to the control group, intervention group A, or intervention group B, with 30 patients per group. The study will begin after ethics approval and continue for approximately 10 months. Screening and written informed consent will be completed before enrollment, and follow-up will continue until 1 month after surgery. Scale assessments and wound recovery evaluations at 1 month will be completed during an in-person hospital visit. Telephone or online communication will be used for contact and supplementary follow-up.

3.2.1 Randomization and Blinding

(1) Random sequence generation: A departmental secretary who is not involved in clinical enrollment or intervention delivery will use SPSS 27.0 to generate the allocation sequence. Allocation will be in a 1:1:1 ratio to the control group (C), intervention group A (A), or intervention group B (B).

(2) Allocation cards: Sequentially numbered allocation cards will be prepared from the random sequence. Each card will show the participant's sequence number and corresponding group code. Group codes identify allocation only; allocation concealment depends on the procedures for storing and opening sealed envelopes.

(3) Allocation concealment: Each card will be placed in a sequentially numbered, opaque, sealed envelope. Only the sequence number will appear on the outside. The departmental secretary will retain the envelopes. Investigators responsible for recruitment and screening will not access allocation results before informed consent and eligibility confirmation are completed.

(4) Allocation implementation: After eligibility is confirmed and written informed consent is obtained, the corresponding envelope will be issued and opened in enrollment order. The intervention will follow the allocation card. Sequence numbers will not be skipped, and assigned groups will not be changed.

(5) Blinding: This is an open-label trial. Participants and treating physicians who deliver the interventions will know the allocation. Outcome assessors will remain unaware of allocation and record postoperative recovery measures, scale scores, and laboratory results according to standardized requirements. Treating

physicians will make discharge decisions based on the clinical condition. The study will record the actual discharge date; treating physicians will not be described as blinded personnel.

3.2.2 Study Endpoints and Outcome Measures

(1) Sole primary endpoint: Postoperative length of stay (LOS), measured in days. The day of surgery is day 0, and the first postoperative day is day 1. LOS is recorded through actual discharge from the index hospitalization. It is calculated as "LOS = actual discharge date − surgery date" using calendar days, rather than completed 24-hour periods. For example, surgery on May 1 followed by actual discharge on May 6 gives an LOS of 5 days. Measurement ends at actual discharge, rather than at the 1-month postoperative follow-up. The date on which discharge criteria are met will not be separately distinguished.

(2) Secondary endpoints: All measures below are secondary endpoints and are not co-primary endpoints alongside LOS.

(i) Postoperative recovery measures: Time to first flatus, time to first bowel movement, postoperative drainage volume, drain duration, time to first ambulation, and wound recovery. Wounds will be observed during hospitalization and reassessed at the in-person 1-month postoperative visit.

(ii) Complications: Infections within 30 days after surgery (surgical wound, pulmonary, urinary tract, and deep tissue infections), gastrointestinal symptoms (abdominal distension, constipation, and diarrhea), poor wound healing, lower-extremity deep vein thrombosis, renal insufficiency, and pressure ulcers. The occurrence, timing, treatment, and outcome of each event category will be recorded separately.

(iii) Anthropometric measurements, scale scores, and laboratory parameters are listed below.

Anthropometric measurements include body mass index (BMI), triceps skinfold thickness, mid-upper arm circumference, mid-upper arm muscle circumference, handgrip strength, waist circumference, hip circumference, and waist-to-hip ratio.

Scale measures include the Mini Nutritional Assessment (MNA), simplified gastrointestinal function score, Visual Analog Scale (VAS), Japanese Orthopaedic Association (JOA) low back pain score, Nutritional Risk Screening 2002 (NRS 2002), and brief dietary assessment. Pain and lumbar function scores will be recorded according to the requirements of the corresponding instruments [32].

Scale assessments are scheduled within 2 hours after admission, on postoperative day 3, before discharge, and at 1 month after surgery. At 1 month, patients must attend the hospital for scoring and necessary examinations. Telephone or online communication will be used only for contact and supplementary information.

Laboratory parameters include white blood cell count, C-reactive protein, erythrocyte sedimentation rate, serum albumin, total lymphocyte count, total cholesterol, hemoglobin, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, prealbumin, transferrin, retinol-binding protein, and serum creatinine. Controlling Nutritional Status (CONUT) and the Prognostic Nutritional Index (PNI) will also be calculated.

3.3 Study Population

3.3.1 Participant Age Range

Participants must be aged at least 18 years and younger than 75 years, i.e., $18 \leq \text{age} < 75$ years.

3.3.2 Inclusion Criteria

(1) Diagnosed with a noninfectious lumbar disorder and scheduled for elective open posterior lumbar fusion in this department.

(2) No marked abnormalities in recent dietary intake and no recent use of probiotic preparations.

(3) Surgery under general anesthesia, with fusion involving 1–3 levels.

(4) Aged 18 to <75 years, willing to participate voluntarily, and able to provide written informed consent.

3.3.3 Exclusion Criteria

(1) Chronic kidney disease, a history of malignancy, or infectious diseases such as pulmonary or spinal infection. Stable, controlled hypertension or diabetes mellitus does not automatically lead to exclusion under the broad term “chronic disease.” Eligibility will be determined using the corresponding criteria in this section.

(2) Impaired immune function, immunodeficiency, or use of immunosuppressive medication for a medical condition.

(3) Preoperative malnutrition or hypoalbuminemia (serum albumin <35 g/L). Malnutrition and hypoalbuminemia will be recorded separately and will not be treated as the same diagnosis.

(4) High bleeding risk, such as coagulation abnormalities, preoperative anemia, severe cardiac, hepatic, or renal dysfunction, or recent use of antiplatelet or anticoagulant medication.

(5) Lower-extremity deep vein thrombosis at admission.

(6) Intolerance or allergy to the medications or nutritional supplements used in this study.

(7) A disease causing severe impairment of digestion or absorption.

(8) Poorly controlled diabetes mellitus or hypertension.

(9) Emergency surgery.

(10) Any other condition that, in the investigator's judgment, prevents the patient from meeting study requirements.

3.3.4 Participant Withdrawal and Loss to Follow-up

All enrolled participants have the right to withdraw from the study at any time. Reasons for withdrawal or discontinuation include:

(1) The participant requests withdrawal and no longer wishes to participate.

(2) The participant is lost to follow-up.

(3) The participant refuses further follow-up visits.

(4) The investigator considers the participant unsuitable for continued participation for another reason.

3.3.5 Retention and Handling of Participants in the Analysis

After randomization, patients will be retained in their originally assigned groups. They must not be excluded entirely during statistical analysis solely because a test was not completed, an intervention was stopped, or an abnormal measurement occurred.

(1) If an eligibility error, protocol deviation, or data issue is identified, original records will be retained and the reasons documented. Participants must not be selected for analysis retrospectively according to outcomes.

(2) Missing data and outliers will be checked, documented, and handled as described in Section 5.4.

4. Study Procedures

After admission, patients who meet the eligibility criteria and provide written informed consent will be randomized to the control group, intervention group A, or intervention group B. Patient information will be registered, and comprehensive assessments and routine preoperative examinations will be completed. Scale assessments are scheduled within 2 hours after admission, on postoperative day 3, before discharge, and at 1 month after surgery. Anthropometric measurements will be obtained at admission and before discharge. Laboratory tests are scheduled preoperatively and on postoperative days 1, 3, and 6. Scoring

and wound assessment will be completed during the in-person hospital visit at 1 month after surgery. Telephone or online communication will be used for contact and supplementary follow-up.

(1) The study will be conducted jointly by clinicians, physicians from the Department of Nutrition, and designated nurses. Clinicians will be responsible for clinical care, safety assessments, and examination arrangements. Physicians from the Department of Nutrition will participate in nutritional screening, assessment, dietary counseling, and development of individualized supplementation regimens. Designated nurses will assist with intervention delivery and documentation. Outcome assessors will not participate in intervention delivery and will remain unaware of group allocation.

(2) Control group: Patients will follow the routine management pathway used in this department at study initiation. After admission assessment, physicians from the Department of Nutrition and treating physicians will provide dietary counseling. Food and fluids will be withheld for more than 8 hours before surgery. Oral feeding will begin after the first postoperative passage of flatus and progress from a liquid diet to a semiliquid diet and then a regular diet. Treating physicians will provide necessary routine treatment based on the patient's condition and test results. No additional study-specific ONS, carbohydrate loading, or probiotic supplementation is planned for this group. Clinically necessary rescue care and nutritional therapy will remain available, and any such co-interventions will be documented accurately.

(3) Intervention group A: A combined strategy incorporating ONS, perioperative carbohydrate loading, and optimized feeding timing will be implemented with reference to the consensus on perioperative nutritional management in orthopaedics [18]. (i) Intervention timing: ONS will begin on preoperative day 2 and continue from postoperative day 1 through day 5. (ii) Nutritional targets: Physicians from the Department of Nutrition will develop a regimen based on body weight, dietary intake, and clinical condition. Daily targets will be approximately 30 kcal/kg for energy and 1.5–2.0 g/kg for protein, adjusted as appropriate. (iii) ONS: Complete nutritional powder and whey protein prepared by the hospital's Department of Nutrition will be used. Patients with diabetes mellitus will receive a corresponding specialized formula. Preparations will be mixed with warm water and taken orally between meals. The actual formulation, supplemental amount, and adjustments will follow nutritional prescriptions and medical orders. (iv) Preoperative feeding: Food will be withheld for more than 8 hours before surgery. A 12.5% carbohydrate drink will be given at approximately 10 hours and 2 hours before surgery, in volumes of 400 mL and 200 mL, respectively. Actual administration times will depend on surgical and anesthetic arrangements. (v) Postoperative feeding: A 200-mL carbohydrate drink will be given after the patient returns to the ward and regains consciousness following anesthesia. Diet will then progress, as tolerated, from semiliquid to soft food and subsequently a regular diet. Physicians from the Department of Nutrition will adjust ONS and dietary regimens.

(4) Intervention group B: Patients will receive the same ONS, carbohydrate loading, and feeding management as group A. In addition, they will take Jinshuangqi (Bifidobacterium and Lactobacillus triple viable bacteria tablets) orally from preoperative day 2 through postoperative day 5, at 2 g per dose three times daily, equivalent to four tablets per dose. The manufacturer is Inner Mongolia Shuangqi Pharmaceutical Co., Ltd.; the Chinese drug approval number is S19980004; each tablet contains 0.5 g. The preparation contains Bifidobacterium longum, Lactobacillus bulgaricus, and Streptococcus thermophilus. Each tablet contains at least 0.5×10^7 colony-forming units (CFU) of B. longum and at least 0.5×10^6 CFU each of L. bulgaricus and S. thermophilus. Orders will be entered through the hospital information system. The preparation will be stored as required, and actual administration will be recorded.

(5) Outcome measures and assessment schedule: LOS is the primary endpoint. All other measures are secondary endpoints, classified as specified in Section 3.2.2.

(i) Anthropometric measurements: BMI, triceps skinfold thickness, mid-upper arm circumference, mid-upper arm muscle circumference, handgrip strength, waist circumference, hip circumference, and waist-to-hip ratio will be assessed at admission and before discharge.

(ii) Scales: VAS, JOA low back pain score, NRS 2002, MNA, brief dietary assessment, and simplified gastrointestinal function score will be assessed within 2 hours after admission, on postoperative day 3, before discharge, and at 1 month after surgery.

(iii) Laboratory tests: Results from routine clinical testing preoperatively and on postoperative days 1, 3, and 6 will be used. Parameters include white blood cell count, C-reactive protein, erythrocyte sedimentation rate, serum albumin, total lymphocyte count, total cholesterol, hemoglobin, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, prealbumin, transferrin, retinol-binding protein, and serum creatinine. CONUT and PNI will be calculated. No additional tests will be performed for the study.

(iv) Postoperative recovery: Time to first flatus, time to first bowel movement, drainage volume, drain duration, time to first ambulation, and wound recovery will be collected from original nursing and clinical records. LOS will be recorded separately as the primary endpoint.

(v) Complications: Infections within 30 days after surgery, gastrointestinal symptoms, poor wound healing, lower-extremity deep vein thrombosis, renal insufficiency, and pressure ulcers will be recorded. Events will be verified using inpatient records and the in-person 1-month postoperative visit.

4.1 Informed Consent and Enrollment

Before randomization and study interventions, research staff will explain the study objectives, management measures in each group, random allocation, potential risks and benefits, cost coverage, data use, and withdrawal rights. Patients may be enrolled only after eligibility is confirmed and written informed consent is obtained. Telephone or online communication will be used for subsequent contact and supplementary follow-up. It does not replace written informed consent obtained before enrollment in this interventional study.

4.2 Participant Identification Numbers

Each participant will be assigned a unique identification number consisting of the initials of the participant's name in Hanyu Pinyin plus a numeric code. This identifier will be used in all study documents, including case report forms and clinical records. Under data privacy regulations, a unique identifier is permissible provided it does not combine information that could identify the participant. For example, combining the participant's initials with their date of birth is not permitted.

4.3 Data Sources and Data Collection

Data sources include original medical records, medical orders, nursing records, examination reports, assessment scales, and follow-up records. Outcomes will be assessed by assessors who are not involved in intervention delivery and remain unaware of allocation. Data will be entered into case report forms (CRFs) according to standardized requirements. Two staff members will enter data independently and reconcile discrepancies. Data entry and verification must not involve arbitrary changes to source records. All corrections will retain supporting evidence and an audit trail.

The following data will be recorded:

(1) Demographic data, including date of birth, sex, height, and weight.

(2) Medical, medication, smoking, and alcohol-use histories during the 6 months before the current visit, including smoking, heavy alcohol consumption, hypertension, hyperlipidemia, and diabetes mellitus.

(3) Anthropometric measurements: BMI, triceps skinfold thickness, mid-upper arm circumference, mid-upper arm muscle circumference, handgrip strength, waist circumference, hip circumference, and waist-to-hip ratio.

(4) Scale scores: VAS, JOA, NRS 2002, MNA, brief dietary assessment, and simplified gastrointestinal function score.

(5) Laboratory tests: Routine clinical tests preoperatively and on postoperative days 1, 3, and 6, using the parameters listed in Section 4. Original reporting units and sampling dates will be retained.

(6) The primary endpoint, LOS, and secondary endpoints, including time to first flatus, time to first bowel movement, drainage volume, drain duration, time to first ambulation, and wound recovery.

(7) Complications: Infection within 30 days (surgical wound, pulmonary, urinary tract, and deep tissue infections), gastrointestinal symptoms (abdominal distension, constipation, and diarrhea), poor wound healing, lower-extremity deep vein thrombosis, renal insufficiency, and pressure ulcers.

4.4 Criteria for Study Termination or Suspension

(1) The study sponsor has the right to terminate or suspend the study. Before termination or suspension, the sponsor must notify the investigators, ethics committee, and relevant regulatory authorities and explain the reasons. Resumption after premature termination or suspension requires ethics committee review and approval.

(2) Termination or suspension required by the ethics committee.

4.5 Bias Control and Management of Protocol Deviations

4.5.1 Measures to Prevent Bias

Random allocation and allocation concealment will reduce selection bias. Blinded outcome assessment and standardized measurement procedures will reduce measurement bias. Randomization does not guarantee complete balance in every baseline characteristic. Interpretation must consider the sample size, between-group differences, and co-interventions that may affect outcomes. Any supplementary adjusted analysis must explain its rationale and relationship to the original analysis plan.

4.5.2 Monitoring and Management of Deviations

An independent data monitoring committee (DMC) will monitor data quality, safety, and protocol implementation according to study arrangements. Membership and monitoring records will be retained. If a protocol deviation is identified, its causes, effects, and corrective measures will be verified. Randomized allocation must not be changed, and the sample size must not be increased retrospectively to eliminate observed between-group differences. Substantive protocol changes will follow ethics committee and hospital requirements and be documented accurately.

4.5.3 Protocol Amendment Process

If recruitment difficulties, technical issues, or other circumstances require protocol amendment, investigators must submit a written application detailing the reasons, proposed changes, and effects on the study. After ethics committee review, all research staff and participants will be informed promptly, and the protocol and related documents will be updated to maintain scientific validity and compliance.

4.6 Adverse Event Monitoring and Management

4.6.1 Definition and Classification of Adverse Events

An adverse event is any unfavorable medical occurrence during a participant's involvement in the study, regardless of a causal relationship with the intervention. Severity will be recorded as mild, moderate, or severe based on symptoms and functional impact. Seriousness will be assessed separately. Death, a life-threatening event, hospitalization or prolonged hospitalization, and persistent or significant disability are criteria relevant to seriousness. “Severe” must not be equated with “serious adverse event.” The possible relationship between each event and the study intervention will be recorded.

4.6.2 Adverse Event Monitoring and Reporting

Adverse events will be monitored through symptom inquiries, clinical records, and routine examinations. Events will be assessed and managed promptly. As required by the original protocol, reporting documentation will be completed within 24 hours, and reports will follow ethics committee and hospital requirements. Serious adverse events require immediate initiation of the appropriate reporting and emergency care procedures. Event onset, manifestations, severity, seriousness, relatedness, management, and outcome will be documented fully.

4.6.3 Management of Adverse Events

For mild adverse events, participants will be monitored closely and receive symptomatic treatment when necessary. For moderate events, the study intervention will be suspended and appropriate treatment provided. Continued participation will be reassessed after symptoms improve. For severe events, the study intervention will be stopped immediately, emergency treatment provided, and the emergency response plan activated. All management procedures will be documented in detail to safeguard participant safety.

4.6.4 Potential Adverse Events and Management Measures

(1) Risk of disclosure of participants' private information: Improper data storage, transmission vulnerabilities, or staff misconduct may result in unlawful access to, alteration of, or disclosure of names, identity card numbers, contact details, health records, or other private information. Management measures: (i) Immediately activate the data security emergency response plan, stop the source of disclosure, and thoroughly investigate and repair affected systems. (ii) Immediately notify affected participants, explain the situation, and offer necessary remedial advice, such as identity protection or password resets. (iii) Report the incident to relevant regulatory authorities, cooperate with investigations, and assume responsibility as required by regulations. (iv) Strengthen staff training and improve encryption, access controls, and other security measures to prevent recurrence.

(2) Surgery-related adverse events: Anesthetic complications, bleeding, or nerve injury may occur intraoperatively. Infection, poor wound healing, pain, or functional impairment may occur after surgery. Close intraoperative monitoring and postoperative observation will support timely identification and symptomatic treatment of complications. Multidisciplinary consultation will be arranged when necessary.

(3) Risks associated with nutritional supplementation and probiotics: Possible symptoms include abdominal distension, nausea, vomiting, diarrhea, constipation, or allergy. If intolerance occurs, the treating physician and physicians from the Department of Nutrition will assess the patient. Supplementation will be adjusted or suspended and symptomatic treatment provided when necessary. Suspected severe allergy or another serious event requires priority treatment and prompt reporting. Necessary treatment must not be delayed to complete the intervention.

5. Statistical Methods

5.1 General Principles

Statistical analyses will be performed using SPSS 27.0. Continuous variables will be summarized as mean ± standard deviation or median (interquartile range), according to their distribution. Categorical variables will be summarized as counts and percentages. Continuous variables across the three groups will be compared using one-way analysis of variance or the Kruskal–Wallis test, depending on distribution and variance. Categorical variables will be compared using the χ^2 test or Fisher's exact test. The two prespecified primary endpoint comparisons are group A versus the control group and group B versus the control group. Bonferroni correction will be applied, with a two-sided α of 0.025 for each comparison. If adjusted P values are reported, significance will be assessed against adjusted $P < 0.05$, without applying correction twice. Group B versus group A is exploratory and does not form part of the primary comparison family. Secondary endpoint analyses and comparisons across multiple time points are exploratory. The

scope and method of adjustment for each set of comparisons must be specified. Paired before-and-after data will be analyzed using a paired t test or the Wilcoxon signed-rank test. Repeated measurements will be handled using the originally planned repeated-measures analysis of variance or Friedman test. Significance within one group and nonsignificance within another cannot establish a between-group difference. Effect sizes, 95% confidence intervals, and exact P values will be reported. Any supplementary models or sensitivity analyses must be identified separately.

The numbers screened, randomized, undergoing surgery, completing follow-up, and included in analyses will be described, together with relevant reasons. Baseline characteristics, including age, sex, diagnosis, fusion levels, and comorbidities, will be described by randomized group. Baseline P values will not determine whether patients are retained.

5.2 Sample Size Estimation

Sample size estimation is based on postoperative LOS as the primary endpoint. The original protocol cited LOS data from Xu et al. [22]: 94 patients in the nutritional management group, 9.03 ± 2.33 days; and 93 controls, 11.54 ± 3.18 days. These data correspond to a difference of 2.51 days, a pooled standard deviation of approximately 2.785 days, and Cohen's d of approximately 0.901. Under an equal-allocation, two-sided independent-samples t-test framework, the original protocol estimated that at least 25 evaluable patients per group were required for 80% power. This estimate used Bonferroni-corrected $\alpha = 0.025$ for each primary comparison: group A versus the control group and group B versus the control group. Allowing for 10% attrition increased the requirement to 28 patients per group, or 84 overall. The final planned enrollment is 30 patients per group, or 90 overall. This rationale applies to the two comparisons with the control group. It does not ensure power for the exploratory comparison of group B versus group A.

5.3 Statistical Analysis Set

The units of analysis are all participants admitted, enrolled, and providing signed informed consent.

5.4 Handling of Missing Data and Outliers

(1) Missing data: If omissions are identified during verification, original records will first be reviewed. Reasons for missingness and the methods used to handle missing data will be disclosed accurately.

(2) Outliers: Box plots or scatter plots will be used to examine data distributions. Ranges of ±3 standard deviations or ±1.5 interquartile ranges will be used to identify outlying measurements. If an abnormal value is clearly present, its cause will be considered and discussed among the investigators. Once confirmed as an outlier, the value will be removed from statistical analysis.

5.5 Analysis of Outcome Measures

5.5.1 Primary Endpoint Analysis

The sole primary endpoint is postoperative LOS, defined and calculated as specified in Section 3.2.2. LOS distributions will be described separately for the three groups. The two prespecified comparisons, group A versus the control group and group B versus the control group, will be conducted. Between-group differences and 95% confidence intervals will be reported. Each comparison will use a two-sided α of 0.025, or Bonferroni-adjusted P values will be reported.

5.5.2 Secondary Endpoint Analysis

(1) Postoperative recovery and complications: Time to first flatus, time to first bowel movement, drainage volume, drain duration, time to first ambulation, and wound recovery will be analyzed. Counts and proportions will be reported separately for infections, gastrointestinal symptoms, poor wound healing, lower-extremity deep vein thrombosis, renal insufficiency, and pressure ulcers within 30 days after

surgery. Different event types will be reported separately; one patient may experience events in multiple categories.

(2) Anthropometric measurements: BMI, triceps skinfold thickness, mid-upper arm circumference, mid-upper arm muscle circumference, handgrip strength, waist circumference, hip circumference, and waist-to-hip ratio will be compared at admission and before discharge. Predischarge measurements occur at different postoperative times, so interpretation should consider the actual measurement dates.

(3) Scales: VAS, JOA low back pain score, NRS 2002, MNA, brief dietary assessment, and simplified gastrointestinal function score will be analyzed at admission, on postoperative day 3, before discharge, and at 1 month after surgery. Each instrument's scoring range, direction, and actual assessment time will be retained.

(4) Laboratory tests: Routine test results obtained preoperatively and on postoperative days 1, 3, and 6 will be analyzed, together with CONUT and PNI calculated from those results.

5.6 Safety Analysis

Adverse events associated with nutritional supplementation, probiotic use, or the perioperative period will be summarized by randomized group. Severity, seriousness, possible relatedness, and management outcomes will be recorded. The sample size is based on LOS. An absence of observed differences cannot establish equivalent risks of rare adverse events or demonstrate safety adequately.

In-hospital adverse event incidence: A patient experiencing multiple adverse events will be counted once when calculating overall incidence. Repeated occurrences of the same adverse event in one patient will also count once for that event's incidence. Incidence will be calculated by symptom or sign as the number of participants experiencing a particular adverse event at least once. If the same adverse event occurs repeatedly in a participant, its severity will be recorded using the most severe occurrence.

6. Ethics

6.1 Ethical Requirements

The study will comply with GCP, the Declaration of Helsinki, applicable regulations, and ethics committee review requirements. Investigators must ensure that the study is reviewed and approved by a qualified ethics committee that meets GCP requirements.

Before study initiation, investigators will submit the protocol and other required materials to the ethics committee for review and approval. The committee's signed approval will be retained in the investigator's files. The committee will issue a clear written opinion identifying the clinical study, reviewed documents with version numbers, and dates. Documentation must also identify the date of the approval meeting, attending members, and voting members.

Any additions or amendments to the protocol or related documents during the study must obtain further written ethics committee approval in accordance with regulations.

Investigators may begin the study only after receiving ethics committee approval.

Investigators are responsible for reporting study progress to the ethics committee.

6.2 Informed Consent

Informed consent will be obtained before enrollment and study interventions and will remain an ongoing process throughout participation. Using ethics committee-approved materials and plain language, research staff will explain study objectives, random allocation, intervention procedures, risks, expected benefits, cost coverage, privacy protection, and withdrawal rights. Participants will have sufficient time to consider participation and ask questions. Participants will sign and date the consent form voluntarily, and research staff will countersign to confirm the process. A copy will be provided to each participant. New

information that may affect willingness to continue will be disclosed promptly and documented. Materials will be updated and consent obtained again when required.

If investigators obtain new information that may affect continued participation, they will promptly inform the participant or guardian and document the communication. If the protocol is amended, the consent form will be updated as appropriate. After ethics committee approval, renewed informed consent will be obtained promptly.

Written informed consent must be obtained before random allocation and study interventions. Telephone or online communication will be used for contact and supplementary follow-up. If audio recordings or similar materials are collected, their purpose must be explained separately, consent obtained, and the materials stored in accordance with privacy requirements. Consent to telephone follow-up does not replace written informed consent obtained before enrollment.

6.3 Privacy of Personal Data

Personal data collected and processed from study participants will be used only for this research and related publications, reports, and dissemination of findings.

Adequate data collection and processing measures will ensure that security and confidentiality comply with applicable privacy laws and regulations. Appropriate technical and organizational safeguards will protect personal data against leakage, unauthorized disclosure or access, accidental or unlawful destruction, and accidental loss or alteration. Research staff whose duties require access to patient data must keep participant identities confidential.

The study team will ensure that personal data are:

(i) Processed fairly and lawfully.

(ii) Collected for the legitimate purposes specified in the protocol and not processed in ways incompatible with those purposes.

(iii) Adequate, relevant, and appropriate for the stated purposes.

(iv) Accurate and, where necessary, kept up to date.

Before collecting personal data, investigators will obtain consent from participants or guardians for data processing and direct access to source medical records and source data during study-related monitoring, audits, ethics committee reviews, and inspections by drug regulatory authorities.

Participants have the right to request their personal data from investigators and to request correction of inaccurate or incomplete data. Reasonable action will be taken in light of the nature of the request, study circumstances, and applicable laws and regulations.

7. Study Management

7.1 Quality Control and Quality Assurance

7.1.1 Quality Control Procedures

Before study initiation, eligibility criteria, random allocation, intervention procedures, and outcome recording requirements will be clarified. Standardized training will be provided, and CRFs will be checked against source records. Reasons for deviations and their management will be documented promptly. Eligibility criteria must not be changed in response to known outcomes.

At the protocol discussion meeting before the clinical study formally begins, the principal investigators will review the protocol and CRFs with all participating investigators.

During the study, investigators must ensure site compliance with the protocol and GCP, complete and accurate CRF data, and coordinated study progress. They must also ensure that study-related medications are stored, dispensed, returned, and counted according to specified requirements.

Investigators are responsible for completing CRFs within 3 days after each patient visit and ensuring consistency with source materials such as medical records.

Investigators will retain CRFs securely alongside other study documents, including the protocol and protocol amendments.

7.1.2 Training

Before study initiation, the principal investigators will train all participating investigators at the study site. Training will cover, but is not limited to, informed consent, the clinical research protocol, and study-related standard operating procedures (SOPs). Investigators must become familiar with the protocol, understand GCP principles, use consistent recording methods and assessment criteria, and follow the protocol strictly.

7.2 Protocol Changes

Protocol changes or additions must be documented in a traceable written record. Substantive changes involving participant safety, interventions, eligibility criteria, the primary endpoint, or analysis arrangements must follow ethics committee and hospital requirements.

Editorial changes, terminology harmonization, and document management updates must also retain version numbers and dates. Whether ethics committee submission is required will be determined under hospital procedures. Editorial revisions after study completion must not replace or overwrite the originally approved protocol or its amendment records.

7.3 Data Recording and Document Retention

Investigators will prepare comprehensive and accurate source documents for every participant, recording all examination results and other relevant data.

Participant information collected in CRFs will be recorded using the initials of each participant's name in Hanyu Pinyin plus a numeric code. Participants will be identified by this code.

All information required by the protocol must be entered into CRFs, and any omissions must be explained. CRFs must be completed within 3 days after each patient visit to facilitate verification of completeness and accuracy. Investigators must sign the CRFs.

All CRF entries must be completed legibly using a fountain pen or other ink pen. Errors may be corrected by drawing a single horizontal line through the incorrect entry so that it remains readable, then writing the corrected entry beside it. The investigator must sign or enter their name and date beside the correction. Correction fluid is not permitted.

Study documents, including the protocol and amendments, completed CRFs, signed informed consent forms, and original medical records, must be retained and managed in accordance with Chinese GCP requirements. Documents must be stored appropriately for future access and data traceability, with consideration of security and environmental risks.

Investigators will retain the relevant documents for 5 years after study completion.

8. Investigator Responsibilities

Investigator responsibilities include, but are not limited to, the following:

(1) Draft and sign the protocol, submit relevant study materials for ethics committee approval, and implement the study after approval.

(2) Ensure that participants are selected according to the protocol.

(3) Understand the characteristics, actions, efficacy, and safety of study medications, including relevant preclinical information. Investigators must also remain informed of all new medication-related information identified during the study.

(4) Conduct the study in a medical institution with appropriate clinical facilities, laboratory equipment, and staffing. The institution must have all facilities necessary to manage emergencies and ensure patient safety. Laboratory results must be accurate and reliable.

(5) Obtain agreement from the medical institution or supervising organization and ensure sufficient time to oversee and complete the study within the protocol-defined period. Investigators must explain study information, requirements, and responsibilities to all participating staff and ensure enrollment of sufficient patients meeting protocol criteria.

(6) Take and document the measures necessary to safeguard patient safety.

(7) Ensure that data are entered truthfully, accurately, completely, and promptly into medical records and CRFs.

(8) Ensure the quality of the clinical study.

(9) Prepare, sign, and date a final report after study completion.

9. Confidentiality and Publication of Study Results

Study results may be presented at scientific conferences and published in scientific journals. Authorship will follow the requirements of the International Committee of Medical Journal Editors (ICMJE).

10. Final Report

Investigators are responsible for completing the final report, compiling statistical data and results, summarizing study implementation in detail, and reporting to the ethics committee.

11. Conflict of Interest Statement

Investigators must devote sufficient time to study completion, follow research integrity and authorship requirements, and accurately disclose study-related financial and nonfinancial interests. Nutritional preparations will be funded by the research budget. Product supply, industry support, consultancy, or other relevant interests must be declared separately when applicable. When treating clinicians also serve as investigators, they must explain that voluntary participation or withdrawal will not affect routine care. A blanket statement of “no conflicts of interest whatsoever” must not replace specific disclosure.

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