Study Protocol

Official Title: Bidirectional Cohort of Lower-Limb Sports Injury and Degeneration: The Yongjiang Cohort

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Responsible Institution: Ningbo No. 2 Hospital

Study Site: Ningbo No. 2 Hospital, Ningbo, China

Study Type: Observational, non-interventional, bidirectional cohort study

This document is prepared in English for ClinicalTrials.gov PRS study document upload. It contains no names or identifiers of research participants.

1. Background and Rationale

Musculoskeletal injuries and degenerative joint diseases are major causes of pain, functional limitation, disability, and health-care burden across the life course. Sports-related knee injuries are increasingly common in active populations, while degenerative knee disease, including knee osteoarthritis, is increasingly prevalent in middle-aged and older adults. Both conditions may lead to long-term functional decline, recurrent injury, progressive degeneration, and reduced quality of life.

The Yongjiang Cohort is designed to establish a regional, standardized, real-world clinical cohort covering the continuum from lower-limb sports injury to degenerative progression and functional outcomes. The study will focus on patients with knee-related sports injuries and degenerative knee conditions receiving routine care at Ningbo No. 2 Hospital. The cohort will integrate clinical information, laboratory tests, patient-reported outcome measures, structural and quantitative imaging, functional assessments, and follow-up outcomes.

Compared with single-disease or single-time-point studies, this cohort emphasizes longitudinal observation of injury characteristics, degeneration, tissue changes, functional recovery, reinjury, reoperation, and age-related functional decline. The study will also include a sarcopenia-related assessment module for participants aged 50 years or older to explore associations among degeneration, body composition, gait, and prognosis.

2. Study Objectives

- To establish a standardized bidirectional clinical cohort covering lower-limb sports injury and degenerative knee disease.
- To collect laboratory, imaging, questionnaire, and functional assessment data from patients with knee-related disease or injury.
- To describe baseline characteristics and longitudinal outcome trajectories across age groups and disease spectra.
- To assess functional outcomes, imaging-based degeneration progression, reinjury, and reoperation at approximately 6, 12, and 24 months after treatment or surgery.
- To explore relationships among sarcopenia-related indicators, degeneration, body composition, gait changes, and prognosis in participants aged 50 years or older.
- To provide real-world evidence for risk stratification, treatment evaluation, and secondary prevention strategies for lower-limb sports injury and degenerative knee disease.

3. Study Design

Study type	Non-interventional, observational, bidirectional cohort study
Study model	Cohort
Time perspective	Bidirectional: baseline and available historical clinical information may be collected, and participants will be followed prospectively.
Study site	Ningbo No. 2 Hospital, including orthopedic and sports medicine outpatient, emergency, and inpatient pathways.
Estimated enrollment	Approximately 500 participants
Planned study period	Preparation: April to June 2026; enrollment: July 2026 to December 2027; follow-up: January 2027 to December 2029; final analysis by December 2029.

No randomization, blinding, or study-assigned intervention will be used. Treatment decisions will be made by treating physicians according to routine clinical practice.

4. Study Population

4.1 Target Population

The study will enroll patients admitted to or treated at Ningbo No. 2 Hospital for knee-related diseases or injuries, including sports injuries and degenerative knee conditions. Participants will be managed according to age-stratified data collection pathways.

4.2 Inclusion Criteria

- Patients scheduled to receive relevant clinical evaluation or treatment at Ningbo No. 2 Hospital and able to complete baseline assessment.
- Patients with a clinical diagnosis of knee-related injury or degenerative knee disease.
- Patients willing to provide informed consent and participate in follow-up.

4.3 Exclusion Criteria

- Patients unable to complete core baseline assessments or with substantial missing key information.
- Patients with severe comorbidities or cognitive impairment that may interfere with outcome assessment or follow-up.
- Patients judged by the investigators to be unsuitable for enrollment.

4.4 Withdrawal Criteria

- Voluntary withdrawal by the participant.
- Loss to follow-up or withdrawal of informed consent.
- Other circumstances that make continued follow-up or assessment impossible.

5. Groups and Cohorts

Sports Injury Cohort	Participants with knee-related sports injuries as the main clinical condition. This cohort will be observed for injury characteristics, treatment patterns, tissue repair, functional recovery, and subsequent degenerative changes.
Degenerative Knee Disease Cohort	Participants with degenerative knee conditions, including knee osteoarthritis or related degenerative disorders, as the main clinical condition. This cohort will be observed for degeneration severity, symptom burden, imaging progression, body composition, gait changes, and clinical outcomes.
Age stratification	Participants younger than 50 years will follow a sports injury and functional recovery-oriented pathway. Participants aged 50 years or older will additionally undergo sarcopenia-related assessments when applicable.

6. Observational Procedures and Data Collection

Data will be collected using standardized case report forms, a unified data dictionary, and standard operating procedures. The following information may be collected as part of the study:

- Demographic information, medical history, comorbidities, prior treatment, medication use, sports exposure, and lifestyle factors.
- Laboratory measures, including serum free fatty acids, ferritin, interleukin-6, insulin-like growth factor 1, cortisol, and adrenocorticotropic hormone.
- Patient-reported outcome measures: KOOS and IKDC for participants younger than 50 years; WOMAC and IKDC for participants aged 50 years or older; PHQ-9 and GAD-7 for both age groups.

- Imaging measures: bilateral standing knee X-rays, full-length lower-limb radiographs, 3.0T bilateral knee MRI including 3D DESS, and additional T1rho/T2 mapping and PDFF sequences when available according to the clinical pathway.
- Intraoperative tissue samples, when participants undergo routine surgery and provide appropriate consent; small amounts of synovial and cartilage tissue may be retained without changing the planned operation or increasing surgical risk.
- Functional assessments for participants aged 50 years or older, including grip strength, DXA bone mineral density and body composition testing, and gait assessment.
- Treatment or surgery-related process information, complications, readmissions, reoperations, and follow-up outcomes.

7. Follow-up Schedule

Follow-up will combine remote follow-up, including telephone, text message, or electronic tools, with outpatient reassessment when applicable. Follow-up visits are planned at approximately 6 months, 12 months, and 24 months after treatment or surgery. A suggested time window of approximately plus or minus 2 to 4 weeks will be used when feasible.

Baseline	Informed consent; demographic and clinical data; laboratory tests; questionnaires; imaging; and functional assessments as applicable.
6 months	Questionnaire follow-up, clinical outcome review, pain and quality-of-life assessment, reinjury or reoperation status, and other clinically indicated assessments.
12 months	Questionnaire follow-up, clinical outcome review, imaging or functional reassessment when applicable, and sarcopenia-related reassessment for participants aged 50 years or older when applicable.
24 months	Final planned follow-up for functional outcomes, imaging-based degeneration progression when available, reinjury, reoperation, falls, and functional decline.

8. Outcome Measures

8.1 Primary Outcome Measures

- Change in knee function scores from baseline, assessed using KOOS and/or IKDC in participants younger than 50 years and WOMAC and/or IKDC in participants aged 50 years or older. Time frame: baseline, 6 months, 12 months, and 24 months after treatment or surgery.
- Change in imaging-based knee degeneration, assessed using Kellgren-Lawrence grading on X-ray and quantitative MRI-related measures when available according to the protocol. Time frame: baseline, 6 months, 12 months, and 24 months after treatment or surgery.

8.2 Secondary Outcome Measures

- Reinjury during follow-up.
- Reoperation during follow-up.
- Changes in pain and quality-of-life-related measures.
- Falls during follow-up.
- Changes in bone mineral density, body composition, and gait measures in participants aged 50 years or older.
- Perioperative complications, readmissions, and other clinically relevant events when applicable.

9. Data Management and Confidentiality

Study data will be collected using standardized case report forms and a unified data dictionary. Research data will be managed using coded participant identifiers. Direct identifying information will be stored separately from research data. Access to research data will be controlled by role-based authorization, and data entry, modification, export, and quality-control activities will be traceable when possible.

Sample collection, laboratory testing, questionnaire administration, imaging acquisition, grip strength measurement, DXA testing, gait assessment, and tissue handling will follow standardized operating procedures. If the cohort is later linked to a regional multicenter registry platform, standardized mapping and data quality verification will be performed while maintaining the integrity of the original data.

10. Safety, Risks, and Benefits

This is an observational cohort study and does not assign experimental treatment. Assessments are mainly integrated with routine clinical care and standardized follow-up. Overall risk is expected to be low.

Potential risks include the time burden associated with additional data collection and follow-up, mild discomfort from routine blood sampling or functional assessments, minimal risks associated with imaging or DXA according to standard clinical practice, and the risk of privacy breach. Risk mitigation measures include minimizing additional burden by coordinating study assessments with routine care, training study personnel, using coded identifiers, applying restricted access, and allowing participants to withdraw at any time without affecting routine care.

Participants may benefit from systematic baseline and follow-up assessments, which may help them and their clinicians better understand recovery, degeneration progression, and related risk factors. The study may also generate real-world evidence to improve future risk assessment, treatment evaluation, and secondary prevention strategies.

11. Statistical Analysis Plan Summary

The primary analyses will be descriptive and exploratory, consistent with the observational cohort design. Baseline characteristics will be summarized overall and by cohort, age group, and major clinical diagnosis. Continuous variables will be summarized using mean, standard deviation, median, interquartile range, minimum, and maximum as appropriate. Categorical variables will be summarized using counts and percentages.

Longitudinal changes in functional scores and imaging measures will be described at the planned follow-up time points. When appropriate, paired analyses, regression models, or mixed-effects models may be used to evaluate changes over time and associations between baseline variables and outcomes. Potential predictors may include demographic factors, clinical diagnosis, laboratory markers, imaging features, treatment-related variables, and age-related functional indicators such as body composition and gait measures.

Secondary outcomes, including reinjury, reoperation, falls, and clinically relevant events, will be summarized using incidence proportions or rates when applicable. Time-to-event analyses may be considered if sufficient event numbers and follow-up data are available. Missing data will be described, and appropriate methods, such as complete-case analysis, sensitivity analysis, or model-based approaches, may be used depending on the amount and pattern of missingness.

All analyses will be interpreted as observational. No causal effect of a study-assigned intervention will be inferred because the study does not assign treatments.

12. Study Governance

The study will be conducted as a single-center investigator-initiated study at Ningbo No. 2 Hospital. Study activities will be coordinated through a project management structure that includes clinical enrollment, imaging, laboratory, rehabilitation assessment, and data management functions. All study personnel will be trained according to their assigned responsibilities and the study standard operating procedures.

13. References

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