Shanghai Sixth People's Hospital

Clinical research project plan

Project Title: A Retrospective Study on the Relationship Between Mortality Rates of Fractures in Different Sites and Factors such as Age, Metabolism, and Nutritional Status in Elderly Patients: A single-center retrospective study

NCT Number Not yet assigned

Project start and end time April 2025 ~ June 2026

Version date: June 23, 2025

1、Summary of the scenario

Objectives of the study	This study retrospectively analyzed the post-fracture mortality rate of elderly fracture patients aged 60 years and above, and explored the effects of different fracture sites, different ages, metabolic and nutritional statuses on mortality, and provided a basis for clinical prevention and intervention strategies.
Study design	Single-center, retrospective, cohort study
Sample size	All cases that met the inclusion and exclusion criteria at the National Orthopedic Medical Center of Shanghai Sixth People's Hospital from January 1, 2010 to December 31, 2019.
The study population and grouping	Elderly fracture patients aged 60 and above were grouped according to fracture site, age, metabolic and nutritional status.
Selection criteria	① Cases from January 1, 2010 to December 31, 2019 at the National Orthopedic Medical Center of Shanghai Sixth People's Hospital; ② Age ≥ 60 years; ③ Shanghai household registration; ④ Diagnosed with fractures of the limbs and spine and underwent surgical treatment at Shanghai Sixth People's Hospital.
Exclusion Criteria	① Multiple fractures; ② Conservative treatment selected; ③ Incomplete case data.
Interventions	None
Primary endpoint index	• All-cause mortality • Fracture-related mortality

2. Basis for establishment

(Including analysis of current research status at home and abroad, literature summary, significance of research topics, etc., with main references)

Fractures in the elderly refer to bone fractures that occur in older patients, typically resulting from bone fragility or low-energy trauma, such as falls from a standing height. As individuals age, bone density diminishes, leading to osteoporosis, a condition that significantly increases the risk of fractures among older adults.

Fractures can lead to a decline in functional status and independence, severely impacting quality of life. They result in various adverse outcomes, including impaired physical function, chronic pain, reduced social engagement, and mental health issues in the short term[1-3]. Furthermore, they elevate the likelihood of disability and mortality in the long term. Research has demonstrated a correlation between lower extremity fractures and increased mortality rates; for instance, older adults who suffer hip fractures face a heightened risk of death for years following the incident[4,5]. Additionally, epidemiological data indicate that as the population ages, the incidence of nearly all types of fractures among the elderly is rising globally[6]. This trend imposes a substantial burden on the economic development and social governance of many countries. It is projected that by 2025, the annual medical expenses associated with osteoporosis-related fractures in the United States alone could reach $25.3 billion[7]. Currently, as our country experiences deepening aging, the number of elderly patients with fractures is increasing. Consequently, how to implement effective follow-up treatment and care to minimize the incidence of complications, enhance patients' quality of life, and prolong their survival will become a critical issue.

Existing research indicates that factors contributing to increased mortality include pre-existing comorbidities and functional health conditions. Older adults with fractures frequently experience a range of health issues that heighten their vulnerability to post-fracture complications such as infections or declines in overall health[4,8]. Furthermore, the study revealed that individuals with fractures in critical bone regions, such as the hip, exhibit significantly higher mortality rates compared to those with fractures in other areas, suggesting that the location and severity of fractures are crucial factors influencing prognosis[9]. In clinical practice, we observe that elements such as metabolic and nutritional status, as well as the presence of postoperative complications, can significantly affect patient prognosis.

Early intervention has been shown to play a vital role in mitigating the risk of long-term mortality associated with fractures[10]. The initial management of fractures, whether surgical or conservative, can substantially influence long-term outcomes. Thus, it is essential to implement targeted measures to enhance patient outcomes. However, the findings concerning relevant factors are relatively fragmented, and most conclusions are drawn from data pertaining to European and American populations. The limited collection and analysis of data from our country's patient population restrict the clinical applicability of these findings in our context. Therefore, conducting a study of considerable scale within the Chinese population is imperative. This study aims to evaluate the long-term mortality risk of elderly fracture patients treated surgically and further analyze the association of related factors with patient prognosis, thereby providing a foundation for the development of clinical prevention and intervention strategies.

References:

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[10]Bigoni M, Turati M, Leone G, et al. Internal fixation of intracapsular femoral neck fractures in elderly patients: mortality and reoperation rate[J]. Aging Clinical and Experimental Research, 2020, 32(6): 1173-1178. DOI: 10.1007/s40520-019-01237-z.

3. Foundation of preliminary research work

(Explain the existing research foundation of our team, such as preclinical research, etc.)

Shanghai Sixth People's Hospital is a long-established tertiary first-class general hospital that was approved as a national orthopedic medical center in 2022. The hospital has consistently adhered to the principles of innovation and leadership in medical science and technology. It provides high-value, high-quality medical services and benchmarks against international first-class medical centers. Furthermore, the hospital has explored and improved its medical service model to align with current social developments and meet the diverse health needs of the population.

The orthopedic headquarters of our hospital, the Shanghai Trauma Orthopedic Clinical Medical Center, is recognized as the "cradle" of severed limb replantation worldwide and the birthplace of microsurgery in China. It accomplished the world's first "amputated limb replantation" operation, an event of great significance in the history of global surgery. In 1978, Yu Zhongjia's team pioneered a series of full-hand reengineering technologies, which earned them the first "National Invention First Prize" in the medical category in our country. Currently, the center boasts three national key clinical specialties, which are designated as the "top priority" construction disciplines in Shanghai, reflecting a robust foundation in discipline development. At present, the center encompasses eight orthopedic surgery subdisciplines, five orthopedic subdisciplines, two national research platforms, two comprehensive scientific research platforms, two international training centers, and one medical science popularization platform. Over the past five years, the hospital's annual outpatient and emergency volume has exceeded 5.3 million, with nearly

180,000 annual discharges and over 120,000 annual inpatient surgeries, providing a sufficient patient base to support the completion of this study.

4. Research objectives and research content

(including research objectives, main research contents, technical routes, implementation plans, feasibility analysis, etc.)

4.1 Purpose of the study

This study aims to retrospectively analyze the post-fracture mortality rate of elderly fracture patients aged 60 years and above, and explore the effects of different fracture sites, different ages, metabolic and nutritional status and other factors on mortality, and provide a basis for clinical prevention and intervention strategies.

4.2 Main research content

4.2.1 Overall research design and planning

This study is a single-center, retrospective, cohort study

4.2.2 Study population

4.2.2.1 Selection criteria

① Cases from January 1, 2010 to December 31, 2019 at the National Orthopedic Medical Center of Shanghai Sixth People's Hospital;
② Age ⩾ 60 years;
③ Shanghai household registration;
④ Diagnosed with fractures of the limbs and spine and underwent surgical treatment at Shanghai Sixth People's Hospital.

4.2.2.2 Exclusion Criteria

① Multiple fractures;
② Conservative treatment selected;
③ Incomplete case data.

4.2.2.3 Elimination criteria

① In-hospital death.

4.2.3 Number of cases and grouping

1) Fracture site grouping: The cases that meet the inclusion criteria are categorized into three distinct groups based on fracture sites: upper limb fractures, spinal fractures, and lower limb fractures. Each category is further subdivided into 20 specific groups. For upper limb fractures, the groups include scapular fractures, clavicle combined with proximal humerus fractures, middle humerus fractures, distal humerus fractures, upper ulnar radius fractures, middle ulnar radius fractures, ulnar radius fractures, and hand fractures. In the spinal fracture category, fractures are classified into cervical spine fractures, thoracic spine fractures, and lumbar spine fractures. Lastly, lower limb fractures are organized into pelvic fractures, femoral neck combined with femoral trochanteric fractures, middle femur fractures, distal femoral fractures, patella combined with tibial plateau fractures, mid-tibia fractures, distal tibia combined with distal fibula fractures, and foot fractures.
2) Age grouping: According to the age of the patients at the time of surgery, they were divided into five groups: 60-64 years old, 65-69 years old, 70-74 years old, 75-89 years old and 80 years and above.
3) Metabolic and nutritional status grouping: grouping is based on indicators of response, energy metabolism, and nutritional status that can be obtained from medical history. Specific assessment indicators include but are not limited to weight, BMI, blood glucose, triglycerides and cholesterol, liver and kidney function, serum albumin, etc. The grouping was further determined by literature review or expert consensus.

4.2.4 Research steps and related inspections

After confirming that the patient meets the inclusion criteria for enrollment, the subsequent information will be collected and recorded based on a review of the medical history records:

1) Basic patient information and preoperative data
   - Basic information: Age, gender.
   - Fractures: Fracture side (left/right), fracture classification.

- Metabolic and nutritional status: heightweight, blood sugar, triglycerides and cholesterol, liver and kidney function, serum albumin, etc.

2) Surgery-related data

- Choice of surgical method。
- Operative time, intraoperative blood loss, postoperative hospital stay.
- Whether there is blood transfusion during and after surgery, the number of blood transfusions, and the amount of blood transfusion.

3) Complications and reoperation data

- All complications that occur postoperatively are recorded, primarily including infections and fracture nonunion.
- For patients requiring reoperation, details such as the reason for reoperation, the duration of the operation, and the specific surgical procedure performed are documented.

4.2.5 Endpoint indicators

Primary endpoints

1. **All-cause mortality**

- To evaluate the long-term (e.g., 1 year, 3 years, 5 years) survival rates of elderly fracture patients treated with surgery.
- To compare the effects of different fracture sites (e.g., hip, femur, spine, etc.) on mortality.

2. **Fracture-related mortality**

- The proportion of deaths due to fractures, either directly or indirectly (e.g., postoperative complications, infections, cardiovascular events, etc.) was analyzed.

Secondary endpoints

1. Postoperative complication rate

- Including deep vein thrombosis (DVT), pneumonia, urinary tract infection (UTI), pressure ulcer, surgical site infection (SSI), etc.

2. Functional recovery situation

- The functional recovery was assessed at 6 months and 12 months after surgery using the Barthel index (ADL score) or the Harris hip score (HHS, for hip fractures).
- Assess whether the patient can regain independent walking ability (eg, with a walker or completely independent).

3. **Recurrent fracture rate**

- The proportion of recurrent fractures within 1 and 3 years after surgery was recorded.

4. Influence of nutritional and metabolic indicators

- The association between preoperative and postoperative serum albumin (Alb), vitamin D (25-OH-D), bone mineral density (BMD) and other indicators with mortality and complications was analyzed.

5. Impact of comorbidities (**Charlson Comorbidity Index, CCI).**

- To assess the impact of underlying diseases such as diabetes, cardiovascular disease, chronic kidney disease, etc. on prognosis.

6. Quality of life (**QoL) assessment**

- The SF-36 or EQ-5D scale was used to evaluate the changes in postoperative quality of life.

7. Length of hospital stay and readmission rate

- Record the readmission rate at 30 and 90 days after surgery, and analyze the reasons for readmission (such as infection, heart failure, etc.)

4.2.6 Criteria for suspension of clinical research

Complete follow-up and data collection of all cases that meet the inclusion criteria.

4.3 Statistical analysis

4.3.1 Sample size estimation

All cases that met the inclusion criteria from January 1, 2010 to December 31, 2019 at the National Orthopedic Medical Center of Shanghai Sixth People's Hospital.

4.3.2 Statistics and analysis of research data

This study used a multi-stage statistical analysis method to systematically evaluate the prognosis of elderly patients with fracture surgery. In the descriptive analysis phase, the baseline characteristics of the patients (age, fracture type, CCI score, etc.) will be reported comprehensively, with mean± standard deviation or median (IQR) for continuous variables according to distribution, and categorical variables presented as frequencies (percentages). For the primary endpoint all-cause mortality, in addition to the conventional Kaplan-Meier curve and Log-rank test, the following supplementary analyses were set up: 1) the Fine-Gray competitive risk model was used for data with competitive risk (such as non-death loss to follow-up); 2) the dynamic discriminative ability of predictors was evaluated by time-dependent ROC curves; 3) Stratified analysis was performed according to fracture site, age (e.g., $\geqslant$ 75 years old), and nutritional status.

The multivariate analysis phase will be implemented in three steps: first, the univariate Cox regression variable ($p<0.1$) is used to identify independent predictors, focusing on the influence of age, fracture site (hip/spine), perioperative nutritional indexes (albumin<3.5g/dL), postoperative complications (DVT/infection) and other variables. The model validation process includes: Schoenfeld residual test proportional risk assumption, 1000 bootstrap method to calculate Harrell's C index (95% CI), draw calibration curve to evaluate prediction accuracy. Finally, a Nomogram model containing core predictors was established based on the regression coefficient, which could calculate the individualized 1/3/5-year mortality risk probability.

For the secondary endpoints, the following special analyses were used: 1) Multivariate logistic regression was used to control for confounding factors such as length of hospital stay for postoperative complications; 2) Functional recovery was

analyzed by linear mixed model to analyze the longitudinal changes of ADL scores. 3) The re-fracture rate analysis uses a competitive risk model (death as a competitive event). All analyses were set to two-sided $\alpha=0.05$ with Bonferroni correction for multiple comparisons. Statistical analysis will be done using R language (survival/cmprsk/rms package) to ensure the correct handling of complex situations such as competitive risk, time-varying covariates, etc. The scheme design can comprehensively identify risk factors and provide clinical decision-making tools with time-series prediction capabilities.

4.4 Technical route and implementation plan

This study is a retrospective study, and the data collection and entry of patient data are planned to be carried out first (data from Shanghai Sixth People's Hospital). First, the batch of data was sorted out by researchers (2-3 residents), and the patient's ID card information was used to correlate the death outcome, and the data was sorted into an electronic database to deal with missing values and outliers. The data were grouped by age group, nutritional status, and presence or absence of comorbidities. Then two senior attending physicians will review and correct this batch of data, and finally hand over this batch of data to one chief surgeon for unified processing, and after confirming that the description is correct, it will be handed over to the statistical analyst for corresponding statistical analysis.

4.5 Feasibility analysis

The project team has accumulated many years of clinical experience in the treatment of diseases related to lower limb fractures, and has made sufficient preparations for breakthroughs in most key technologies to ensure the smooth development of the project. The project team has been conducting a new model of diagnosis and treatment of lower limb fractures for many years, with rich research

experience and a solid research foundation. The hospital has accumulated a large amount of relevant data in the early stage of the clinical cases of calcaneal fracture disease required for the completion of the project research, and the number of orthopedic outpatient and emergency departments is large every year, which provides resources for the acquisition of subsequent clinical cases and provides resource guarantee for the successful completion of this project. At the same time, the team is fully equipped with clinicians and clinical researchers, and has the ability to carry out follow-up data collection and analysis.

5. Explanation of subject expenses, pre-assessment of project risks and risk disposal plans

(Modified according to the actual situation)

5.1 Description of the cost of subjects involved in the study

This study is a retrospective study that only collects data and does not involve new tests, treatments, or other medical procedures without incurring costs.

5.2 Pre-assessment of project risks and risk disposal plans

This study is a retrospective study that only collects data and does not involve new tests, treatments, or other medical procedures that pose no risk to patients.

5.2.1 Definition of adverse events

This study is a retrospective study that only collects data and does not involve new tests, treatments, or other medical procedures without adverse events.

6. Quality management plan

(The quality management plan can include the following contents: establishing an organizational management system and standard operating procedures (SOP), strictly following the research plan and various SOPs, establishing a quality control system, electronic management of research data, etc.)

This study is a retrospective study, and the data collection and entry of patient data are planned to be carried out first (data from Shanghai Sixth People's Hospital). First, the batch of data is analyzed by researchers (2-3 residents), each case data is described in detail, and then the data is reviewed and corrected by 2 senior attending physicians, and finally this batch of data is handed over to a chief surgeon for unified processing, and after confirming that the description is correct, it is handed over to the statistical analyst for corresponding statistical analysis.

7. Research related ethics

7.1 Ethics Committee review

This protocol and written informed consent and information directly related to the subjects must be submitted to the ethics committee and approved in writing by the ethics committee before the study can be officially carried out. The investigator must submit an annual report of the study to the Ethics Committee at least annually, if applicable. Upon study discontinuation and/or completion, the investigator must notify the Ethics Committee in writing; The investigator must promptly report to the Ethics Committee all changes occurring in the study work (such as revisions to the protocol and/or number of informed consents) and must not perform these changes without the approval of the Ethics Committee, except to eliminate changes that are made to eliminate obvious and immediate risk to the subject. In the event of such a situation, the Ethics Committee will be notified.

7.2 Informed consent

7.2.1 Procedures for obtaining informed consent

Applying for an exemption from informed consent meets the following conditions: the subject can no longer be found for research using personally identifiable human data, and the research project does not involve personal privacy and commercial interests.

8. Data confidentiality and security supervision plan

The results of this research may be published in medical journals, but we will keep patients' information confidential as required by law, unless required by relevant laws, patients' personal information will not be disclosed. When necessary, government management departments, hospital ethics committees, and their relevant personnel may consult the patient's information in accordance with regulations. Briefly describe subject privacy and confidentiality measures.

9. The expected progress and completion date of the research project

The project is scheduled to be completed in June 2026, and the specific planned progress is as follows:

April - June 2025: Conduct literature search, background research, and formulate overall plans;

July - September 2025: Collect and organize patient data.

October - December 2025: Analyze and organize data and draw conclusions.

January - March 2026: Summarize relevant data and conclusions, write and revise the paper.

April - June 2026: Submit and publish papers.