Study Protocol

Project Name： The influence of central sensitization in endometriosis disease

Name of the Sponsor: Sun Yat-Sen Memorial Hospital of Sun Yat-Sen University

Version number: Version 3.0

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Project Leader: Yingchen Wu

Plan sign-off confirmation: Yingchen Wu

Compliance Statement

Comply with the Good Clinical Practice for Drug Trials and the Management Measures for Investigator-Initiated Clinical Research in Healthcare Institutions (Trial), as well as the Helsinki Declaration. We commit to implementing this study according to the protocol. Participants must be trained and the study can only proceed after obtaining written approval from the ethics committee and informed consent from the participants. Any revisions to the protocol require

re-approval.

Abstract

Endometriosis and adenomyosis are included in endometriotic diseases. Adenomyosis is similar to endometriosis, both being associated with chronic pelvic pain (CPP), and the involved pain mechanisms are relatively complex. Currently,Surgical treatment (such as lesion resection, hysterectomy) is still a common method for treating endometriotic diseases. However, some patients still have persistent pain after surgery.Recent studies have shown that central sensitization (CS) may play a significant role in persistent postoperative pain among patients with endometriosis. Central sensitization refers to the abnormal response of the central nervous system to pain stimuli, a mechanism that can amplify pain perception, potentially causing pain to persist even after the lesion has been surgically removed. It is therefore reasonable to hypothesize that central sensitization may also be a potential contributor to persistent postoperative pain in adenomyosis patients. Furthermore, the efficacy of different postoperative medications in alleviating central pain among endometriosis patients remains unclear. Thus, this study aims to investigate the role of central sensitization in postoperative pain following hysterectomy in adenomyosis patients, evaluate the pain-relieving effects of different medications after lesion resection in endometriosis patients, and provide new insights for postoperative pain management.

Introduction

2.1 Background

Endometriosis and adenomyosis are included in endometriotic diseases. Endometrial tissue appears outside the uterine is called endometriosis. Adenomyosis is a common gynecological disease in reproductive-aged women. Its characteristic is that endometrial glands and stroma invade the uterine myometrium, accompanied by the proliferation of surrounding smooth muscle cells. 20.9% to 34% of reproductive-aged women have adenomyosis detected by ultrasound examination. Most patients with endometriotic diseases will experience various forms of pain, such as dysmenorrhea, dyspareunia, chronic pelvic pain, dyschezia, or back pain, etc. Surgical treatment (such as lesion resection, hysterectomy) is still a common method for treating endometriotic diseases. However, some patients still have persistent pain after surgery.

The mechanism of central sensitization may explain why about 30% of endometriosis

patients have persistent CPP after traditional surgical treatment. Previous study indicates that almost half of endometriosis patients (42%) have CS, and CS is independently associated with moderate to severe chronic pelvic pain, and the score of the Central Sensitization Inventory (CSI) at the baseline before surgery is significantly correlated with persistent CPP after surgery. Therefore, it is reasonable to speculate that central sensitization may also be a potential cause of persistent pain after adenomyosis surgery. However, there is currently no relevant study indicating whether central sensitization plays a role in persistent pain after hysterectomy in adenomyosis patients, nor is there any relevant study indicating the pain relief of different medications after lesion resection in endometriosis patients. In this study, we will explore the role of central sensitization in pain after hysterectomy in adenomyosis patients, explore the pain relief of different medications after lesion resection in endometriosis patients, and provide new ideas for postoperative pain management.

2.2 Risk and Benefit Assessment

2.2.1 Potential risks

This study did not involve clinical interventions, thus there are no risks arising from clinical procedures.

2.2.2 Known potential benefits

We will explore the role of central sensitization in pain after hysterectomy in adenomyosis patients, explore the pain relief of different medications after lesion resection in endometriosis patients, and provide new ideas for postoperative pain management.

Research Objectives and Endpoints

3.1 Purpose

Include 200 or more patients with endometriosis diseases;

Explore the role of central sensitization in postoperative pain of patients with adenomyosis, that is, the relationship between central sensitization and postoperative pain outcomes (chronic pelvic pain, dyspareunia, dyschezia, back pain);

Evaluate whether the baseline CSI score can predict the severity of postoperative pain;

Explore the pain relief of different medications after lesion resection in patients with endometriosis.

3.2. Research indicators

3.2.1 Key Indicators and Definitions

Baseline (preoperative), 1, 3, and 6-month follow-up CSI scores.

3.2.2 Secondary indicators and definitions

Baseline (preoperative), 1, 3, and 6-month follow-up dysmenorrhea scores, chronic pelvic pain scores, dyspareunia scores, dyschezia scores, back pain scores.

3.2.3 Safety indicators

None.

3.2.4 Other collected metrics

Relevant clinical data such as age, BMI, educational level, history of other diseases, surgical history, smoking and drinking history, pregnancy and childbirth history, pain duration, preoperative CA125 level, hemoglobin, surgical methods (laparotomy / laparoscopy), endometriosis stage, endometriosis location.

Study population

4.1 Inclusion Criteria:

Patients admitted to the gynaecological ward of Sun Yat-sen Memorial Hospital from March 2025 to March 2027;

Age 18-50 years old;

Endometriosis focus excision or hysterectomy (with or without bilateral salpingo-oophorectomy, with excision of any complicated lesion) ;

The pathology was adenomyosis or endometriosis.

4.2 Exclusion Criteria:

Postmenopausal (spontaneous or surgical) ;

Hysterectomy and/or bilateral salpingo-oophorectomy (before baseline) ;

Lack of CSI or CPP score;

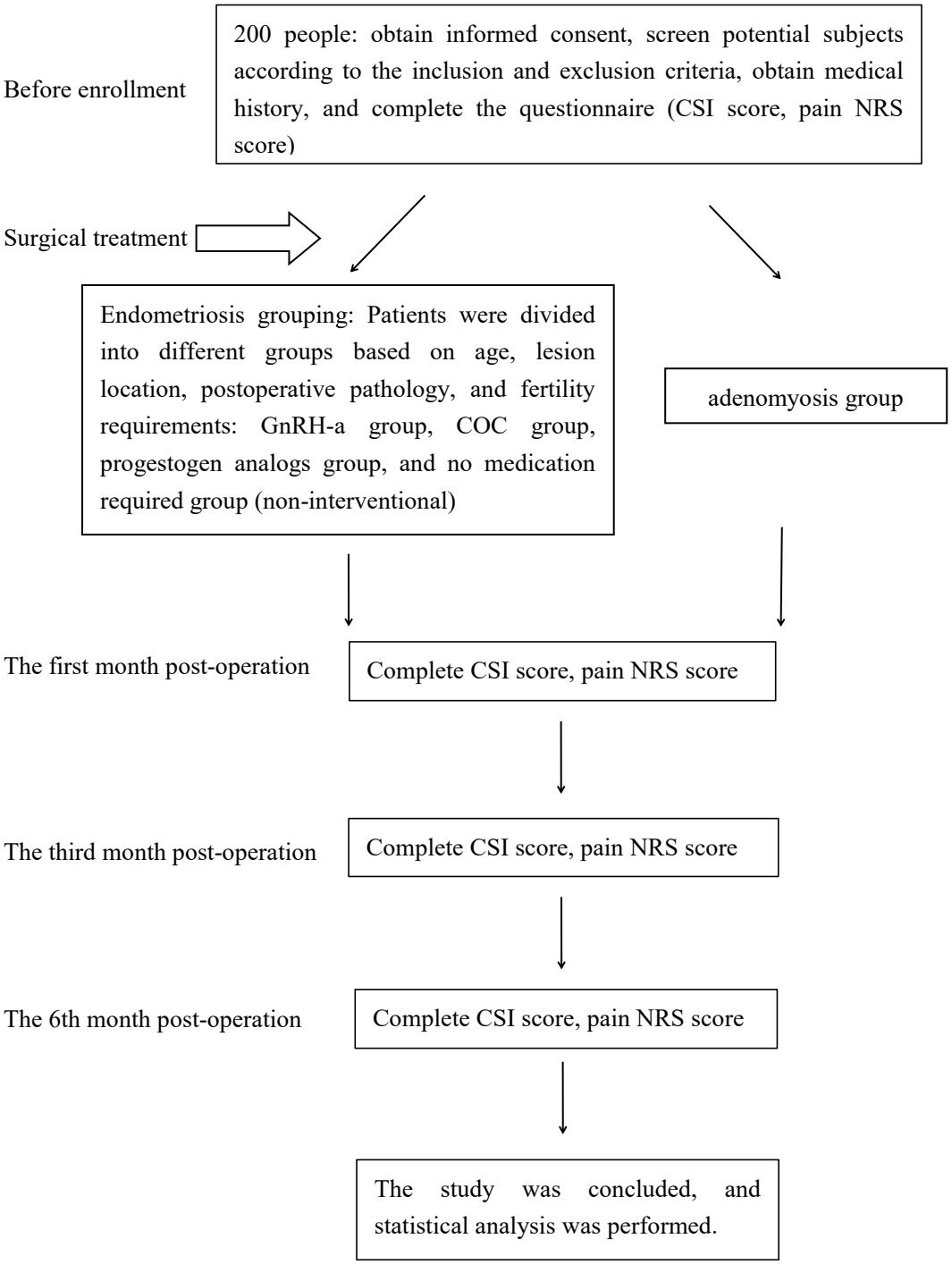
The postoperative follow-up time was less than 6 months.

Research Design

5.1 Overall Design

Inclusion period: From March 2025 to March 2027, a prospective cohort study was conducted on patients with endometriosis or adenomyosis undergoing surgical treatment in the gynecology inpatient department of Sun Yat-sen Memorial Hospital, Sun Yat-sen University.

5.2 Research design process



5.3 Methods to reduce bias

Multivariate regression analysis was employed to control for potential confounding variables such as age and BMI, thereby reducing their impact on the results; through standardized questionnaires (CSI and NRS) and clear evaluation criteria, data collection was ensured to be consistent across all participants to avoid measurement bias.

5.4 Definition of study completion

The last study subject completed the final follow-up.

5.5 Statistical analysis

5.5.1 Sample size

Exceeds 200 cases;

5.5.2 Data analysis set

This study adopts the Per-Protocol Set (PPS): valid case samples. It is defined as patients among the subjects who completed all planned treatments, follow-ups, and data collection on schedule. Any protocol violations or loss to follow-up during the study will result in exclusion from the Per-Protocol Set.

5.5.3 Statistical Analysis Plan

The statistical analysis software is IBM SPSS Statistics for Windows version 26. Descriptive statistics will be performed using means and standard deviations for continuous variables, and frequency analysis for categorical variables. Multiple regression analysis will be employed to assess the relationship between baseline CSI scores and postoperative pain outcomes (adjusted for baseline pain levels). Survival analysis or Kaplan-Meier curves will be utilized for comparative evaluation of the association between postoperative pain relief and central sensitization.

Data collection and management

6.1 Electronic data record

6.2 Data management

The data collection will be conducted in the form of questionnaires; the storage medium is electronic.

Ethical requirements

This study complies with the "Good Clinical Practice" and the "Management Measures for

Clinical Research Initiated by Researchers in Healthcare Institutions" (Trial Implementation), as well as the Declaration of Helsinki. Before the commencement of the trial, the study protocol must be approved by the ethics committee of our institution. During the research process, if protocol amendments are necessary, the revised protocol must be resubmitted to the ethics committee for review. Researchers must wait for the ethics committee's approval before implementing the new protocol.

This study will collect clinical data and personal information of the research subjects for scientific research purposes, which may involve patients' privacy rights. All participants and data analysts involved in this study have signed confidentiality agreements and will not disclose patients' personal information or disease-related details to any individuals or institutions unrelated to the research. The collected patient data will be uniformly managed to prevent any leakage of personal privacy.

References

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