BMJ Open  Perioperative sleep disorders in gynaecological daycase surgery patients and analysis of risk factors: protocol for a cross-sectional study

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ABSTRACT

Introduction  Sleep disorders are clinical syndromes of disturbed sleep-wake rhythms and abnormal sleep quality. They have various causes, but their main manifestations are difficulty falling asleep, sleep disruption and daytime fatigue. These are common clinical symptoms in perioperative patients, especially in gynaecological patients. There is a lack of research on the factors influencing perioperative sleep disorders in gynaecological patients. The aim of this study is to assess the prevalence of sleep disorders in gynaecological surgery patients and to analyse the possible factors influencing them to provide new ideas for improving sleep disorders in this patient population.

Methods and analysis This cross-sectional, descriptive and observational survey is planned to include 480 gynaecological day surgery patients. All patients who meet the inclusion criteria are eligible to join the study. The study will record preoperative diagnosis, surgical procedure, duration of surgery, type of anaesthesia, anaesthetic drugs, sleep quality, anxiety and depression levels and pain indices 30 days before and 1, 2, 3 and 30 days after surgery.

Ethics and dissemination The study was approved by the Ethics Committee of Beijing Shijitan Hospital Affiliated with Capital Medical University (Approval Number: sjtyylx-2022(109)) before the start of recruitment. The results of the study will be disseminated through peer-reviewed publications and conference presentations.

Trial registration number ChiCTR2200064533.

INTRODUCTION

Sleep disorders are clinical syndromes caused by various disturbances in the rhythm of sleeping and waking and by abnormal sleep quality, which are found in 13.9% of people. Sleep disorders not only affect quality of life but also increase morbidity and mortality from many chronic diseases. Patients with sleep disorders also have higher rates of multiple cancers than those without sleep disorders. As a result, increasing research is now focusing on sleep disorders.

Sleep disorders are highly prevalent psychiatric disorders in women, and perioperative sleep disorders and anxiety are more common in gynaecological patients than in other kinds of patients. Sleep disorders in women are associated with a variety of factors. First, female sex is an independent risk factor for insomnia. Women’s transition to menopause combined with the development of other comorbidities may trigger episodes of insomnia. Hormonal changes in women are highly correlated with sleep disorders. During hormonal changes, women are at increased risk of developing sleep disorders. Loss of ovarian hormones from middle age to old age can make sleep disorders more likely. Sleep regulation changes in gynaecological patients under pathological conditions, so sleep disorders in gynaecological patients may be related to gynaecological diseases. This study will focus on the incidence of perioperative sleep disorders in women with gynaecological diseases requiring surgery and explore its influencing factors.
Sleep disorders are a common clinical symptom in perioperative patients during the treatment process, mainly manifesting as difficulty falling asleep, sleep disruption and daytime fatigue. The process of sleep includes rapid-eye-movement (REM) sleep and non-rapid-eye-movement (NREM) sleep, of which NREM can be divided into stages N1, N2 and N3. The selection of anaesthesia mode and anaesthetic drug during surgery can cause sleep disorders by affecting different sleep periods. The binding of opioids to opioid receptors in the brain nuclei that are involved in sleep regulation can cause sleep disorders by reducing REM and slow-wave sleep. General anaesthesia can also affect the sleep-wake cycle by affecting various endogenous sleep-wake-related substances. Gamma-aminobutyric acid (GABA) A receptors (GABAARs) play a central role in modern anaesthesia. Many GABAAR agonists, including propofol, etomidate and isoﬂurane, are used for anaesthesia and sedation since they positively regulate the inhibitory function of the neurotransmitter GABA. Under this mechanism, propofol can increase N3 sleep and produce hypnotic sedative effects, while etomidate can induce hypnosis by increasing alpha-beta frequency electrocor-tical activity and increased spindle-like oscillations during NREM. Ketamine enhances wakefulness and inhibits NREM sleep, while isoprotenerol inhibits wakefulness and enhances NREM sleep. Dexmedetomidine stimulates the α2 receptor in the endogenous sleep-inducing pathway to promote N3 sleep, which can produce effects similar to natural sleep. In summary, numerous studies have demonstrated a strong correlation between anaesthesia and sleep conditions. We believe that sleep disorders can be improved through interventions in the choice of anaesthesia mode and anaesthetic drug.

Perioperative sleep disorders in female patients are detrimental to recovery. Gynaecological patients with chronic postoperative sleep disorders were more likely to have clinical complications, longer hospital stays and a worse prognosis. The purpose of this study was to investigate the incidence of perioperative sleep disorders in patients undergoing gynaecological daycase surgery, analyse the impact of different anaesthesia methods and different anaesthetic drugs on sleep disorders and summarise the risk factors related to perioperative sleep disorders.

**METHODS AND ANALYSIS**

**Study design and population**

This is an observational, cross-sectional, descriptive study. People who intend to undergo day surgery (including induced abortion, ring removal, diagnostic curettage, cervical conisation, polyp removal, uterine myomectomy, etc), living in the catchment area of Beijing Shijitan Hospital, will be recruited to the study over approximately 12 months starting July 2023. After surgery, researchers will follow-up each patient for a few days or weeks to check on their sleep.

**Participants**

**Inclusion criteria**

Patients who meet all of the following criteria are eligible for inclusion:

1. Age 18–60 years.
3. Planned gynaecological day surgery (including induced abortion, ring removal, diagnostic curettage, cervical conisation, polyp removal and uterine myomectomy).
4. Willingness to participate and sign the informed consent form.

**Exclusion criteria**

1. A history of mental or neurological diseases or complications with craniocerebral injury and inability to communicate normally;
2. Contraindication to surgery (cervicitis, genital bleeding, acute pelvic inflammatory disease);
3. Combined malignant tumour;
4. Participants with Parkinson’s disease, restless legs syndrome, obstructive sleep apnoea, narcolepsy and other diseases that may lead to pre-existing chronic insomnia;
5. Participants taking regular night sedatives, evening gabapentinoids or other evening neurodepressant medications;
6. History of alcoholism or illicit drug use;
7. Hearing impairment and aphasia;
8. Various other reasons for not being able to complete the questionnaire; and
9. Refusal to sign the informed consent form.

**Control participants**

Before enrolment, patients will be fully informed about the trial background, purpose, method, risks and benefits, exit mechanism, confidentiality mechanism and other relevant information. Under the condition of full communication with the subjects, patients can voluntarily complete the relevant questionnaire after signing the informed consent form and the questionnaire will be anonymous. The above should be reflected in the informed consent form. Informed consent shall be reviewed and approved or waived by the institutional review board. If the patient is unable to complete the questionnaire, chooses to withdraw from the trial at any time, or refuses to cooperate with the questionnaire and follow-up, withdrawal from the trial will not affect the follow-up treatment of the patient. Patients and the public will provide clinical data as participants but will not be involved in the design, conduct, reporting or dissemination of the study (figure 1).

**Questionnaire information**

The clinician will obtain the following relevant assessment contents from the participant in the form of a questionnaire:
Demographic data, including age, body mass index (BMI), menstrual history (history of dysmenorrhea, menopausal status, age at menopause), reproductive history (pregnant or not, fertile or not) and prior history (history of disease, anaesthesia, surgery).

Particular attention should be given to a history of diabetes, hypertension, coronary artery disease, gynaecological disease, chronic pain and other related chronic conditions.

The Pittsburgh Sleep Quality Index (PSQI) is a recognised method of assessing sleep quality and consists of 19 self-rated and 5 other rated entries, usually used to assess the subject’s sleep in the past month. Participants rate each item on a 4-point scale ranging from 0 (none) to 4 (≥3 times/week). The items are divided into seven dimensions depending on their meaning, and the seven dimensions are scored separately and summed to give a total score, higher scores indicating poorer sleep quality.

The 5-point Likert Sleep Scale is a simple scale to assess sleep. Sleep quality is assessed by the question ‘How would you rate the quality of your sleep over the past 24 hours?’ They report disorders using a 5-point Likert scale where 1=very good, 2=good, 3=not necessary, 4=poor and 5=very poor.

The Patient Health Questionnaire-9 (PHQ-9) is a simple scale used in clinical settings for initial screening of depression. It has nine questions, and the scores are summed to give a total score, higher scores indicating a greater tendency towards depression. Questions 1 and 4 are the core symptoms of depression, and a score of more than 2 should be given special attention.

The Generalised Anxiety Disorder Scale-7 (GAD-7) is a simple scale used in clinical practice to initially screen for anxiety. It assesses anxiety symptoms over the past 2 weeks using a seven-symptom programme. Each item is scored on a scale of 0–3, and the total score is a combination of seven items, with a score of ≥10 indicating generalised anxiety disorder.

The Numerical Rating Scale (NRS) is a simple scale for rating a patient’s level of pain. It is a scale from 0 to 10.
1 to 10, higher numbers indicating greater pain: 0 indicates no pain, 1–3 indicates mild pain, 4–6 indicates moderate pain and 7–10 indicates severe pain. The scores can be used in clinical practice to gauge a patient’s level of pain.

Recruitment and assessment procedures
Day surgery is a planned, non-urgent procedure performed on selected and prepared patients who are discharged within a few hours of the procedure. With advances in surgical and analgesic techniques and the rising costs of healthcare, day surgery is steadily increasing to reduce the cost of patient care and save healthcare resources. Therefore, our study will include gynaecological day surgery patients.

Patients who undergo gynaecological day surgery at Beijing Shijitan Hospital will be recruited as study subjects through electronic means to participate in a cross-sectional study of sleep disorders associated with gynaecological day surgery. We plan to enrol 480 eligible female patients into the study. The forms of gynaecological day surgery included in this study will include induced abortion, ring removal, diagnostic curettage, cervical conisation, polyp removal and uterine myomectomy. The aim of our study is to determine the incidence of perioperative sleep disorders in gynaecological surgery patients and to analyse the factors that may contribute to them, such as the mode of anaesthesia.

Table 1 provides an overview of the data collection and evaluation time points.

Table 1  Data collection schedule of gynaecological surgery patients

<table>
<thead>
<tr>
<th>Time point</th>
<th>Enrolment</th>
<th>Preoperative</th>
<th>Post-allocation</th>
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<tbody>
<tr>
<td></td>
<td>T0</td>
<td>T1</td>
<td>T2</td>
</tr>
<tr>
<td>Enrolment</td>
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<td></td>
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<tr>
<td>Informed consent</td>
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<td>Inclusion/exclusion criteria</td>
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<td>5-point Likert Sleep Scale</td>
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<tr>
<td>NRS</td>
<td>X</td>
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</table>

GAD-7, Generalised Anxiety Disorder Scale-7; NRS, Numerical Rating Scale; PHQ-9, Patient Health Questionnaire-9; PSQI, Pittsburgh Sleep Quality Index; T0, at the end of surgery; T1, postoperative day 1; T2, postoperative day 2; T3, postoperative day 3; T4, postoperative day 30.
record system and aggregated with the questionnaire results. The basic information includes demographic data (age, BMI, menstrual history, reproductive history and previous history).

For the surgical procedure, the day before the operation, the anaesthetist will visit the patient on the ward for a preoperative overview and discuss the method of anaesthesia with the operating physician and gynaecologist based on the medical history. On the day of the operation, the anaesthetist will open the patient’s peripheral intravenous access, deliver oxygen by mask and check the method of anaesthesia again before starting the anaesthetic. For gynaecological patients, the usual anaesthetic is lumbar or general anaesthesia. Intraoperative anaesthesia is at the discretion of the anaesthetist, who decides which anaesthetic drugs to use to maintain sedation, analgesia and muscle relaxation and to safeguard the patient’s life. The researcher will obtain relevant intraoperative information through the surgical anaesthesia system. This information includes the preoperative diagnosis; surgery type; type of anaesthesia; types and amounts of analgesics; sedatives and muscle relaxants; duration of anaesthesia; intraoperative fluid replacement; urine volume and blood loss.

Patients will be assessed a second time by the researcher on the first, second and third postoperative days by telephone follow-up. The follow-up visit will include NRS and 5-point Likert Sleep Scale.

The last assessment is 30 days postoperatively, and the researcher will follow-up with the PSQI, PHQ-9 and GAD-7 by telephone. On completion of the follow-up, the patient will be informed that all follow-up had been completed and will be thanked.

**Data collection**

We plan to start recruiting patients in July 2023 and complete data collection and entry for all cases within 12 months. Data analysis and statistical processing will begin in June 2024, and the research paper will be written.

Throughout the trial, the anaesthetists involved in the procedure will be completely independent of the data collectors. To ensure the integrity of data entry, four data collectors will be trained in this study to enter questionnaire data in a standardised manner and will be fully responsible for the preparation, maintenance and management of the database. Data collection will include objective clinical data from patients and preoperative and postoperative questionnaires and follow-ups. Anonymous data will be collected in numerical or alphabetical order on a case report form (CRF). On completion of the anonymised CRF form, the data collector will confirm the authenticity and validity of all data and provide a reasonable explanation for any missing data. In addition, we will have an independent statistical analyst on-hand who will be ready to process the data.

**Sample size**

This research is cross-sectional, descriptive and observational. For statistical analysis, preoperative, intraoperative and postoperative data indices will be recorded. Patients’ sleep patterns before and after surgery will be investigated, and the underlying causes will be examined. Multiple linear regression will be employed to examine the risk factors and sleeping habits of patients undergoing gynaecological day surgery. The present study is an exploratory study and there is no literature report on related studies, therefore the exact parameters for calculating the sample size through the sample size formula were missing and the event per variable ratio method was used to calculate the sample size. Based on the event per variable ratio method, the expected model accuracy is 90% (Events per Variable (EPV)=10), and approximately 20% of women will report experiencing sleeplessness. **Gynaecological diagnoses, menopause status, BMI, age, haemoglobin level, anaesthetic mode, anxiety index, pain index, etc, will be the main covariates, CI=95%.** A total of 400 patients will need to complete the study; therefore, 480 patients need to be enrolled in the study because it is an investigative study, and 20% of the patients are expected to be lost to follow-up.

**Statistical analysis**

The relationships between the sleep index and risk factors among patients undergoing gynaecological day surgery will be the study’s main outcomes. A multiple linear regression model will be used to assess the continuous dependent variable: the sleep index. Stepwise regression will be carried out using a prediction model. To recreate the model using the step technique and perform a collinearity diagnosis across all factors, useless factors will be eliminated, while meaningful factors will be kept. Principal component regression will be used if there is an excessive amount of collinearity. Multiple imputation can be used to replace missing data of variables. This statistical approach is rational and scientifically supported.

**Limitations**

The planned study has several limitations. First, it will be a cross-sectional survey, and its findings may provide clues and aetiological hypotheses for longitudinal outcomes, but it cannot detect causal relationships between the disease states and the variables of interest. Second, this study will use an online questionnaire to collect data, which could result in a low response rate and may also be subject to non-response bias. People who do not answer the questions asked for various reasons are referred to as non-responders. Non-responders may differ from responders in some important characteristics or exposures. More than a certain percentage of non-responders will lower the veracity of the results. To avoid this limitation, the following efforts will be made: First, a bulletin with the survey content and the QR code of the questionnaire will be posted in the corridors of the wards for 2 months to promote the survey, and a person will...
be responsible for introducing the survey to patients on a one-to-one basis and for obtaining informed consent. Second, to simplify the questionnaire and increase the response rate, we will use the most popular questionnaire collection application in the country to collect the questionnaire and will give as many multiple-choice questions as possible to ensure complete and correct responses. The questionnaire will follow a voluntary response procedure, and we expect that patients presenting with sleep disorders will be more motivated to complete the questionnaire, resulting in a higher prevalence of sleep disorders among the participating gynaecological patients than among the non-participating patients. To avoid bias, we will invite an equal number of eligible patients to participate in the survey and ensure that each patient is as likely to participate as possible through multiple reminders.

**Patient and public involvement statement**

Patients and the public are not involved in the design, execution and analysis of the study.

**DISCUSSION**

This is a cross-sectional study. In this study, the occurrence of gynaecological day surgery and perioperative sleep disorders will be analysed together for the first time. The aim is to determine the incidence of perioperative sleep disorders in gynaecological surgery patients and to analyse the impact of different risk factors on perioperative sleep disorders in them.

The occurrence of perioperative sleep disorders in gynaecological patients may be associated with a variety of factors. The mechanisms by which sleep disorders occur in perioperative female patients can be explained by the occurrence of hormonal fluctuations or circadian rhythm changes. A decline in oestrogen is one of the causes of sleep disorders in menopausal women, and the use of hormone replacement therapy can alleviate the extent of sleep disorders. Song et al found that morning surgery required higher doses of anaesthetic drugs than evening surgery and that postoperative sleep disorders were more common in patients who had evening surgery than those who had morning surgery. In addition, sleep disorders may be caused by the original disease itself. Notably, sleep disorders are often associated with anxiety or depression.

Intraoperative anaesthesia may have an impact on perioperative sleep disorders. In a study of women who had undergone caesarean section, the incidence of sleep disorders was higher with general anaesthesia than with neuraxial anaesthesia, and the risk of depression was significantly increased. The incidence of sleep disorders was significantly lower after intraoperative use of esetamine than after its non-use. In addition, the use of sedative analgesics reduces the incidence of sleep disorders. Fujii et al showed that patients with sleep disorders experienced a significant improvement in sleep quality after receiving chlorpromazine injections. This trial will take these factors into account to investigate the occurrence of perioperative sleep disorders in patients undergoing gynaecological surgery and provide new possibilities for alleviating postoperative sleep disorders in them.

**ETHICS AND DISSEMINATION**

**Privacy and confidentiality**

Participation is voluntary, and all participants must provide informed consent. Researchers, all participants and the trial registrar will be informed if there are significant changes to the study protocol. All data collected will be kept strictly confidential, no personal information will be disclosed and participants will not be identified when the study results are published. Participants are allowed to withdraw at any time, and this will not affect any of their medical or other interests.

**Publication plan**

The study results will be disseminated through peer-reviewed publications and international conference presentations.

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**Contributors**

WZ contributed to the conception of the research protocol and will participate in the execution and analysis of the study.

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