STUDY PROTOCOL

Official Title:
Evaluation of the Effects of Intraoperative Ventilation Modes on Perioperative Atelectasis in Patients Undergoing Hysterectomy by Lung Ultrasonography

NCT Number:
NCT07413575

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Version 1.0

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Sponsor:
Sehit Prof. Dr. Ilhan Varank Sancaktepe Training and Research Hospital

Study Location:
Istanbul

1. Background and Rationale

Postoperative pulmonary complications, including atelectasis, pneumonia, pulmonary embolism, pleural effusion, pulmonary edema, and pneumothorax, are associated with prolonged hospitalization and increased morbidity and mortality.

Atelectasis occurs in approximately 80–100% of patients receiving general anesthesia. Mechanical ventilation, while essential, may contribute to ventilator-induced lung injury (VILI) through atelectotrauma, barotrauma, volutrauma, and biotrauma.

Mechanical power represents the total energy transferred from the ventilator to lung tissue and is influenced by tidal volume (Vt), airway pressures, respiratory rate (RR), inspiratory flow, and positive end-expiratory pressure (PEEP).

Hysterectomy procedures present a particularly high risk for perioperative atelectasis due to the abdominal surgical approach, prolonged operative duration, Trendelenburg positioning, and pneumoperitoneum-related diaphragmatic displacement.

Lung ultrasonography is a sensitive bedside modality for detecting anesthesia-related atelectasis and allows dynamic perioperative monitoring without radiation exposure.

Flow-controlled ventilation (FCV) is a ventilation mode delivering constant inspiratory and expiratory flow, enabling precise assessment of dynamic lung compliance and individualized ventilatory settings. Comparative clinical data between FCV and conventional ventilation modes remain limited.

2. Study Objectives

Primary Objective

To determine whether intraoperative ventilation mode affects the development of perioperative atelectasis measured quantitatively by lung ultrasonography.

Secondary Objectives

To compare ventilation modes with respect to:

- Mechanical power of ventilation
- Oxygenation parameters

3. Study Design

This study is observational in nature; the choice of ventilation mode was determined solely by the attending anesthesiologist as part of routine clinical care, and no study-driven intervention was applied.

- **Study Type:** Observational
- **Design:** Prospective cohort
- **Time Perspective:** Prospective
- **Number of Groups:** 3

- **Enrollment:** 78 patients
- **Sampling Method:** Non-probability sampling
- **Study Period:** September 15, 2024 – August 05, 2025
- **Setting:** Single center

Patients were grouped according to the ventilation mode selected by the attending anesthesiologist as part of routine clinical care. No intervention was assigned by the study protocol.

4. Study Population

Inclusion Criteria

- Female patients ≥45 years of age
- Scheduled for elective hysterectomy
- Expected surgery duration >2 hours
- American Society of Anesthesiologists (ASA) Physical Status I–III
- Planned total intravenous anesthesia

Exclusion Criteria

- ASA Physical Status ≥IV
- Body mass index (BMI) >35 kg/m²
- Planned postoperative intensive care admission
- Neuromuscular disease
- Uncontrolled asthma
- Chronic obstructive pulmonary disease (GOLD stage IV)
- Chest wall deformity or scoliosis
- Prior pulmonary resection
- History of spontaneous pneumothorax
- Preference for inhalational anesthesia
- Inability to provide informed consent

5. Study Groups

Flow-Controlled Ventilation (FCV)
Constant inspiratory and expiratory flow with linear pressure changes and inspiratory-to-expiratory ratio of 1:1.

Pressure-Controlled Ventilation (PCV)
Peak airway pressure predetermined; inspiratory time and respiratory rate fixed.

Volume-Controlled Ventilation (VCV)
Fixed tidal volume delivered with constant flow; airway pressure varies.

6. Study Procedures

Recorded Parameters

Hemodynamic and Monitoring Data

- Heart rate (HR)
- Mean arterial pressure (MAP)
- Peripheral oxygen saturation (SpO_2)
- BIS monitoring (depth of anesthesia)

Respiratory and Ventilator Parameters

- Peak airway pressure (Ppeak)
- Plateau pressure
- Positive end-expiratory pressure (PEEP)
- Tidal volume (Vt)
- Respiratory rate (RR)
- End-tidal carbon dioxide ($EtCO_2$)
- Fraction of inspired oxygen (FiO_2)
- Flow rate

Calculated Respiratory Mechanical Parameters

- Mechanical power (J/min)

- Lung compliance (mL/cmH_2O)

Arterial Blood Gas Parameters

- Partial pressure of arterial oxygen (PaO_2, mmHg)
- PaO_2/FiO_2 ratio (mmHg)
- Partial pressure of carbon dioxide ($PaCO_2$, mmHg)

Lung Ultrasonography Assessment

- Lung Ultrasound Score (LUS)

Postoperative Clinical Assessment

- Pain intensity assessed using the Visual Analog Scale (VAS)

Measurement Time Points

Lung Ultrasonography (LUS) Measurements

- Preoperatively (baseline value)
- At transfer from the PACU to the ward

- Postoperative 2nd hour
- Postoperative 24th hour

Changes from preoperative baseline values were used to evaluate perioperative atelectasis.

Pain Assessment (VAS Scores)

- Postoperative 2nd hour
- Postoperative 6th hour
- Postoperative 12th hour
- Postoperative 24th hour

Timing of Intraoperative and Perioperative Parameter Measurements

- Preoperative period
- After anesthesia induction
- Before and after pneumoperitoneum
- Before and after surgical positioning
- At 30-minute intervals during the intraoperative period
- During the Post-Anesthesia Care Unit (PACU) period

7-Outcome Measures

PRİMARY OUTCOME MEASURES

Perioperative atelectasis

Description:
Perioperative atelectasis will be quantified using Lung Ultrasound Score obtained via standardized bedside lung ultrasonography. Each lung region will be graded using a validated aeration scoring system (0 = normal aeration to 3 = consolidation). Total score range: **0–36 points**.

Outcome Metric:
Difference between postoperative and preoperative total LUS (ΔLUS, points).

Measurement Time Points:

- Preoperative baseline
- At discharge from Post-Anesthesia Care Unit (PACU)
- Postoperative 2 hours
- Postoperative 24 hours

Time Frame: 24 Hours

SECONDARY OUTCOME MEASURES

Evaluation of Oxygenation and Mechanical Power

Description:

Mechanical power and oxygenation were evaluated across three different ventilation modes based on the ventilation parameters set by the anesthesiologist. Mechanical power was assessed at predefined time intervals throughout mechanical ventilation. Oxygenation was evaluated preoperatively and in the post-anesthesia care unit (Post-Anesthesia Care Unit, PACU) using the partial pressure of oxygen (pO_2) and the ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO_2/FiO_2 ratio).

Unit of Measure: Joules per minute (J/min), representing the mechanical power applied to the respiratory system.

Oxygenation will be assessed using arterial blood gas analysis measuring: • PaO_2 (mmHg) • PaO_2/FiO_2 ratio (mmHg)

Time Frame: Perioperative period

8. Statistical Analysis Plan

8.1 General Principles

All statistical analyses will be conducted using **NCSS (Number Cruncher Statistical System) 2020 Statistical Software** (NCSS LLC).
Statistical significance will be assessed using two-sided tests, with a significance level of $\mathbf{p < 0.05}$. Results will be reported with **95% confidence intervals (CI)**.

8.2 Sample Size Determination

Sample size was calculated using **G*Power (v3.1.9.7)** (Heinrich Heine University Düsseldorf).
Assuming:

- Type I error (α): 0.05
- Statistical power: 80%
- Three-group comparison design

The minimum required sample size was **22 patients per group (total n = 66)**.
To account for potential **data loss, protocol deviations, or dropouts**, the study planned to enroll **78 participants**.

8.3 Data Presentation

- **Continuous variables** will be summarized as:
    - Mean ± standard deviation (SD)
    - Median
    - Minimum–maximum values

- **Categorical variables** will be expressed as:
    - Frequency (n)
    - Percentage (%)

8.4 Assessment of Normality

Distribution of continuous variables will be evaluated using:

- **Shapiro–Wilk test**
- Skewness and kurtosis values
- Visual inspection of **box plot graphs**

8.5 Between-Group Comparisons

For comparisons among the three ventilation groups:

Normally distributed variables

- One-Way Analysis of Variance (**One-Way ANOVA**)
- **Bonferroni post hoc test** to identify pairwise differences

Non-normally distributed variables

- **Kruskal–Wallis test**
- **Dunn test** for multiple comparisons

8.6 Within-Group (Repeated Measures) Analysis

To evaluate intraoperative and perioperative changes over time:

Normally distributed repeated measurements

- **Repeated Measures ANOVA**

Non-normally distributed repeated measurements

- **Friedman test**

8.7 Analysis of Categorical Variables

Categorical outcomes (e.g., incidence of postoperative findings) will be analyzed using:

- **Pearson's Chi-Square test**

8.8 Analysis Population

All enrolled patients with available outcome data will be included in the analysis.
Missing data will not be imputed; analyses will be performed using available-case data.

8.9 Software and Reporting Standards

All analyses will follow accepted biostatistical standards for observational clinical studies. Results will be reported in accordance with CONSORT-style recommendations where applicable.

9. Ethical Considerations

The study was reviewed and approved by the Clinical Research Ethics Committee of Sehit Prof. Dr. Ilhan Varank Sancaktepe Training and Research Hospital, affiliated with the University of Health Sciences (Approval No: 2024/241).

Written informed consent was obtained from all participants.

The study adhered to:

- Declaration of Helsinki
- Good Clinical Practice principles

10. Data Management and Confidentiality

- No biospecimens retained.
- Data anonymized prior to analysis.
- Only study investigators had access to coded datasets.

11. Safety Considerations

As an observational study, all interventions were part of routine anesthesia care.
No additional risk beyond standard clinical management was introduced.

No study-specific adverse event monitoring was required because all procedures were part of standard clinical practice.

12. Study Completion

- Primary Completion Date: June 26, 2025
- Study Completion Date: August 05, 2025
- Recruitment Status: Completed

INFORMED CONSENT FORM (ICF)
FOR THE RESEARCH STUDY ENTITLED:
"Evaluation of the Effects of Intraoperative Ventilation Modes on Perioperative Atelectasis in Patients Undergoing Hysterectomy by Lung Ultrasonography"

PLEASE READ CAREFULLY!

You are being invited to participate in this study.
Before agreeing to take part, you should understand the purpose of the study and make your decision freely after being informed.
Please read this information prepared specifically for you with care.
Feel free to ask any questions and request clear answers.

WHAT IS THE PURPOSE OF THE STUDY?

In hysterectomy operations, factors such as abdominal surgery, prolonged duration of the procedure, and the head-down position during surgery may cause a lobe or a certain part of the lungs to collapse and not fill with air after the operation. This condition is defined as **atelectasis**.

In this study, we aim to evaluate the effects of ventilation modes—routinely used in the operating room and not proven to be superior to one another—that help maintain breathing during surgery, on the development of postoperative atelectasis using lung ultrasonography.

WHAT ARE THE CONDITIONS FOR PARTICIPATION?

To participate in this study, you must:

- Be **45 years of age or older**,
- Be scheduled to undergo a hysterectomy expected to last **longer than 2 hours**,
- Be in the patient category for whom **total intravenous anesthesia (anesthesia administered entirely through intravenous medications)** is preferred by the responsible anesthesiologist.

WHAT WILL BE DONE AND HOW WILL IT BE PERFORMED?

During this research, no intervention or treatment other than the treatment planned by your responsible physicians will be applied to you or your relatives.

Only the data recorded during routine procedures will be analyzed after the data collection phase of the study is completed.

HOW MANY PARTICIPANTS WILL BE INCLUDED?

Approximately **78 patients** will be included in this study.

HOW LONG WILL THE STUDY LAST?

The study is expected to last approximately **1 year**.

WHAT ARE THE POSSIBLE BENEFITS OF PARTICIPATING?

The aim of the study is to evaluate the effects of ventilation modes routinely used in the operating room on the development of postoperative atelectasis.
Although there may be no direct benefit to you, the results may contribute to improving medical practice in the future.

WHAT ARE THE POSSIBLE RISKS OF PARTICIPATING?

This is an **observational study**.
No additional treatment will be applied other than the procedures required for your medical care. Therefore, participation does not pose any additional risk beyond the standard risks associated with anesthesia and surgery.

WHO SHOULD I CONTACT IF I EXPERIENCE ANY PROBLEMS DURING THE STUDY?

Dr. Tuğçe Türkan Tanman
Department of Anesthesiology and Reanimation
Phone: +90 216 603 33 00 (Extension: 1751)

WILL ANY COSTS BE COVERED WITHIN THE STUDY?

All treatments applied during the study are part of your routine care, and no additional expenses will arise.

WILL I RECEIVE ANY PAYMENT FOR PARTICIPATING?

Participants will not receive any payment.

WHAT SHOULD I DO IF I DO NOT WANT TO PARTICIPATE OR WISH TO WITHDRAW?

Participation in this study is entirely voluntary.
You may refuse to participate or withdraw from the study at any time.

The results of the research will be used for scientific purposes.
If you withdraw or are removed from the study, your data will not be used for scientific purposes.

WILL MY INFORMATION BE KEPT CONFIDENTIAL?

All your medical and personal information will be kept confidential. Even if the research is published, your identity will not be disclosed.

However, study monitors, auditors, ethics committees, and official authorities may access your medical records when necessary. These records will remain confidential. By signing this informed consent form, you authorize such access.

Your information will not be disclosed to the public. Even if study results are published, your identity will remain confidential. If new information that may affect you becomes available, you will be informed in a timely manner.

CONSENT TO PARTICIPATE

I have read the above information, which must be provided to volunteers before participation, and have also listened to the verbal explanation given by the physician named below.

I have asked all questions that came to mind and fully understood the written and verbal explanations provided to me.
I was given sufficient time to decide whether or not to participate.

I voluntarily agree to participate in this research without any pressure or coercion.

Under these conditions, I authorize the study investigator to review, transfer, and process my medical information and accept the invitation to participate in this research entirely of my own free will.

By signing this form, I understand that I do not waive any rights granted to me by local laws.

A signed and dated copy of this form has been given to me.

PARTICIPANT

Name and Surname: _____
Signature: _____
Address: _____
Phone: _____
Date: _____

INVESTIGATOR

Name and Surname: _____
Signature: _____
Date: _____

WITNESS (WHEN REQUIRED)

Name and Surname: _____
Role: _____
Signature: _____
Date: _____