# Effect of Positive end-Expiratory Pressure on Pulmonary Compliance and Pulmonary Complications in Patients Undergoing Robot-Assisted Laparoscopic Radical Prostatectomy

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## Abstract

# Purpose

To observe the effects of different levels of positive end-expiratory pressure (PEEP) ventilation strategies on pulmonary compliance and complications in patients undergoing robotic-assisted laparoscopic prostate surgery.

# Methods

A total of 120 patients with American Society of Anesthesiologists Physical Status Class I or II who underwent elective robotic-assisted laparoscopic prostatectomy were enrolled. The patients were randomly divided into three groups of 40 patients each: control (PEEP = 0 $cmH_2O$), low-level (PEEP = 5 $cmH_2O$), and high-level (PEEP = 10 $cmH_2O$). Volume control ventilation with an intraoperative deep muscle relaxation strategy was used intraoperatively. Respiratory mechanics indexes were recorded at six time points: 10 min after anesthesia induction, immediately after pneumoperitoneum establishment, 30 min, 1 h, 1.5 h, and at the end of pneumoperitoneum (T1-T6). Arterial blood gas analysis and oxygenation index calculation were performed at T1, T4, and after tracheal extubation (T7). Postoperative pulmonary complications were also recorded.

# Results

After pneumoperitoneum, peak inspiratory pressure (Ppeak), plateau pressure (Pplat), mean pressure (Pmean), driving pressure (ΔP), and airway resistance (Raw) increased significantly and pulmonary compliance (Crs) decreased, persisting during pneumoperitoneum in all groups. Between T2–T5, the low-level group had the highest Crs value and the lowestΔP (driving pressure) value relative to the high-level and control groups ($P < 0.05$). At T4 and T7, the $PaCO_2$ and $PaO_2/FiO_2$ did not significantly differ among the three groups. There was no significant difference in postoperative pulmonary complications among the three groups.

# Conclusion

High levels of intraoperative PEEP increased lung compliance without significantly reducing postoperative pulmonary complications.

## 1. Background

The International Agency for Research in Oncology (IARC) estimated 1,414,259 new cases of prostate cancer and approximately 375,304 prostate-cancer-related deaths worldwide in 2020 [1]. With the continuous advancement of minimally invasive surgery and the rapid development of artificial intelligence-assisted systems, an increasing number of studies have shown that robotic-assisted laparoscopic radical prostatectomy (RARP) is superior to traditional open radical prostatectomy or pure laparoscopic radical prostatectomy in aspects such as in providing a clearer field, a more delicate operation execution, less trauma, less blood loss, and complete radical treatment [2]. While the da Vinci robot-assisted surgery has benefited prostate cancer patients, the anesthetic management of patients undergoing RARP surgery, especially managing the physiological changes due to pneumoperitoneum and a steep head-down position, has become one of the main recent topics in anesthesiology [3, 4]. The establishment of pneumoperitoneum and head-down position can cause serious interference with pulmonary function: first, it affects

diaphragm elevation, causing decreased thoracopulmonary compliance, reduced functional residual air volume, and pulmonary atelectasis. This increases the possibility of hypoxemia. Ventilation pressure increases significantly as well, which may damage the lungs and increase the occurrence of postoperative pulmonary complications. Pulmonary complications occur in about 5% of patients undergoing surgical procedures under general anesthesia with tracheal intubation, leading to prolonged postoperative recovery and increased hospital costs [5]. There are many causes of postoperative pulmonary complications, including barotrauma during general anesthesia [4, 5]. Therefore, the anesthetic management of perioperative pulmonary protection is an important component for rapid patient recovery. Pulmonary protective ventilation, which combines a low tidal volume (6–8 mL/kg) and positive end-expiratory pressure (PEEP) ventilation, was initially used in patients with respiratory distress syndrome and is now considered beneficial in "normal lung" patients under general anesthesia with tracheal intubation [5, 6]. For laparoscopic procedures requiring $CO_2$ pneumoperitoneum, a "permissive hypercapnia," where small tidal volume ventilation is applied and the arterial blood $CO_2$ partial pressure is allowed to reach ≥ 60–70 mmHg for a short period, was proposed to avoid lung damage from high ventilation pressure [6]. In a study of 40 cases of patients who underwent elective abdominal surgery with individual PEEP value monitoring by thoracic image scanning, a PEEP of 6–16 $cmH_2O$ with a median of 12 $cmH_2O$ is required to improve pulmonary compliance and reduce pulmonary atelectasis [7]. It has also been suggested that high PEEP levels (10 $cmH_2O$) significantly improve lung compliance and reduce the incidence of atelectasis during mechanical ventilation compared to low PEEP levels and no PEEP ventilation [8, 9].

Most anesthetized patients treated with RARP surgery have a healthy level of pulmonary function with good lung compliance. There is a lack of systematic studies on whether intraoperative PEEP is needed to improve oxygenation and reduce postoperative pulmonary complications in this group. It is important to guide clinical anesthesiologists in managing respiratory function of patients undergoing RARP surgery with safer and more effective mechanical ventilation parameters by finding the appropriate PEEP values. In this study, we investigated the feasibility of a PEEP ventilation strategy in patients undergoing RARP surgery and its effects on ventilation, oxygenation, and postoperative rehabilitation.

## 2. Patients And Methods

This prospective randomized double-blind controlled trial was reviewed and approved by the IIT Ethics Review Panel of the Clinical Research Ethics Committee of the First Hospital of Zhejiang University School of Medicine on May 6, 2020 (Session No. 48). The study was registered in the China Clinical Trials Registry (Registration No. ChiCTR2000033380).

# 2.1. Patients

Written informed consent was obtained from all subjects. The inclusion criteria were ASA classification I-II and no history of serious systemic disease. Exclusion criteria were age > 80 years, history of severe cardiopulmonary, hepatic, and renal disease, history of neuromuscular disease, excessive obesity or malnutrition (body mass index, BMI ≥ 30 or ≤ 20), history of drug allergy, etc. Using SPSS 23 (IBM, Armonk, NY, USA), patients were randomly allocated to three groups (40 patients per group): control group (group A: PEEP = 0), low-level PEEP group (group B: 5 $cmH_2O$), and high-level PEEP group (group C: 10 $cmH_2O$). Randomization was performed by a researcher not involved in the anesthesia or statistical analysis. The attending anesthetist was given an envelope containing the allocation results. The patient, the surgeon, and the resident anesthetist responsible for the records were blinded to the PEEP level. A flowchart of the study is shown in Fig. 1.

## 2.2. Anesthesia method

After the patient was admitted to the operating room, an invasive arterial puncture was performed in addition to routine monitoring and preoperative blood gas analysis. Induction of anesthesia took place through intravenous administration of etomidate, fentanyl, rocuronium bromide 0.6 mg/kg, followed by tracheal intubation and mechanical ventilation. Ventilation was set to volume-controlled breathing (60% oxygen concentration, mixed air) with an initial tidal volume of 7 mL/kg and a frequency of 12 breaths/min. The PEEP was set to 0, 5, and 10 $cmH_2O$ according to the grouping. The parameters were adjusted before pneumoperitoneum to maintain an end-expiratory carbon dioxide partial pressure of 30–35 mmHg. When end-expiratory carbon dioxide reached ≥ 60 mmHg (expected blood carbon dioxide partial pressure of 70 mmHg), hypercapnia was permissive during pneumoperitoneum to increase respiratory rate at first. If end-expiratory carbon dioxide could not be reduced or continued to rise, hypercapnia can continue to increase tidal volume when. No pulmonary resuscitation strategy was used for any ventilation mode. Intraoperative rocuronium bromide 0.6 mg/kg/h was pumped intravenously to maintain deep muscular relaxation at 0 train of four (TOF) stimulation response and 1–2 post tonic counts (PTC). Rocuronium was discontinued at the end of pneumoperitoneum.

## 2.3. Monitoring

Pulse oximetry, electrocardiogram (ECG), temperature measurement, bispectral index (BIS) monitoring, invasive arterial pressure monitoring, end-expiratory carbon dioxide measurement, pressure-volume loop measurement, accelerometer monitoring of muscle relaxation, and blood gas analysis were performed. Data were recorded for patients in all groups at six time points: after induction (T1), pneumoperitoneum establishment (T2), 0.5 h after pneumoperitoneum (T3), 1 h after pneumoperitoneum (T4), 1.5 h after pneumoperitoneum (T5), and at the end of pneumoperitoneum (T6). Data obtained include tidal volume, respiratory rate, end-expiratory carbon dioxide partial pressure, peak airway pressure, plateau pressure, lung compliance, airway resistance, pulse oximeter, blood pressure, heart rate, duration of surgery, among others. Blood gas analysis was performed after anesthesia induction, 1 h after pneumoperitoneum, and after tracheal extubation. Follow-up visits were performed on postoperative days 1, 3, and one month after surgery. Indicators for postoperative pain and postoperative complications were monitored and recorded.

Table 1
Basic patient characteristics

| PEEP (cmH2O) | 0 $cmH_2O$ | 5 $cmH_2O$ | 10 $cmH_2O$ | P-value |
|---|---|---|---|---|
| N | 27 | 33 | 29 | |
| Age (years) | 65 (60–72) | 70 (65–73) | 69 (63–72) | 0.063 |
| Body weight (kg) | 69 (65–71) | 66 (61–71) | 66 (61–70) | 0.592 |
| Height (cm) | 170(165–172) | 170 (165–171) | 170 (165–173) | 0.839 |
| BMI (kg/m2) | 24 (23–26) | 24 (22–25) | 23 (22–25) | 0.446 |
| Surgery time(min) | 157(144–174) | 159 (128–176) | 150 (130–172) | 0.514 |
| Data are expressed as median (interquartile range) | | | | |

## 2.4. Statistical Analysis

The Kolmogorov-Smirnov test was used to test the normality of the distributions of all variables. The values of peak inspiratory pressure (Ppeak), mean pressure (Pmean), pulmonary compliance (Crs), airway resistance (Raw),partial pressure of carbon dioxide in artery ($PaCO_2$) and ratio of partial pressure of O2 in arterial blood to fraction of inspired oxygen ($PaO_2/FiO_2$) at different timepoints are expressed as median and interquartile ranges, where the data were not normally distributed. Patient characteristics, time to pneumoperitoneum, time to surgery, and time to extubation were expressed as median and interquartile ranges. Differences between multiple time points were analyzed using Kruskal-Wallis and one-way analysis of variance (ANOVA) post hoc tests. The Mann–Whitney U test was used to analyze the differences between two time points and groups. χ2 tests were used to compare the number of patients with agitation upon awakening and that of those with postoperative pulmonary complications in all groups.

To determine the sample size, a pretest was performed. The mean Crs during pneumoperitoneum (Pnp) of 0, 5, 10 $cmH_2O$ of PEEP were 27 mL/$cmH_2O$, 32 mL/$cmH_2O$, and 34 mL/$cmH_2O$ with standard deviations of 7, 9, and 10, respectively. Considering P value = 0.05 and a degree of certainty of 0.90, to distinguish the Crs of each group, at least 28 patients were required per group.

Crs: respiratory compliance (mL/cmH2O); ΔP: driving pressure (cmH2O); PEEP: positive end-expiratory pressure (cmH2O); data are expressed as medians. T1 post-induction; t2: immediate post-pneumoperitoneum; t3: 0.5 h post-pneumoperitoneum; t4: 1 h post-pneumoperitoneum; t5: 1.5 h post-pneumoperitoneum; t6: end of pneumoperitoneum. * $P < 0.05$, for the 10 $cmH_2O$ group compared with the 0 and 5 $cmH_2O$ groups at this time point.

Table 2
Arterial blood gas variables at different time points

| | $PaCO_2$(mmHg) | | | $PaO_2/FiO_2$(mmHg) | | |
|---|---|---|---|---|---|---|
| | 0$cmH_2O$PEEP | 5$cmH_2O$PEEP | 10$cmH_2O$PEEP | 0$cmH_2O$PEEP | 5$cmH_2O$PEEP | 10$cmH_2O$PEEP |
| **T1** | 40.9(37.9–44) | 41.1(39.3–42.5) | 41.9(39.7–44.5) | 463(367–532) | 480(407–530) | 440(355–503) |
| **T4** | 51.1(48.2–74.5) | 56.1(51.9–59.9) | 54.7(46.4–57.9) | 435(335–504) | 422(330–475) | 403(340–483) |
| **T7** | 44.9(42.8–47.1) | 46.7(45–49) | 44.7(41.5–47.1) | 292(245–423) | 363(227–305) | 262(231–355) |
| **t7: after tracheal extubation.** | | | | | | |

# 3. Results

Patient characteristics such as height, weight, age, BMI, pneumoperitoneum time, and operative time (Table 1) were not significantly different among groups.

After establishment of the pneumoperitoneum, Peak, Pmean, Raw, Plat, and ΔP (driving pressure) increased while Crs decreased. These changes persisted during pneumoperitoneum in all groups. At the end of the pneumoperitoneum, these indices improved but did not return to post-induction levels (Table 1). At T2, T3, T4, and T5, the 10 $cmH_2O$ PEEP group had the highest Crs ($P < 0.05$) and the smallest ΔP values ($P < 0.05$) relative to the other groups (Fig. 2). During T2–T5, there was no significant difference in Peak, Mean, and Raw between the 0 and 5 $cmH_2O$ PEEP groups ($P > 0.05$). At T1, T4, and T7, there was no significant difference in $PaCO_2$ and $PaO_2$ among groups ($P > 0.05$, Table 2). There was no difference in $SpO_2$ and VAS scores or in the rate of pulmonary complications at 1 and 3 post-operative

days (P > 0.05, Fig. 3, Table 3). Extubation and PACU times were significantly longer in the 5 $cmH_2O$ PEEP group (P < 0.05), but there was no significant difference in agitation during the awakening period and hospital stay among groups (P > 0.05, Table 4).

VAS score, visual analog pain scoring method; Day 1: One day after surgery; Day 3: Three days after surgery; $SpO_2$, transcutaneous oxygen saturation; PEEP, positive end-expiratory pressure ($cmH_2O$). Data are expressed as means.

Table 3
Pulmonary complications on the first and third postoperative days

| | One day after surgery | | | | Three days after surgery | | | |
|---|---|---|---|---|---|---|---|---|
| | 0$cmH_2O$ PEEP | 5$cmH_2O$ PEEP | 10$cmH_2O$ PEEP | p | 0$cmH_2O$ PEEP | 5$cmH_2O$ PEEP | 10$cmH_2O$ PEEP | p |
| Cough(n) | 24(85.7%) | 23(76.6%) | 21(72.4%) | 0.349 | 19(70.3%) | 19(57.5%) | 12(41.3%) | 0.234 |
| Secretions(n) | 10(37.0%) | 11(33.3%) | 10(34.4%) | 0.775 | 4(14.8%) | 9(27.2%) | 6(20.6%) | 0.220 |
| Shortness of breath (n) | 3(11.1%) | 8(24.2%) | 5(17.2%) | 0.416 | 1(3.7%) | 3(9.1%) | 4(13.7) | 0.419 |
| Fever(n) | 3(11.1%) | 6(18.8%) | 4(13.7%) | 0.734 | 0 | 2(6.1%) | 1(3.4%) | 0.433 |
| Data are number of patients (percentage). PEEP: positive end-expiratory pressure. | | | | | | | | |

Table 4
Postoperative indicators

| | 0$cmH_2O$PEEP | 5$cmH_2O$PEEP | 10$cmH_2O$PEEP | p |
|---|---|---|---|---|
| Time of extubation(min) | 35(22-48.5) | 50.5(35-66.5) | 39(20-57.5) | 0.019 |
| Time in PACU(min) | 74(62-86.5) | 92(76-112.5) | 74(55–90) | 0.02 |
| Restlessness during the awakening period(n) | 4 | 6 | 4 | 0.865 |
| Length of hospitalization(day) | 7(7–8) | 7(7–8) | 7(6–8) | 0.863 |
| Data are expressed as median (interquartile range) or number of patients; PEEP: positive end-expiratory pressure. | | | | |

# 4. Discussion

Laparoscopic patients under general anesthesia are prone to pulmonary atelectasis and postoperative pulmonary complications after mechanical ventilation [10, 11]. In RARP, the incidence of atelectasis often increases due to the patient's older age and the surgical position. To obtain the best surgical view, RARP requires a Trendelenburg position > 30˚, with intra-abdominal organs compressing the diaphragm and lungs. In addition, the elderly tend to have poor lung compliance and a higher incidence of postoperative pulmonary atelectasis compared to younger patients [12, 13]. Furthermore, our previous study showed that use of deep neuromuscular blockade during RARP did not increase pulmonary compliance and reduce pulmonary complications [14].

We used continuous dynamic pulmonary respiratory mechanics monitoring and found that the establishment of pneumoperitoneum and the change in surgical position decreased pulmonary compliance in patients, which is

consistent with the results of related studies [15]. This may be due to a decrease in pulmonary compliance caused by diaphragmatic elevation, restricted thoracic motion due to pneumoperitoneal pressure, and the effect of gravity in the Trendelenburg position, which increases pulmonary stasis, further disturbing pulmonary ventilation/flow ratio. Patients administered either 5 cm$H_2O$ or 10 cm$H_2O$ in this study showed an increase in lung compliance, presumably because a certain PEEP level counteracts the effects of manual pneumoperitoneum and the Trendelenburg position on lung compliance in RARP patients. These results are consistent with current clinical findings [16]. Most studies on intraoperative protective mechanical ventilation have not individualized the PEEP level applied. An arbitrary selection of PEEP levels in different patient populations and surgical approaches can lead to heterogeneity of results [17]. The choice of PEEP level should be based on the patient's characteristics, the specific surgical access site, and the patient's position [18]. In a study of obese patients undergoing laparoscopic bariatric surgery, the use of an individualized stepwise PEEP approach with lung ultrasound improved lung compliance and oxygenation [19].

In addition, the present study observed that 10 cm $H_2O$ PEEP did not significantly improve the key intraoperative oxygenation index nor significantly reduce the incidence of postoperative pulmonary complications, showing a limited protective effect on the lungs. Similarly, Van Hecke et al. reported that in laparoscopic bariatric surgery, optimizing lung compliance by PEEP did not reduce the incidence of postoperative hypoxemia [20]. In contrast, combining pulmonary resuscitation strategies with PEEP significantly reduced perioperative pulmonary complications compared with PEEP alone in elderly patients undergoing RARP [21]. We hypothesized that appropriate PEEP can increase end-expiratory alveolar volume, reduce intrapulmonary shunts, increase lung compliance, and improve oxygenation. However, an inappropriately high PEEP results in higher airway and plateau pressures, which may produce hyperbaric lung injury [22]. An excessively high PEEP level increases thoracic pressure, which can significantly affect right ventricular outflow resistance [23], in turn can cause an imbalance in ventilatory flow ratio. Future studies should investigate and implement lung-protective low ventilation strategies with electrical impedance tomography (EIT) of the chest or lung ultrasound to help determine the appropriate PEEP values.

This study also has limitations: First, postoperative pulmonary function and lung CT monitoring, which can help evaluate the incidence of pulmonary complications accurately, were not performed. Second, intraoperative cardiac output values, which would allow to understand the effect of different PEEP values on hemodynamics, were not recorded. Third, we did not individualize PEEP settings [24]. The use of individualized titrated PEEP setting for perioperative lung protection may be a trend in the future.

# 5. Conclusion

Applying a high-level PEEP (10 cm$H_2O$) in robotic-assisted laparoscopic prostatectomy under deep muscle relaxation increased lung compliance and decreased driving pressure values after pneumoperitoneum. However, it did not improve oxygenation 1 h after pneumoperitoneum nor did it significantly reduce postoperative pulmonary complications. Individualized pulmonary protective ventilation strategies are needed in the future.

# Declarations

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**Competing Interests**: The authors have no relevant financial or non-financial interests to disclose

**Author Contributions**: All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Lifeng Ni , Menglan Chen and Ling'er Huang. The first draft of the manuscript was written by Lifeng Niand all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript

**Ethics approval**: This prospective randomized double-blind controlled trial was reviewed and approved by the IIT Ethics Review Panel of the Clinical Research Ethics Committee of the First Hospital of Zhejiang University School of Medicine on May 6, 2020 (Session No. 48). The study was registered in the China Clinical Trials Registry (Registration No. ChiCTR2000033380).

**Consent to participate**: Written informed consent was obtained from all subjects.

**Consent to publish**: The authors affirm that human research participants provided informed consent for publication of the images in Figure 1, 2and 3.

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# Figures

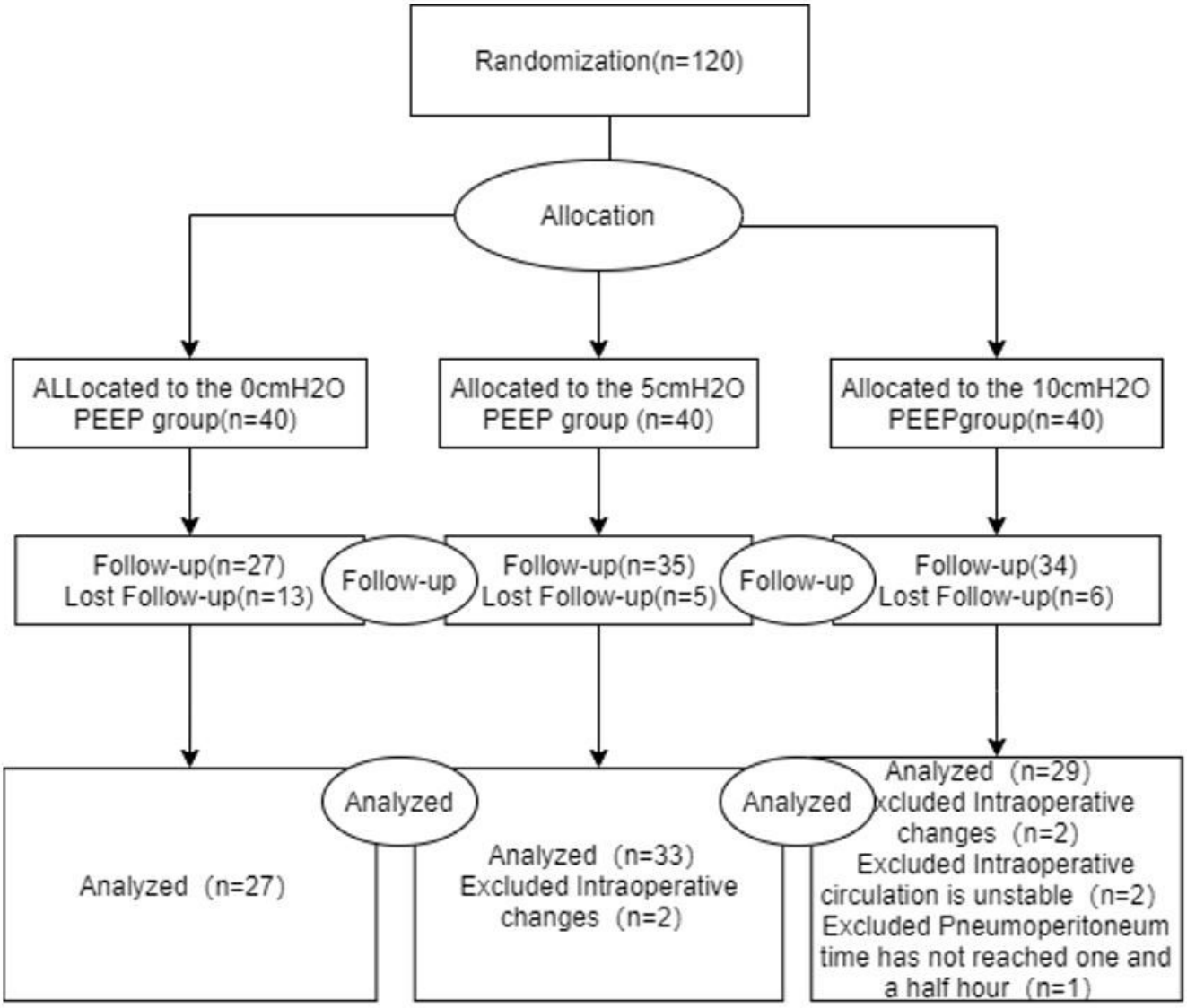
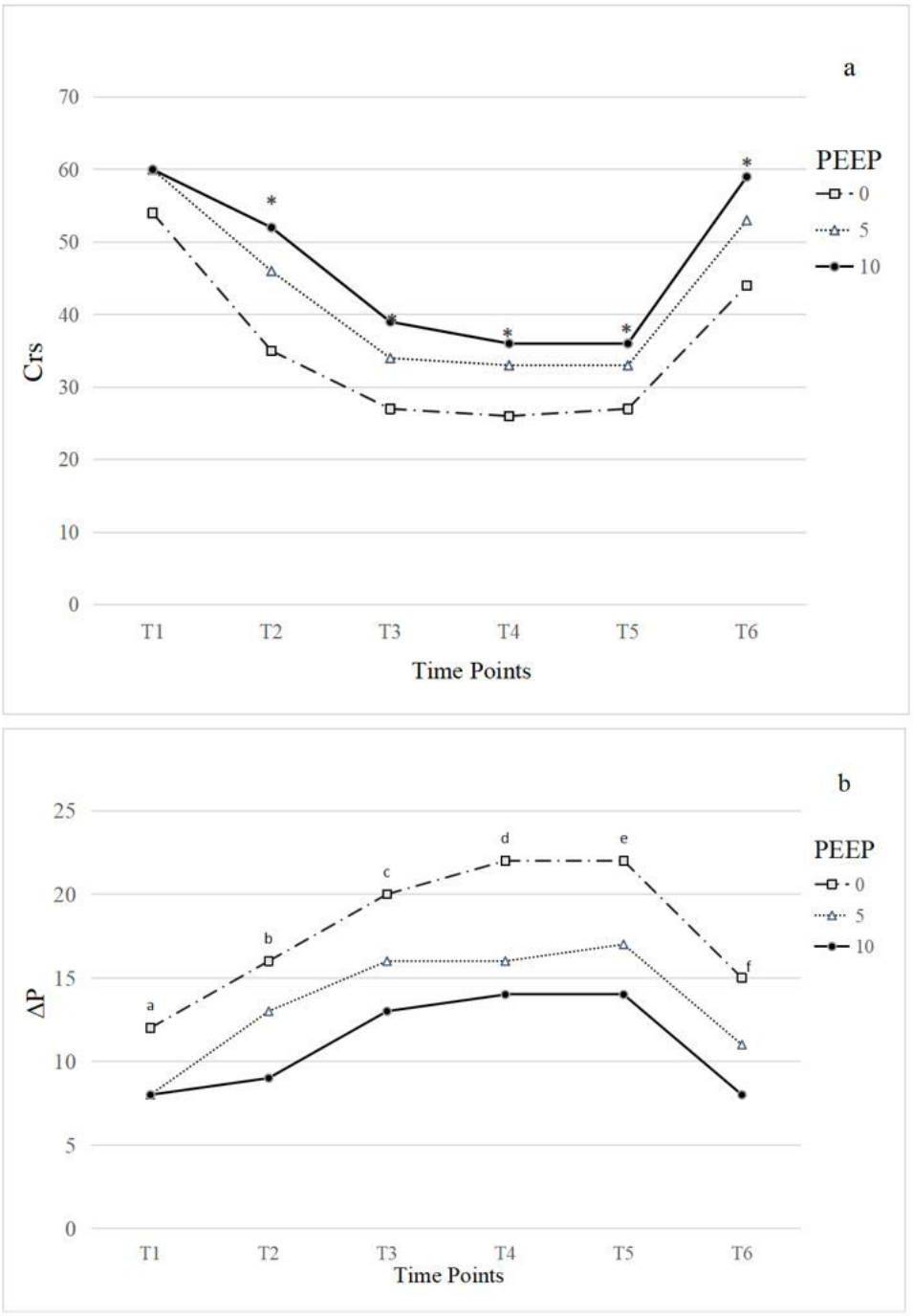



**Figure 1**

Experimental flow chart




## Figure 2

Respiratory mechanics at different time points during surgery

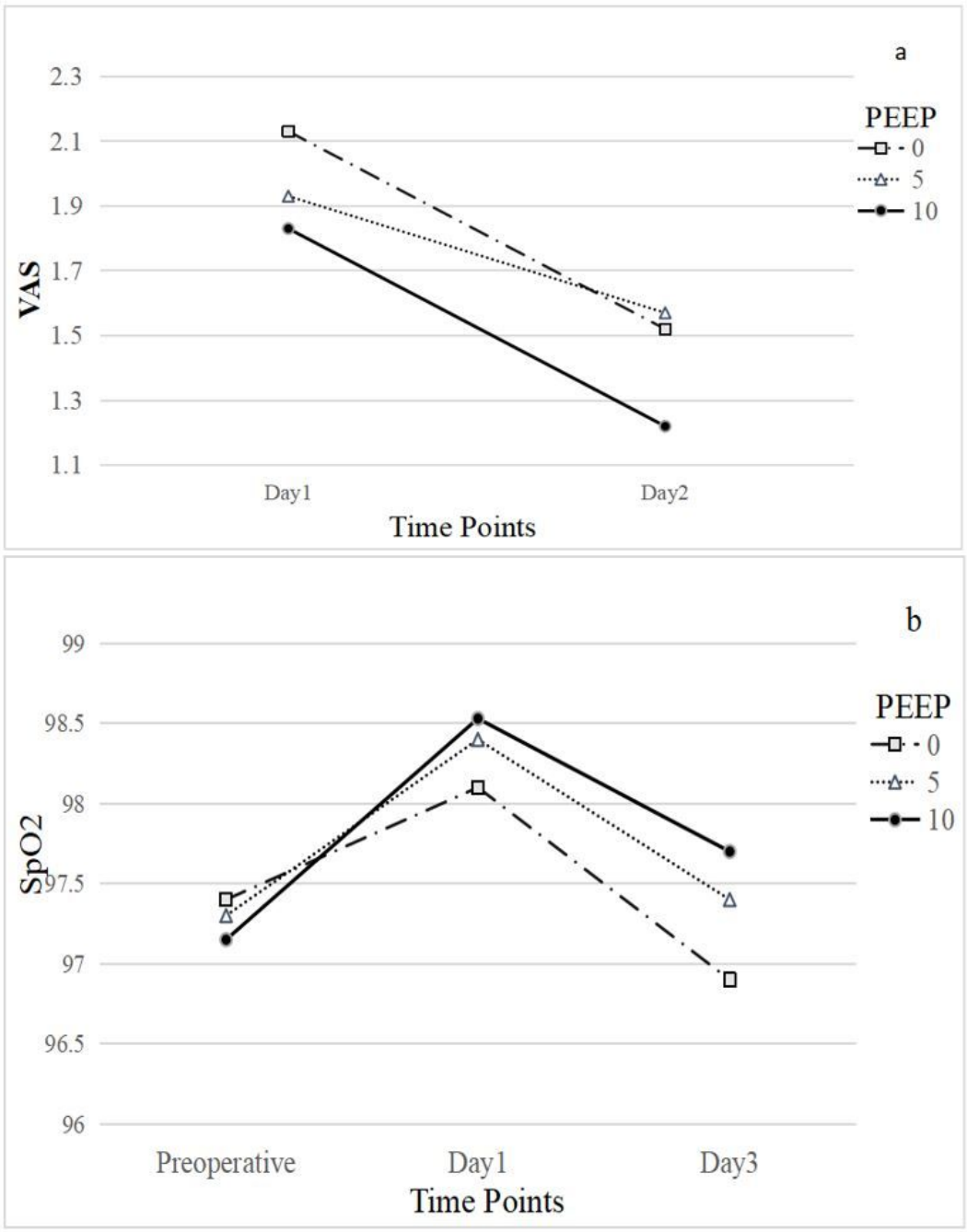



**Figure 3**

$SpO_2$ and VAS scores of the three groups at one and three days postoperatively

## Supplementary Files

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