



Effect of recruitment maneuver on arterial oxygenation in patients undergoing robot-assisted laparoscopic prostatectomy with intraoperative 15 cmH₂O positive end expiratory pressure

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Background: This randomized, controlled study was designed to compare the effects of recruitment maneuvers (RMs) with a 15 cmH₂O positive end-expiratory pressure (PEEP) on the systemic oxygenation and lung compliance of patients with healthy lungs following robot-assisted laparoscopic prostatectomy (RALP).

Methods: Sixty patients undergoing a RALP with an intraoperative 15 cmH₂O PEEP were randomly allocated to an RM or a Control group. The patients in the RM group received a single RM through the application of a continuous positive airway pressure of 40 cmH₂O for 40 s 15 min after being placed in the Trendelenburg position. The arterial oxygen tension (PaO₂, primary endpoint) and the pulmonary dynamic and static compliances (secondary endpoints) were measured 10 min after the anesthetic induction (T1), 10 min after establishment of the pneumoperitoneum (T2), 10 min after establishment of the Trendelenburg position (T3), 10 min after the RM (T4), 60 min after the RM (T5), and 10 min after deflation of the pneumoperitoneum in the supine position (T6).

Results: The intergroup comparisons of the PaO₂ showed significantly higher values in the RM group than in the Control group at T4 and T5 (193 ± 35 mmHg vs. 219 ± 33 mmHg, P = 0.015, 188 ± 41 mmHg vs. 214 ± 42 mmHg, P = 0.005, respectively). However, the PaO₂ at T6 was similar in the two groups (211 ± 39 mmHg vs. 224 ± 41 mmHg, P = 0.442). Moreover, there were no statistical differences between the groups in the dynamic and static compliances of the lungs at any time point.

Conclusions: The arterial oxygenation of the patients with a healthy lung function who had undergone a RALP with intraoperative 15 cmH₂O PEEP was improved by a single RM. However, this benefit did not last long, and it did not lead to an amelioration of the lung mechanics.

Key Words: Pneumoperitoneum, Recruitment maneuver, Robot-assisted laparoscopic prostatectomy, Steep Trendelenburg position.

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Introduction

It is well known that the incidence of a pneumoperitoneum with CO₂ insufflation during laparoscopic surgery elevates the intrathoracic pressure through the elevation of the diaphragm, which in turn decreases the lung compliance [1]. Additionally, the Trendelenburg position influences the abdominal pressure through gravity, thereby increasing the airway pressure and reducing the functional residual capacity, which causes further changes in the respiratory system [2].

Since the introduction of computer-enhanced robotic surgical systems in 2001, robot-assisted laparoscopic prostatectomy (RALP) has been commonly used in the surgical treatment of prostate cancer. RALP presents a number of advantages over conventional surgery, including nerve sparing, shorter hospitalization times, reduced blood loss, and lower postoperative pain [3,4]. However, in order to improve the surgical visual field to the maximum, RALP usually requires the patient to be placed in a steep Trendelenburg position with a pneumoperitoneum, which results in a significantly elevated airway pressure [5].

Clinical data have demonstrated that a mechanical ventilatory strategy using lower tidal volumes (V_T) and positive end-expiratory pressure (PEEP) decreases the risks of pulmonary complications by minimizing the alveolar stretching at the end of inspiration and avoiding possible inflammation or alveolar collapse [6]. Recent clinical studies have also reported that mechanical ventilation using PEEP with or without recruitment maneuvers (RMs) could help improve the intraoperative PaO₂ and lung compliance and decrease the pulmonary shunt fraction [7,8]. Meanwhile, postoperative pulmonary complications arising from mechanical ventilation – which is essential in surgeries requiring general anesthesia – are common in surgical patients, with an incidence of up to 5% [9]. However, there has been a lack of evidence for the effect of RM on the pulmonary function and clinical outcomes of surgical patients with healthy lungs managed with a protective ventilatory strategy at a higher PEEP.

Therefore, this study conducted a randomized, controlled trial to test the hypothesis that a single RM can improve the systemic oxygenation and lung compliance of surgical patients with a healthy lung function undergoing a RALP in a steep Trendelenburg position with a pneumoperitoneum when used in conjunction with a protective ventilatory strategy and a higher PEEP level (15 cmH₂O) during the surgery.

Materials and Methods

After receiving approval from the Institutional Review Board, we obtained informed consent forms from all enrolled adult patients (20–75 years) scheduled for a RALP between May 2013 and August 2014. Sixty patients were prospectively included and

were randomly assigned to the Control group (n = 30) or the RM group (n = 30) one day prior to the surgery by a computerized randomization table created by a staff member who was not involved in the study. Patients with a known history or with clinical evidence of chronic obstructive pulmonary disease or respiratory insufficiency from preoperative medication or in the pulmonary function test, of renal or hepatic dysfunction, or of emergency operations were excluded. The flow chart used for randomization of the patient enrolment is provided as Fig. 1. The group allocation was concealed from the staff members who provided clinical care for the participants while they collected the clinical data for the study. The intervention protocol was registered at <http://cris.nih.go.kr>.

All patients received standardized anesthetic and ventilation management. Upon arrival in the operating room, standard monitoring devices were applied. These included a FloTrac/Vigileo[®] system (Edwards Lifesciences, Irvine, CA, USA) that was connected to the right radial artery and the right internal jugular vein for continuous monitoring of the cardiac index (CI), the stroke volume variation (SVV), and the central venous oxygen saturation (ScvO₂). The general anesthesia was induced with 1.5 mg/kg of propofol and 0.5–1 µg/kg of remifentanyl, and was maintained with a continuous infusion of propofol and remifentanyl to sustain bispectral index scale (BIS) values of 40–60. The tracheal intubation was facilitated with 0.6 mg/kg of rocuronium bromide. The patients were intubated and mechanical ventilation was initiated when their train of four (TOF) response disappeared. The initial dose was followed by a continuous infusion of rocuronium bromide (0.3–0.6 mg/kg/h), which was adjusted in order to maintain a deep block with a TOF response of 0 and post-tetanic counts under 10 throughout the procedure. During the surgery, the hemodynamic response was stabilized with a target-controlled infusion device (Orchestra[®], Fresenius Vial, Brezins, France). At the end of the surgery, the infusions of propofol and remifentanyl were discontinued, and the residual neuromuscular paralysis was reversed with pyridostigmine 0.2 mg/kg and glycopyrrolate 0.04 mg/kg. After successful extubation and recovery, the patients were transferred to the post-anesthesia care unit (PACU). The mechanical ventilation parameters during the anesthesia were standardized in order to maintain normocarbia (respiratory rate: 8–12 breaths/min, V_T : 6 ml/kg, fraction of inspired oxygen: 0.4, PEEP: 15 cmH₂O). Moreover, during the intraoperative period, standardized fluid management was performed in all patients using a crystalloid solution (lactated Ringer's solution; B. Braun, Melsungen, Germany) at a rate of 20 ml/kg/h immediately before the anesthetic induction and until the patient was placed in the Trendelenburg position, followed by 5 ml/kg/h until the end of the surgery. The occurrence of intraoperative hypotension (mean blood pressure [MBP] < 65 mmHg or a decrease in MBP > 20% of baseline

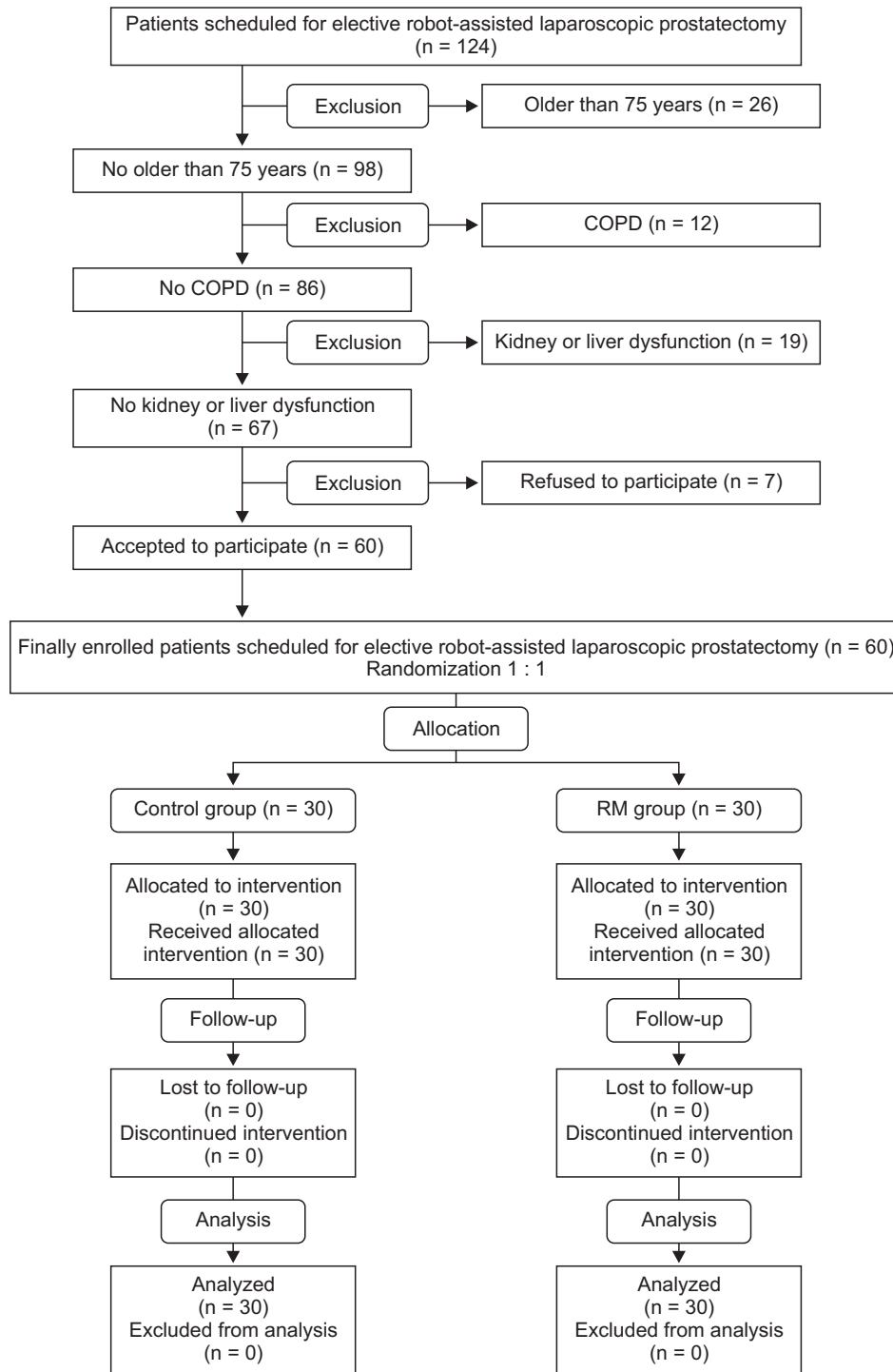


Fig. 1. Flow chart of patient participation. COPD: chronic obstructive pulmonary disease, RM: recruitment maneuver.

for more than 5 min) was managed with a bolus of a 10 ml/kg colloid solution (Voluven®; Fresenius Kabi, Bad Homburg, Germany) for maintenance of the SVV values at 8–15% and/or with an incremental administration of intravenous vasoactive drugs (ephedrine 4 mg or phenylephrine 50 µg), as appropriate.

In all enrolled patients, a pneumoperitoneum was established

using CO₂ with an intra-abdominal pressure of 12 mmHg in the supine position. The patients in the RM group then received a single RM, which was conducted by applying a continuous positive airway pressure of 40 cmH₂O for 40 s 15 min after placing the patients in the Trendelenburg position. The patients in the Control group did not receive the RM. The intervention was

performed by a single nurse who was not otherwise involved in the study, and the attending anesthesiologists and surgeons were blinded to the details of the intervention allocation.

The primary endpoint was the PaO₂ as measured 10 min after deflation of the pneumoperitoneum in the supine position (T6). The pulmonary dynamic compliance (V_T/ [peak airway pressure – PEEP]) and static compliance (V_T/ [plateau airway pressure – PEEP]) and the clinical outcomes, including the length of hospital stay, were assessed as secondary endpoints. All pulmonary parameters were evaluated 10 min after the anesthetic induction (T1), 10 min after establishment of the pneumoperitoneum (T2), 10 min after establishment of the Trendelenburg position (T3), 10 min after the RM (T4), 60 min after the RM (T5), and 10 min after deflation of the pneumoperitoneum in the supine position (T6). The hemodynamic variables of the MBP, CI, SVV, and ScvO₂ were also recorded at the same time points as the pulmonary variables. Finally, the PaO₂ in the PACU, the durations of the PACU and hospital stays, and the number of patients suffering from the development of acute lung injury (ALI) on the second postoperative day were recorded as postoperative clinical data. Postoperative ALI was defined with the following criteria: PaO₂/FIO₂ < 300 mmHg, bilateral pulmonary infiltrates on the chest radiography, and no clinical evidence of further pressure elevation in the left atrium [10]. All the variables involved in this study were evaluated and recorded by an investigator who was blinded to the group allocation details.

SPSS Statistics software ver.18 (SPSS Inc., Chicago, IL, USA) was used for the statistical analyses, and all values were expressed as the number of patients, the means ± standard deviation (SD), or the median (interquartile range), as appropriate. The sample size was calculated according to the primary endpoint, i.e., the comparison of the PaO₂ values between the groups. Based on a preliminary institutional study, we determined that 27 patients would be required in each group in order to detect a 50 mmHg difference in PaO₂ between the two groups at FIO₂ 0.4 with an alpha level of 0.05 and a SD of 60 mmHg using an independent t-test, at an 80% power. Allowing for a 10% drop-out rate during the study period, 30 patients were enrolled in each group. Chi-square statistics or Fisher's exact test were used as appropriate for the categorical variables, and independent t-tests or Mann-Whitney U tests for the continuous variables. As a *post hoc* analysis, the repeatedly-measured values were compared with a repeated-measures ANOVA using Bonferroni's correction. A P value under 0.05 was considered statistically significant.

Results

A RALP was successfully performed on all patients without any incidence of perioperative complications from the anesthesia or surgery. Therefore, the data for all 60 initially enrolled

adult patients was collected and analyzed.

The patient characteristics, including the values of the pre-operative pulmonary function, did not differ statistically significantly between the two groups. Moreover, the operative data, including the intraoperative fluid balance and the surgery duration, were similar between the two groups (Table 1).

The PaO₂ at T5 was significantly lower than its baseline value in the Control group, but not in the RM group. The intergroup comparisons of these variables also showed significantly higher values in the RM group than in the Control group at T4 and T5. However, the dynamic and static compliances of the lungs revealed no statistical differences between the two groups at any time point (Table 2).

Although certain hemodynamic variables – namely, the MBP, the central venous pressure, and the CI, differed statistically from their corresponding baseline value (T1), the difference between the groups remained similar throughout the study period (Table 3). Moreover, although transient hypotension was developed during the RM application, fluid management and/or pharmacologic support was not required to manage this event in any patient.

There were no differences in the postoperative clinical variables, including the PaO₂ in the PACU, the postoperative development of acute lung injury, and the durations of the PACU and hospital stays (Table 4).

Discussion

This randomized, controlled trial evaluated the effect of a single RM of 40 cmH₂O for 40 s on the systemic oxygenation and pulmonary compliance of patients undergoing RALP with an intraoperative PEEP of 15 cmH₂O. The arterial PaO₂ was

Table 1. Patients' Characteristics and Operative Data

	Control (n = 30)	RM (n = 30)	P value
Age (yr)	62 ± 6	63 ± 6	0.833
Height (cm)	169 ± 5	168 ± 6	0.990
Weight (kg)	69 ± 9	69 ± 9	0.690
Hypertension (%)	14 (47)	18 (60)	0.301
Diabetes Mellitus (%)	4 (13)	2 (7)	0.389
Preoperative pulmonary function test			
FVC (L)	2.7 ± 0.3	2.8 ± 0.2	0.531
FEV ₁ (L)	2.2 ± 0.3	2.2 ± 0.2	0.781
FEV ₁ /FVC (%)	81 ± 4	71 ± 5	0.650
Intraoperative crystalloid (ml)	2300 ± 850	2500 ± 800	0.251
Intraoperative colloid (ml)	940 ± 180	990 ± 190	0.305
Operation time (min)	238 ± 31	249 ± 44	0.284

Values are number (proportion) or mean ± SD. FVC: forced vital capacity, FEV₁: forced expiratory volume in one 1 second, RM: recruitment maneuver.

Table 2. Data of Pulmonary Variables

	T1	T2	T3	T4	T5	T6
PaO ₂ (mmHg)						
Control	226 ± 48	222 ± 38	204 ± 47	193 ± 35	188 ± 41*	211 ± 39
RM	214 ± 55	210 ± 43	217 ± 39	219 ± 33 [†]	214 ± 42 [†]	224 ± 41
Cdyn (ml/cmH ₂ O)						
Control	33.8 ± 5.4	23.7 ± 4.8*	21.5 ± 3.6*	21.3 ± 4.3*	22.4 ± 5.7*	33.5 ± 6.9
RM	36.9 ± 6.7	24.5 ± 5.1*	22.1 ± 3.5*	22.0 ± 4.3*	22.3 ± 5.0*	36.0 ± 5.7
Cst (ml/cmH ₂ O)						
Control	51.9 ± 7.1	34.3 ± 9.1*	31.8 ± 9.5*	29.2 ± 5.6*	30.7 ± 8.3*	48.9 ± 6.0
RM	55.5 ± 9.7	33.7 ± 8.4*	31.4 ± 8.0*	31.4 ± 7.9*	33.2 ± 8.5*	52.0 ± 7.4

Values are mean ± SD. T1: 10 min after induction of anesthesia, T2: 10 min after establishing pneumoperitoneum, T3: 10 min after establishing Trendelenburg position, T4: 10 min after recruitment maneuver, T5: 60 min after recruitment maneuver, T6: 10 min after deflation in the supine position. RM: recruitment maneuver, PaO₂: arterial oxygen tension, Cdyn: dynamic lung compliance, Cst: static lung compliance. *P < 0.05 compared with T1. [†]P < 0.05 compared with the Control group.

Table 3. Hemodynamic Data

	T1	T2	T3	T4	T5	T6
mBP (mmHg)						
Control	83 ± 10	96 ± 11*	91 ± 9*	86 ± 10	83 ± 11	86 ± 15
RM	81 ± 11	96 ± 11*	93 ± 11*	86 ± 9	83 ± 9	81 ± 12
Heart rate (beats/min)						
Control	63 ± 9	66 ± 8	62 ± 9	60 ± 9	60 ± 8	62 ± 7
RM	60 ± 5	62 ± 9	61 ± 9	59 ± 8	57 ± 5	61 ± 9
CVP (mmHg)						
Control	11 ± 2	17 ± 3*	15 ± 3*	14 ± 4*	13 ± 3	12 ± 3
RM	10 ± 3	17 ± 5*	16 ± 5*	15 ± 5*	13 ± 5	11 ± 3
CI (L/m ² /min)						
Control	2.8 ± 0.9	3.2 ± 0.8*	3.4 ± 0.8*	3.3 ± 0.8*	2.9 ± 0.9	2.9 ± 0.9
RM	2.5 ± 0.7	3.0 ± 0.7*	3.2 ± 0.6*	3.1 ± 0.7*	2.7 ± 0.8	2.6 ± 0.7
SVV						
Control	10 ± 3	6 ± 2*	7 ± 3	9 ± 2	10 ± 3	10 ± 4
RM	9 ± 3	7 ± 3	8 ± 2	8 ± 2	8 ± 2	9 ± 2
ScvO ₂ (%)						
Control	78 ± 6	82 ± 6	81 ± 7	80 ± 8	78 ± 7	76 ± 8
RM	80 ± 7	84 ± 6	84 ± 7	83 ± 7	81 ± 7	78 ± 9

Values are mean ± SD. T1: 10 min after induction of anesthesia, T2: 10 min after establishing pneumoperitoneum, T3: 10 min after establishing Trendelenburg position, T4: 10 min after recruitment maneuver, T5: 60 min after recruitment maneuver, T6: 10 min after deflation in the supine position. RM: recruitment maneuver, mBP: mean blood pressure, ScvO₂: central venous oxygen saturation, CVP: central venous pressure, CI: cardiac index. *P < 0.05 compared with T1 (baseline value).

Table 4. Postoperative Clinical Data

	Control (n = 30)	RM (n = 30)	P value
PaO ₂ in PACU (mmHg)	102 ± 34	112 ± 36	0.296
Acute lung injury (n)	7	4	0.317
PACU stay (min)	30 ± 6	28 ± 5	0.337
Hospital stay (day)	12 ± 2	12 ± 2	0.764

Values are number or mean ± SD. RM: recruitment maneuver, PACU: post-anesthetic care unit.

found to be significantly higher without hemodynamic disturbances in the RM group. However, this beneficial effect on the oxygenation did not last long, as there were no statistical differences between the two groups 2 hours after the RM. Additionally, there were no statistical differences between the groups in the other pulmonary variables, including the dynamic and static compliances.

In the last few decades, it has been demonstrated that a lower V_T and higher PEEP levels are beneficial to the protection of the lung function and the improvement of the clinical outcomes in patients who require mechanical ventilation in various settings,

including management in intensive care units and during different surgical procedures [11,12]. It has been reported that a single application of 40 cmH₂O for 8 s was sufficient to prevent postoperative atelectasis after anesthetic induction in normal-weight patients [13], and that RMs with a PEEP of 10 cmH₂O significantly improved their intraoperative pulmonary mechanics and oxygenation [14]. However, data on the use of RMs in surgical patients with healthy lungs, particularly in those ventilated with a protective ventilatory strategy, remain insufficient. Consequently, our study investigated whether a single RM could be beneficial to the systemic oxygenation and pulmonary mechanics of healthy patients ventilated at lower V_T levels (6 ml/kg) and higher PEEP levels (15 cmH₂O).

A recent review article demonstrated that RM improved the oxygenation and lung mechanics of patients with acute respiratory distress syndrome (ARDS) [15]. The conclusions of this review echoed those of other studies that demonstrated that RM improved arterial oxygenation, although the benefit was rapidly lost [16,17] or was only sustained for a few hours [18,19]. The post-RM PEEP level may have been the cause of these conflicting results. It has been reported that 15 cmH₂O may be the proper PEEP level for retention of the RM benefits, whereas 5 cmH₂O was insufficient and resulted in a prompt loss of the benefit [20]. On that basis, we chose to apply a PEEP level of 15 cmH₂O in order to maximize the beneficial effect of the RM in this study. However, a recent clinical study demonstrated that a high PEEP level (12 cmH₂O) increased the intraoperative PaO₂ without hemodynamic instability, but not the postoperative PaO₂ [21]. In addition, a recent meta-analysis [22] reported that a higher PEEP level with or without RM during the intraoperative period led to a decrease in the development of lung injuries, including pulmonary atelectasis and infection. Moreover, although the application of PEEP at 8–10 cmH₂O with RM has been reported to improve the lung compliance during surgery [7], a recent study demonstrated that increased PEEP levels (10 cmH₂O) could ameliorate the pulmonary compliance during laparoscopic surgery even without RM [8]. However, the PEEP levels used in these studies were lower than in the current study. These previous findings suggested that the application of a higher PEEP level of 15 cmH₂O to all patients in the current study

would close the gap between the two groups in terms of positive effect of RM on the systemic oxygenation and pulmonary compliance.

Another reason for the minimal or inexistent RM benefits may have been the timing of the RM application. In our study, the RM was conducted 10 min after the establishment of the Trendelenburg position with a pneumoperitoneum, at which point we considered that the lung mechanics and oxygenation would be at their maximal attenuation. However, it has been demonstrated that RM only improves arterial oxygenation when performed early in patients with ARDS. In addition, given that the beneficial effect of a single RM is reportedly insufficient to last [16,17], a recent clinical study suggested repetitive RMs as a way to improve the arterial oxygenation by keeping the alveoli open and improving the aeration [23].

This study was limited by its small sample size. Therefore, although the single RM did not have a beneficial effect on the arterial oxygenation or the respiratory mechanics in our trial, this result is difficult to generalize. Well-powered randomized clinical trials are needed to determine the effect of a RM with protective ventilator support during the intraoperative period more clearly. Indeed, a large-scale multicenter study is presently being conducted to evaluate the effect of higher PEEP levels and RM during surgery on the postoperative complications of adult patients [24].

In conclusion, despite its short-lived nature, a single RM of 40 cmH₂O combined with 15 cmH₂O of PEEP for 40 s improved arterial oxygenation without hemodynamic disturbance in patients with a healthy lung. In addition, this transient benefit did not lead to the amelioration of the lung mechanics or to better clinical outcomes such as shorter hospital stays. Well-powered randomized multicenter trials should be conducted to validate the use of RM with a lung protective ventilation strategy in surgical patients.

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