

Pressure-Controlled Inverse Ratio Ventilation during General Anesthesia for Open Abdominal Surgery Improves Postoperative Pulmonary Function

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Abstract

Background: Studies have shown that pressure-controlled ventilation improves alveolar gas distribution. And inverse ratio ventilation has advantages of improving oxygenation in acute respiratory distress syndrome (ARDS) patients. However, the effects that pressure-controlled inverse ratio ventilation in patients undergoes endotracheal intubation general anesthesia have not been assessed. **Objective:** To investigate whether pressure-controlled inverse ratio ventilation (PIV) would improve ventilatory and oxygenation parameters as well as lung function compared to conventional ventilation in patients undergoing open abdominal surgery. **Interventions:** In the conventional ventilation (CV) group, the ventilation strategy involved zero end-expiratory pressure and volume-controlled ventilation. In the pressure-controlled inverse ratio ventilation (PIV) group, the strategy involved P high starting at 7 cm H₂O, P low starting at 4 cm H₂O, T high at 4 s, T low at 2 s, and an inspiratory-to-expiratory time ratio of 2:1. The ΔP value was adjusted according to V_T . Pressure levels were increased by 2 cm H₂O until a maximal V_T was observed. Inspired oxygen fraction (FIO₂) was 1.0 and tidal volume (V_T) was 6 mL/kg in both groups. **Main Outcome Measures:** The primary outcome is pulmonary function tests. Hemodynamic, ventilatory and oxygenation parameters were measured; visual analog scale (VAS) scores, and nausea and vomiting scores were also measured. **Results:** The PIV group tolerated pressure-controlled inverse ratio ventilation without significant hemodynamic instability. Mean airway pressure and static compliance were significantly higher in the PIV group than those in CV group ($P < 0.05$). Patients in the PIV group showed better pulmonary function test results on postoperative day 1 ($P < 0.05$). VAS and nausea and vomiting scores did not differ significantly between the two groups. **Conclusion:** Pressure-controlled inverse ratio ventilation during open abdominal surgery lasting >2 h was well tolerated and improved respiratory compliance and lung function on the first postoperative day.

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Keywords

Inverse Ratio Ventilation, Conventional Ventilation, General Anesthesia, Lung Function

1. Introduction

The induction of general anesthesia fosters reduced lung volume and atelectasis formation associated with deteriorated gas exchange and respiratory mechanics [1]-[4]. Pressure-controlled ventilation and inverse ratio ventilation are all modes of mechanical ventilation which are best described as partial ventilatory support and based on the management of patients with the adult respiratory distress syndrome (ARDS) [5] [6]. Minimizing the risk of ventilator-induced lung injury (VILI), improving oxygenation and alveolar recruitment are all advantages of inverse ratio ventilation. Although they have advantages in ventilating patients with ARDS, few studies investigated their use during operative mechanical ventilation [7]-[9].

Mechanical ventilation is mandatory in patients receiving general anesthesia with endotracheal intubation, and high tidal volumes may over distend noninjured lungs. During surgical procedures, both general anesthesia and high tidal volumes may strain noninjured lungs and trigger inflammation [10] [11]. By using a small tidal volume (V_T) with positive end-expiratory pressure (PEEP), pressure-controlled inverse ratio ventilation (PIV) may be potential protective ventilation strategy. It has been shown that a small tidal volume (V_T) and PEEP can reduce the incidence of postoperative lung dysfunction and improve intraoperative oxygenation [12]-[15]. However, the potential utility of pressure-controlled inverse ratio ventilation (PIV) has not been studied in patients undergoing general anesthesia. In this exploratory study, we test the hypothesis that PIV improves oxygenation and pulmonary function in patients undergoing open abdominal surgery lasting >2 h.

We hypothesized that in patients with normal lungs scheduled for general anesthesia, PIV might prevent lung function deterioration and lung morphological alterations. Our aim was to investigate the effect of as an intraoperative protective ventilation strategy on oxygenation and pulmonary function tests in this patient population.

2. Materials and Methods

2.1. Patient Data

Patients were recruited between January 2 and November 1 2013 in Shandong Cancer Hospital and Institute. Lung function tests were performed before and after surgery by two blinded physician and anesthesiologists which included the following variable: forced vital capacity (FVC); forced expiratory volume in 1 s (FEV_1); maximal voluntary ventilation (MVV); peak expiratory flow (PEF); forced expiratory flow 25% - 75% ($FEV_{25\%-75\%}$). ALL of the data and follow-up notes were recorded by the anesthesiologists.

The entire protocol (201301102) was approved by the Ethics Committee of Shandong Provincial Cancer Hospital (Chairperson Dr. Shaoping Wang) and written informed consent was obtained from each patient before the study was performed. Exclusion criteria included significant pulmonary disease with obstructive or restrictive pulmonary disease, active asthma, previous lung surgery, home oxygen therapy, significant cardiac dysfunction (left ventricular ejection fraction < 40%), or a body mass index > 35 $kg \cdot m^{-2}$. A total of 60 patients aged 20 - 60 years with an American Society of Anesthesiologists (ASA) physical status grade 1 - 2 who underwent open abdominal surgery were recruited into this study and randomly divided into the pressure-controlled inverse ratio ventilation (PIV) or conventional ventilation (CV) group.

2.2. Anesthesia and Surgery

A standardized anesthesia technique was used in both groups. Anesthesia was induced with propofol (2 - 3 mg/kg), fentanyl (1 - 2 $\mu g/kg$), and rocuronium (0.8 mg/kg) and maintained with propofol (5 - 10 mg/kg/h) or sevoflurane (inspiratory concentration 1.5% - 2%). Analgesia was provided with continuous remifentanyl (0.05 - 0.3 $\mu g/kg/min$) or fentanyl (1 - 3 $\mu g/kg$) as required. Rocuronium was administered every 40 min, and the last administration was at least 1 h before the end of the surgical suturing. In addition to the standard ASA monitors, arterial pressure was measured via a radial artery catheter in all patients. A central venous line was inserted in all patients. Standardized fluid management consisted of 10 mL/kg lactated Ringer solution preoperatively followed

by 6 mL/kg/h perioperatively. Hypotension (mean arterial pressure \leq 60 mmHg) was treated with either ephedrine 5 mg IV or phenylephrine 100 μ g IV. After emerging from anesthesia, all patients received IV patient-controlled analgesia (fentanyl 1500 μ g + ketorolac 180 mg + normal saline 64 mL: bolus, 1 mL; lockout time, 15 min; basal infusion, 1 mL/h).

2.3. Study Protocol of Each Ventilator Strategy

Concealed randomization was conducted to ensure fair intergroup comparisons. To select patients for treatment, we generated a randomization list using Random Allocation Software (Windows version 1.0, May 2004, Saghaei, BioMed Central Ltd.; allocation ratio, 1:1) and inserted the group identifying paper into envelopes that were then sealed and clouded to not reveal the allocation.

The ventilation protocol consisted of volume-controlled mechanical ventilation (CV group) and pressure-controlled inverse ratio ventilation (PIV group) (Aestiva/5 Advance Ventilator Datex-Ohmeda, Madison, WI, USA) and a respiratory rate adjusted to normocapnia (end-tidal carbon dioxide partial pressure, 30 - 40 mmHg). In the CV group, the FIO₂ was 1.0, the ventilator included a V_T 6 mL/kg ideal body weight, and a PEEP was set at 0 cm H₂O (actual PEEP was \sim 2.5 cm H₂O due to the intrinsic PEEP of the mechanical ventilator). In the PIV group (SIMV-PC, P support = 0, inspiratory-to-expiratory [I:E] time ratio = 2:1), the ventilation settings after tracheal intubation were V_T 6 mL/kg ideal body weight, and P high started at 7 cm H₂O, P low started at 4 cm H₂O, T high was set at 4 seconds, and T low was set at 2 seconds. The Δ P was adjusted according to V_T. Pressure levels were increased by 2 cm H₂O until a rational V_T was observed. After tracheal intubation, the patients were randomly assigned to the CV or PIV group.

The anesthesiologists were allowed to change the ventilation protocol at any point on the surgeon's request or if there was any concern about patient safety.

2.4. Measurements

Heart rate, systolic arterial pressure, and diastolic pressure were detected before anesthesia (T₀) and 10 min (T₁), and 60 min (T₂) after onset of mechanical ventilation. Baseline arterial blood gases were obtained at 5 min after anesthetic induction and at 60 min after tracheal intubation in both groups. During mechanical ventilation, the magnitude of the peak, mean airway pressure (P_{mean}), V_T, and respiratory rate were obtained directly from the ventilator and recorded. The compliance of the respiratory system was calculated as V_T/(plateau pressure of the respiratory system-PEEP). Before and after surgery, pulmonary function tests were performed at the bedside using a spirometer while the patient was in a comfortable seated position. The forced expiratory volume in one second (FEV₁), forced vital capacity (FVC), peak expiratory flow (PEF), maximal voluntary ventilation (MVV), and forced expiratory flow 25% - 75% (FEF_{25%-75%}) values were measured. We also calculated the predicted values of the pulmonary function tests according to Quanjer *et al.* [14]. Visual analog scale (VAS) pain score was obtained by an attending physician who was blinded to the study. Nausea and vomiting was scored on a scale of 1 - 4 (1, no nausea or vomiting; 2, nausea without vomiting; 3, less than two times vomiting; 4, more than two times severe vomiting) [16] [17].

2.5. Statistical Analysis

Student's *t* test, the Mann-Whitney U test, or the chi-square test was used to analyze patients' baseline characteristics as continuous variables. The Pearson χ^2 or Fisher's exact test was used to examine categorical variables. Data obtained with linear mixed model analysis are presented as $\bar{x} \pm s$. *P* values $<$ 0.05 were considered statistically significant. All statistical analyses were performed using the Statistical Package for the Social Sciences 12.2.2 (SPSS, Chicago, IL, USA).

3. Results

Sixty consecutive patients who were scheduled to undergo an elective surgical procedure $>$ 2 hr were screened. Four patients were excluded from the final analysis because the initial surgical procedure was converted by the surgeon into another shorter ($<$ 2 hr) or longer procedure ($>$ 4 hr). A total of 56 patients completed the study protocol. There were no major differences between groups with regard to baseline characteristics or hemodynamic or operational data (Table 1 and Table 2). However, there were significant differences in respiratory com-

pliance and P_{mean} between the two mechanical ventilation strategies ($P < 0.05$). The other respiratory parameters did not differ between the two study groups (Table 3). VAS and nausea and vomiting scores did not differ significantly between the two groups (Table 4). In the CV group, FVC, FEV₁, MVV, PEF, and FEF_{25%-75%} values decreased from the preoperative to the first postoperative measurement. Spirometric values on the first postoperative day were lower in the CV group than in the PIV group ($P < 0.05$); however, the values no longer differed significantly on postoperative day 3. In the PIV group, there was no reduction in any of the spirometric variables in the first and third postoperative measurements compared to the preoperative measurements (Table 5).

Table 1. Patient characteristics and surgical details.

	CV group (n = 28)	PIV group (n = 28)
Age, yrs	49 ± 9	48 ± 10
Sex, M/F	14/14	13/15
BMI, kg/m ²	24.8 ± 4.1	24.0 ± 4.6
Type of surgery		
Renal	5	2
Hepatic	4	1
Gastrointestinal	16	20
Other	3	5
Duration of operation, min	183 ± 63	180 ± 57
Duration of anesthesia, min	190 ± 60	201 ± 51
Blood loss, mL	240 ± 130	321 ± 201
Amount of fluid, mL	1576 ± 117	1502 ± 121
Urine output, mL	312 ± 108	321 ± 112

Data are expressed as mean ± SD or no. of patients. CV group = volume-controlled ventilation; PIV group = pressure-controlled inverse ratio ventilation; BMI = body mass index; M = male; F = female. There was no significant difference between two groups in baseline and perioperative characteristics ($P > 0.05$).

Table 2. Hemodynamic data (mean ± SD).

	CV group (n = 28)			PIV group (n = 28)		
	T ₀	T ₁	T ₂	T ₀	T ₁	T ₂
SBP, mmHg	132 ± 17	128 ± 16	122 ± 18	140 ± 20	130 ± 19	127 ± 16
DBP, mmHg	75 ± 9	70 ± 14	73 ± 10	74 ± 11	71 ± 9	68 ± 11
HR, bpm	66 ± 10	64 ± 11	70 ± 10	61 ± 11	64 ± 9	61 ± 9

SBP = systolic blood pressure; DBP = diastolic blood pressure; HR = heart rate. Hemodynamic variables were no significant difference between two groups during surgery ($P > 0.05$).

Table 3. Respiratory parameters of the two mechanical ventilation approaches (mean ± SD).

	CV group (n = 28)	PIV group (n = 28)
P_{max} , mmHg	16.17 ± 4.23	15.64 ± 3.81
P_{mean} , mmHg	6.43 ± 1.21	12.23 ± 2.04*
CL, mL·mm·Hg ⁻¹	28.37 ± 9.51	53.03 ± 11.91*
PaO ₂ , mmHg	101 ± 13	110 ± 14

* $P < 0.001$, compared with V-C group; P_{max} = maximal airway pressure; P_{mean} = mean airway pressure; CL = respiratory compliance; PaO₂ = arterial partial pressure of oxygen.

Table 4. VAS and N & V scores (mean \pm SD).

	CV group (n = 28)		PIV group (n = 28)	
	PO day 1	PO day 3	PO day 1	PO day 3
VAS score	2.1 \pm 0.97	3.7 \pm 1.31	2.3 \pm 1.01	3.2 \pm 1.21
N & V score	1.31 \pm 0.50	1.3 \pm 0.61	1.14 \pm 0.36	1.31 \pm 0.47

VAS = Visual analogue scale; N & V = nausea and vomiting; PO = postoperative. VAS score and N & V score were no significant difference between two groups postoperatively ($P > 0.05$).

Table 5. Spirometric test data (mean \pm SD).

	CV group (n = 28)			PIV group (n = 28)		
	Pre	PO day 1	PO day 3	Pre	PO day 1	PO day 3
FVC, L	3.29 \pm 0.47	2.14 \pm 0.56 [#]	2.82 \pm 0.78	3.28 \pm 0.91	2.91 \pm 0.89	2.82 \pm 0.87
FEV ₁ , L	2.85 \pm 0.45	1.87 \pm 0.33 [#]	2.51 \pm 0.43	2.68 \pm 0.71	2.46 \pm 0.73	2.53 \pm 0.85
MVV, L	99.02 \pm 21.53	65.17 \pm 10.89 [#]	98.37 \pm 13.67	97.34 \pm 30.56	85.21 \pm 30.23	89.57 \pm 38.78
PEF, L/min	322.01 \pm 85.50	208.04 \pm 56.19 [#]	306.17 \pm 87.34	314.14 \pm 90.36	289.71 \pm 88.47	290.01 \pm 90.08
FEV _{25-75%} , L/s	3.21 \pm 0.58	2.02 \pm 0.87 [#]	3.12 \pm 0.18	3.29 \pm 0.91	2.76 \pm 1.09	2.92 \pm 1.18

* $P < 0.05$, compared with preoperative values; # $P < 0.05$, compared with the PV group; FVC = forced vital capacity; FEV₁ = forced expiratory volume in 1 s; MVV = maximal voluntary ventilation; PEF = peak expiratory flow; FEV_{25%-75%} = forced expiratory flow 25% - 75%; PO = postoperative.

4. Discussion

The main finding of this study was that compared with a conventional approach to intraoperative ventilation, PIV improved intraoperative pulmonary compliance without changing hemodynamics. These effects on respiratory compliance were associated with better pulmonary function test results on postoperative day 1.

Mechanical ventilation may induce VILI because it can deteriorate pre-existing lung injuries or even injure healthy lungs. Various VILI mechanisms are possible: regional alveolar overdistension by high airway inflation pressures as well as large volumes (volutrauma) [15] and increased shear forces generated by cyclic alveolar collapse–reopening (atelectrauma) [18]. Both these mechanisms can lead to biotrauma and induce local and systemic inflammatory responses [16] [17]. Accordingly, a lung protective ventilation strategy consists of low V_T ventilation, permissive hypercapnia, and open lung ventilation [19]–[22]. However, these support techniques have undergone an impressive evolution within the last two decades and have been used in critical care medicine for the treatment of ALI and ARDS. Judging by the data from the past few decades, it remains unclear how lung injury can be prevented in patients without a pre-existing lung injury.

PIV was not the first application as mechanical ventilation in operation [7]–[9]. The difference between PIV and biphasic positive airway pressure is that the latter does not use inverse I:E ratios. In our study, we used pressure-controlled ventilation and set P high, P low, T high, and T low values in the ventilator. We also set an I:E ratio of 2:1. A higher mean airway pressure was required to maintain lung expansion, and we were concerned that the hemodynamic consequences would not be well tolerated in these patients with PIV. However, no statistical differences in hemodynamics were seen between the groups. No episodes of acute hemodynamics occurred during surgery, which suggests that this strategy was well tolerated.

In our study, we used PIV to ventilate patients, which were different from conventional volume ventilation that limited recruitment to brief cyclical intervals at end-inspiration or plateau pressure, and may produce recurrent shear forces and increased the potential lung injury [23]. PIV is essentially pressure-controlled ventilation. Inspiratory pressure results in alveolar ventilation and increases lung volume, while expiratory pressure like PEEP keeps lung open. Alveolar recruitment is a dynamic phenomenon; therefore, adequate transalveolar pressure may be needed to re-open collapsed alveoli, while continuous high V_T can also return collapsed alveoli to the ideal open state. Progressive extensions of inspiratory time are critical for sustaining alveolar recruitment [24] [25]. During CV, inspiratory V_T must overcome airway impedance and elastic forces of the restricted lung from

a lower baseline resting volume, increasing the pressure required to distend the lung and chest wall. We used appropriate inspiratory positive pressure and PEEP, making it possible to avoid alveolar collapse and decreased shear forces by applying a near-sustained inflation or recruitment state. Inspiratory reserve volume (IRV) has been proposed for the treatment of patients with ARDS because it may better improve gas exchange than the CV approach. IRV may also improve PaO₂ by extending inspiratory time and increasing mean airway pressure. Studies have shown that only an I:E ratio > 2.0 decreases cardiac output [26]. We found the same results in our study in that the hemodynamics did not differ significantly between the two MV approaches. Since patients with chronic obstructive airway diseases have extensive expiratory time, they were not included in our study.

There are two inflection points on the pressure-volume curve. High-volume lung injury occurs as a result of tidal ventilation above the upper inflection point of the pressure-volume curve. Low-volume lung injuries result from ventilation beginning beneath the lower inflection point, meaning that respiratory compliance should be greatest within these two points. Thus, a small change in transpulmonary pressure will achieve normal V_T [27] [28]. According to this theory, we preset the inflating pressure and PEEP and then regulate both by optimizing V_T. An optimal PEEP can prevent atelectasis and lung injury, but how to best determine it remains unknown. Our data suggested that determining optimal PEEP using the pressure-volume curve could be sensible. In our study, inflating pressure and PEEP were 9.32 ± 2.13 cm H₂O and 5.45 ± 0.97 cm H₂O, respectively, which did not change the hemodynamics in patients without cardiac dysfunction.

The high inspiratory pressure and extension of inspiratory time contribute significantly to the mean airway pressure. Mean airway pressure correlates to mean alveolar volume and is critical for diffusive gas movement. As a result, these parameters control oxygenation and alveolar ventilation. One reason that we did not see an intergroup difference in PaO₂ is that we used 100% oxygen.

Postoperative pain intensity plays a major role in preserving pulmonary function after surgery [29] [30]. In the current trial, the VAS pain and nausea and vomiting scores did not differ significantly between the two MV strategies. However, the PIV group had a better overall mean pulmonary function test results on the first postoperative day. The mechanisms by which PIV exerts its beneficial effect on pulmonary function after anesthesia and surgery are through increases in functional residual capacity (FRC), respiratory compliance and mean airway pressure. We assumed that those three factors may contribute to the better pulmonary function on day 1 in PIV group. Because we chose patients without severe respiratory system disease and the surgery time were less than 4 h, so the pulmonary function test were no different after day 1. Additional studies are needed to prospectively compare PIV and CV and to investigate the clinical role of PIV in anesthesia.

This study has two main limitations. First, we did not have the sample size calculation and we did not examine hospitalization duration or the number of postoperative pulmonary complications. Second, different FIO₂ levels might bring further benefits. As such, further studies are required to explore whether this ventilatory strategy ameliorates clinically relevant outcomes.

5. Conclusion

The use of pressure-controlled inverse ratio ventilation during open abdominal surgery increases mean airway pressure, improves respiratory compliance, and leads to better pulmonary function test results.

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Competing Interests

The authors declare no competing interests.

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