

## The effects of volume-controlled ventilation versus pressure-controlled ventilation on hemodynamic and respiratory parameters in patients undergoing lumbar spine fusion surgery: a randomized controlled trial

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**Background:** Hypotension is a common event in patients under general anesthesia during lumbar spine fusion surgery. The reduction of venous drainage followed by the postural changes is the main reason. The venous return reduced when the intrathoracic pressure is positive. Volume-controlled ventilation (VCV) and pressure-controlled ventilation (PCV) are two traditional ventilation modes in operating room, with different respiratory mechanics. The two ventilation modes have different influences on intrathoracic pressure and consequently venous return. A double-blinded, randomized, parallel group controlled clinical trial was conducted to examine the hemodynamic and respiratory effects of two different ventilation modes in lumbar spine fusion surgery.

**Methods:** Forty-eight patients scheduled for posterior lumbar spine fusion surgery at Zhongda Hospital, Southeast University were randomly allocated into two groups to receive either the VCV mode or PCV mode [vital volume ( $V_T$ ) 8 mL/kg, and partial pressure of end-tidal carbon dioxide ( $P_{ET}CO_2$ ) 35–45 mmHg]. The respiratory mechanics [peak airway pressure (Ppeak) and dynamic compliance (Cdyn)] and hemodynamic changes were measured every 10 min for 120 min. All participants and relevant staff were blinded to the randomization.

**Results:** The data of 19 of 22 patients in the VCV group and 18 of 20 in the PCV group were analyzed. Compared to VCV group, cardiac output (CO) and central venous pressure (CVP) in the PCV group were higher; however, the difference was not significant. There's no statistically difference in systemic vascular resistance index (SVRI) values of both the groups. The mean blood pressure (MBP) of the PCV group was higher than that of the VCV group from 90 min after the patients were turned to the prone position until the endpoint. The Cdyn and Ppeak of the PCV group were higher than those of the VCV group. Additionally, there was a positive correlation between Cdyn and CO (r=0.744, P=0.006).

**Conclusions:** With better respiratory mechanic and hemodynamic stability, PCV was a better choice for patients undergoing lumbar spine fusion surgery.

Trial Registration: Chinese Clinical Trial Registry ChiCTR-TRC-14005086.

**Keywords:** Hypotension; pressure-controlled ventilation (PCV); volume-controlled ventilation (VCV); hemodynamic variables; respiratory mechanics

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### Introduction

The prone position provides a better operation view for lumbar spine fusion surgery, and general anesthesia enables better control of the airway and the precise management of hemodynamics. The prone position is not a physical position; when a patient is turned to the prone position under general anesthesia, a frame is needed to support the torso. This positions the heart on top of the body and compresses the chest and belly, which has been shown to compress partial inferior vena cava (1), decrease the venous return (2,3) and reduce the preload of the left ventricular, cardiac index (CI) and stroke volume (SV) (4,5). The abdomen hangs freely to prevent abdominal viscera from compromising the diaphragm movement, which also decreases dynamic compliance (Cdyn) and increases peak airway pressure (Ppeak) (2,6,7), exaggerating the hemodynamic changes associated with respiration (8).

The classic ventilation mode, volume-controlled ventilation (VCV), has been used for many years with a constant flow to deliver a target tidal volume and thus ensure satisfactory minute ventilation; however, VCV mode causes high airway pressure levels when chest compliance decreased, such as in obese patients (9) and lead to ventilation induced lung injury. Pressure-controlled ventilation (PCV) is an alternative mode of mechanical ventilation. By limiting the inspiratory pressure, it can reduce the risk of barotrauma and volutrauma. It also ensures that collapsed alveoli open up by extending the inspiratory time using adequate positive end expiratory pressure (PEEP) levels (10). For some cases, there's no big difference between the two ventilation modes. However, when the following situations occur, researchers cautiously recommend changing the ventilation settings from VCV to PCV: (I) when VCV increases the tidal volume and fails to deliver a targeted vital volume  $(V_T)$ ; and (II) when VCV fails to improve hypoxemia and produces an extremely high airway pressure (11). Additionally, PCV has been show to provide a lower Ppeak and a higher mean airway pressure (12). Finally, PCV can reduce intrathoracic pressure and pulmonary vascular resistance, thereby improving right ventricular function (13).

Hypotension rates are high among patients under general

anesthesia undergoing lumbar spine fusion surgery (4). The maintenance of the prone position requires a Wilson frame to support the torso, which places the extremities on the bottom of the body and compresses the chest and abdomen. In the event of inferior cava vein obstruction, the venous return largely decreases, reducing the cardiac output (CO), which is considered the main reason for hypotension in the prone position (4). Positive pressure ventilation further reduces CO (14). When a patient is turned to the prone position, airway pressure increases and chest wall compliance decreases, and there is a subsequent rise in intrathoracic pressure that further reduces the venous reflux. VCV is conventionally applied by anesthetists in operating rooms. But anesthetists had to set the  $V_T$  to a higher value to make sure adequate ventilation the prone position when there's a decrease in chest wall compliance, which increases airway pressure. PCV has proven to be better than VCV, and has a number advantages, including a lower Ppeak, higher Cdyn and better oxygenation for surgical patients (15). However, no study has examined the effects of different ventilation patterns on hemodynamics in patients undergoing lumbar spine fusion surgery during the whole period of operation. We hypothesized that VCV and PCV would have different hemodynamic effects in the prone position. We sought to find a better ventilation mode to reduce the occurrence of hypotension during lumbar spine fusion surgery. Specifically, this double-blind, randomized clinical trial sought to identify the hemodynamic changes caused by different ventilation patterns in the prone position. We present the following article in accordance with the CONSORT reporting checklist (available at https://dx.doi.org/10.21037/apm-21-1932).

### **Methods**

### Study design

This study, which was a prospective, randomized, parallel group controlled trial, was conducted at the Zhongda Hospital, Medical College of Southeast University, Nanjing, China. Participant recruitment was started in July 2014, and was planned to be finished within 1 year. Patients were classified as having a physical status of I or II according to the American Society of Anesthesiologist (ASA) classification. Patients who were scheduled to have 1- or 2-level lumbar space fusion surgery were recruited to participate in this study, and written informed consent was obtained from the patients before the surgery. Patients who had severe systematic disease, such as coronary heart disease, or who were older than 75 years or younger than 18 years were excluded from the study. The patients were randomly allocated into the following two groups (allocation ratio was close to 1:1) in which different ventilation modes were used after endotracheal intubation: (I) the VCV group; and (II) the PCV group. All surgical procedures were performed by an experienced spine surgeon.

### Ethics

All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Independent Ethics Committee (IEC) for Clinical Research of Zhongda Hospital, Medical School of Southeast University (No.: 2014ZDSYLL076.0) and informed consent was taken from all the patients. And this study was registered in the Chinese Clinical Trial Registry with the identifier ChiCTR-TRC-14005086.

### Informed consent

A member of the research team visited the patients the day before surgery day, if a patient and/or a patient's guardian both agreed to the patient's participating in the research, a written informed consent was obtained. If either the patient or the patient's guardian declined consent, the patient was not entered into the study. All members of the research team were trained in obtaining informed consent in accordance with good clinical practice.

### Study population

## Selection and withdrawal of participants *Recruitment*

Participants were identified and recruited from the orthopedic wards by one investigator. The investigator informed the recruiters of all aspects. The intervention started immediately after the completion of endotracheal intubation. The medical records were reviewed following hospital discharge for in-hospital complications or hospital stays.

### Inclusion criteria

All patients' physical status were ASA I–II. Patients who were scheduled to receive lumbar spine surgery at the Zhong Da Hospital, Southeast University and who were older than 18 years and younger than 70 years were included in the study if their preoperative magnetic resonance imaging showed 1–2 lumbar disc displacements.

## Exclusion criteria

Patients who had severe cardiopulmonary, hepatic, renal disease, or other organ failure, those elder than 75 years old, with a body mass index (BMI)  $\geq$ 30 kg/m<sup>2</sup>, albumin  $\leq$ 30 g/L, or hyperbaric oxygen  $\leq$ 70 g/L were excluded from the study.

### **Randomization and blinding**

All patients were randomly allocated by a computergenerated list of random numbers to receive either VCV or PCV by a technician using a simple randomization method. The allocation sequence was sealed in sequentially numbered, opaque envelopes by a research assistant (Assistant A). Another research assistant (Assistant B) was the only person who received the envelopes on the day of surgery. This research assistant (Assistant B) set up the ventilation mode after endotracheal intubation. All the patients, surgeons, anesthetists, and research assistants who collected the data through the surgery were blinded to the randomization.

### Primary endpoint

The primary endpoint was mean blood pressure (MBP). The primary purpose of this study was to investigate whether VCV and PCV affected MBP differently in patients on the prone position under general anesthesia undergoing lumbar spine surgery, because MBP was closely related to the infusion of organs and tissues. The other hemodynamic variables were central venous pressure (CVP), CO, and the systemic vascular resistance index (SVRI). For both groups, the  $V_T$  was set to 8 mL/kg (of the ideal body weight) without any PEEP, and the initial inspiration pressure of the PCV group was given according to the plat pressure of the VCV of the same patient. The inspiration-to-expiration ratio (I:E) was 1:2, and the respiratory rate (RR) was adjusted to maintain the partial pressure of end-tidal carbon dioxide ( $P_{ET}CO_2$ ) between 35–45 mmHg. Cdvn and Ppeak were recorded by a research assistant. Cdyn of the respiratory system was calculated as  $V_T$ /(Ppeak – autoPEEP). AutoPEEP was measured by an

anesthetic machine (Dragor, Germany). The hemodynamic and respiratory variables were recorded at 10min after the induction of the general anesthesia (Tsupine), 10 min after the patient was turned to the prone position and every 10 min thereafter for 120 min (Tprone10, Tprone20, ..., Tprone120), and then 10 min after the patient was turned to the supine position again (Tsupine2).

## Secondary endpoints

The secondary endpoints were the ventilation mechanic variables, including the Ppeak and Cdyn of both groups. The secondary purpose of this study was to identify the effects of different ventilation patterns in relation to respiratory variables, the occurrence of pulmonary and nonpulmonary side effects, and hospital stay.

## Anesthesia protocol

Electrocardiogram, non-invasive blood pressure, oxygen saturation (monitor, M8005A, Philips Medizin Systeme Boeblingen GmbH) and bispectral index (BIS) value (BIS monitor, Philips, Mansfield, USA; software version 3.3) were measured after the patient was shifted to the operating bed, and 70-80% oxygen (16) was then administrated for 3 min. Induction of anesthesia was achieved by a combination of intravenous agents, started with midazolam (0.05 mg/kg) followed by propofol (0.5-1 mg/kg), and sufentanil (0.4-0.5 µg/kg) then, cisatracurium (0.15 mg/kg). Endotracheal intubation was completed via a visual laryngoscope (TD-C-III, Zhejiang UE Medical Corp., China) when the BIS value was 40-60. The radial artery and right internal jugular vein were cannulated for MBP and CVP monitoring respectively. CO and SVRI were monitored by FloTrac/ Vigilio (Edwards Lifesciences, Irvine, CA, USA). The axillary temperature was kept at 36-37 °C. Anesthesia was maintained with inhalational sevoflurane (1-1.5%)in oxygen (70-80%) and via the continuous intravenous infusion of propofol (2-4 mg/kg/h) remifentanil (4-10 µg/kg/h), and cisatracurium (0.1-0.15 mg/kg/h). The depth of anesthesia was monitored by the BIS [40-50]. Hydration was maintained with a lactate ringer solution and 5% hydroxyethyl starch (HES) (2:1) (4 mL/kg/h), and one-third was transfused before postural changing. Arterial blood gas analysis was measured at Tprone120. The allocation sequence was sealed in sequentially numbered envelopes. A research assistant received the envelope and opened it on the surgery day. The randomization was

concealed from the patients, surgeons, anesthetists, and research assistants who were responsible for subsequent data collection.

## Study intervention

## Ventilation protocol

For the VCV group,  $V_T$  was set to 8 mL/kg of the ideal body weight, which was calculated by the formula:  $50 + 0.91 \times (\text{height in cm} - 152.4)$  for male, and  $45.5 + 0.91 \times (\text{height in cm} - 152.4)$  for female without any PEEP. The I:E was 1:2, and the RR was adjusted to maintain the  $P_{ET}CO_2$  between 35–45 mmHg. The fraction of inspired oxygen (FiO<sub>2</sub>) was 80%. Patients in the PCV group were ventilated at peak inspiratory pressure (PIP), adjusted to the same tidal volume as the VCV group with no PEEP, and I:E was 1:2. RR was also adjusted to maintain the P<sub>ET</sub>CO<sub>2</sub> between 35–45 mmHg. FiO<sub>2</sub> was 80%. Cdyn and Ppeak were recorded by an assistant. Cdyn of the respiratory system was calculated using the following formula: V<sub>T</sub>/Ppeak - (PEEP + autoPEEP). AutoPEEP was measured by an anesthetic machine (Aestiva/5 7900, Datex-Ohmeda, Inc., USA).

## Length of hospital stay

The mean length of hospital stay was calculated for both groups by a research assistant.

## Reporting of adverse events

All participants were observed for adverse events, and which must be recorded and closely monitored until resolution or stabilization, or until it was otherwise explained. Any serious adverse events were informed to the chief investigator immediately. In cooperation with the treating medical practitioners, they together determined the seriousness and causality of the events. As part of annual reports, the Research Ethics Committee received all treatmentrelated serious adverse events. Within the relevant time frames, unexpected serious adverse events were reported to the Research Ethics Committee The chief investigator was ultimately responsible for the reporting of all adverse events.

# Pulmonary complications and extrapulmonary complications measurements

Major pulmonary complications before discharge were defined as pneumonia, a need for invasive or non-invasive ventilation due to acute respiratory failure, the development

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of postoperative atelectasis, pneumonia, acute lung injury, and acute respiratory distress syndrome, defined according to standard criteria (see Appendix 1). Sepsis was defined as life-threatening organ dysfunction caused by a dysregulated host response to infection (17). Organ dysfunction was identified by an acute change in the total Sequential (Sepsisrelated) Organ Failure Assessment (SOFA) score  $\geq 2$  points consequent to an infection.

Patients with a suspected infection who were likely to have a prolonged stay in the intensive care unit or to die in the hospital were promptly identified at the bedside based on SOFA. Extrapulmonary complications included systemic inflammatory response syndrome (SIRS), sepsis, and septic shock, and surgical complications, such as an intraabdominal abscess, anastomotic leakage, and unplanned reoperation (all defined according to consensus criteria) (18,19).

### Statistical analysis

SPSS 13.0 software (IBM, USA) for Windows was used for all the statistical analyses. All numeric data are expressed as mean ± standard deviation. The demographic data of patients and perioperative variables were compared using a one-way analysis of variance (ANOVA). A two-way repeated measurement of ANOVA was used to determine the difference in the hemodynamics and respiratory variables at the designated points of the study. If there was a significant difference, a multivariant analysis [a least significant difference (LSD) or Bonferroni test] was then used to further compare the different groups in terms of the hemodynamics and respiratory variables at the same time point in the prone position. The correlations between the hemodynamic variables (MBP and CO) and respiratory variables (Cdyn and Ppeak) were revealed by two-tailed Pearson tests. Differences were considered to be statistically significant if the P value was <0.05.

### Sample size and justification

The following sample size formula was used to calculate the sample size:

$$N = \frac{2(u\alpha + u\beta)2\sigma 2}{\delta 2}$$
[1]

A sample size of 16 (with 80% power) was needed to detect a significance level (alpha) of 0.05. Twenty percent additional patients were added to each group to account for dropouts during the follow-up period in the experimental period.

## **Results**

### Demographic and intraoperative information

The study was completed on July 30th, 2015. Ultimately, the VCV group comprised 19 patients and the PCV group comprised 18 patients (see *Figure 1*). No statistical differences were found in age and BSA between the two groups. The operation time, blood loss, infusion volume and BIS values for both groups were comparable (see *Table 1*).

### Hemodynamics in the prone position

There were no differences in heart rate (HR), CVP, CO, and SVRI between the two groups, The MBP of the PCV group was significantly higher than that of VCV group in the prone position (P=0.041; Table 2). In the two groups, patients' MBP, CO, and CVP decreased after the postural change and continued to decrease over time in the prone position, while increased to baseline value (before postural change) or higher than baseline value quickly as long as the patients were placed in the supine position. MBP was significantly higher in patients in the VCV than the PCV group after 90 min in the prone position, but the difference was not statistically significant within 80min. At all the time points in the supine position, CO, CVP, and SVRI were slightly higher in the PCV group, compared to the VCV group; however, the differences were not statistically significant (see Figure 2).

### Respiratory variables in the prone position

There was no difference in  $V_{T}$ ,  $P_{ET}CO_2$ , and autoPEEP between the two groups; however, there were significant differences in Ppeak, Cdyn, and arterial partial pressure of oxygen (PaO<sub>2</sub>)/FiO<sub>2</sub> between the two groups (see *Table 3*). In both groups, Ppeak increased from the supine to the prone position while Cdyn decreased. Ppeak, Cdyn, and PaO<sub>2</sub>/FiO<sub>2</sub> were significantly higher in the PCV group in the supine position than the VCV group (see *Figure 3*).

# The effects of ventilation mode on hemodynamics in the prone position

A Pearson correlation analysis revealed a positive correlation between Cdyn and MAP (r=0.744, P=0.006), a positive correlation between Cdyn and CO (r=0.744, P=0.006), and



**Figure 1** Consort flow diagram. Among 48 patients, 3 were excluded from the study because of pulmonary diseases (2 for asthma and 1 for COPD), and 3 because of morbid obesity. A total of 42 patients were randomly assigned to two groups. Three patients in the VCV group were excluded because of large blood loss and noradrenaline infusion. Two patients in the PCV group were excluded because of the long surgery time and lost data. The data of 19 patients in the VCV group and 18 patients in the PCV group were analyzed. COPD, chronic obstructive pulmonary disease; VCV, volume-controlled ventilation; PCV, pressure-controlled ventilation.

Table 1 Demographic data of patients and intraoperative variables

Characteristics	VCV group (n=19)	PCV group (n=18)	P value
Age (yr)	59.85±11.10	55.35±9.57	0.538
BSA (kg/m²)	1.72±0.16	1.69±0.97	0.053
Hydration (mL)	2,145±654.11	2,129.41±427.95	0.117
Blood loss (mL)	482.50±336.96	294.11±262.72	0.111
Urine (mL)	477.5±336.96	481.17±248.79	0.748
Operative time (min)	170.25±54.95	158.05±36.95	0.255
BIS value	44.99±1.04	44.62±1.04	0.063

Variables are mean ± SD. VCV, volume-controlled ventilation; PCV, pressure-controlled ventilation; BSA, body surface area; BIS, bispectral index.

a negative correlation between Ppeak and MAP (r=-0.725, P=0.008).

### Hospital stay and postoperative complications

In relation to the VCV group, surgical site infection occurred in 1 patient and incision inflammation and drainage occurred in 6 patients. In relation to the PCV group, 1 patient had a urinary tract infection and 2 patients had incision inflammation and drainage. The mean hospital stay of patients was 17 days and 15 days in the VCV and PCV groups, respectively. There was no significant difference in terms of hospital stay between the groups, but hospitalization costs differed (see *Table 4*).

### Discussion

This study demonstrated that compared to VCV, which is

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Parameter	VCV group (n=19)	PCV group (n=18)	P value
HR (bpm)	64.22±2.15	64.18±2.27	0.990
MBP (mmHg)	75.72±2.04	82.21±2.28	0.041
CVP (mmHg)	$5.46 \pm 0.60$	6.44±0.72	0.302
CO (L/min)	3.93±0.12	4.14±0.14	0.296

2,427.41±145

Table 2 Hemodynamic data in the prone position

SVRI

Variables are mean ± SD. VCV, volume-controlled ventilation; PCV, pressure-controlled ventilation; HR, heart rate; MBP, mean blood pressure; CVP, central venous pressure; CO, cardiac output; SVRI, systemic vascular resistance index.

2,478.67±150.47



Figure 2 Hemodynamic changes across all time points. (A) From the supine to the prone position, the MBP decreased in both groups and immediately increased in the supine position. Blood pressure decreased over time in the prone position. The MBP of the PCV group was higher than that in VCV group 90 mins after patients were turned to the prone position (P<0.05). (B) With the posture changed from supine to the prone position, CVP decreased sharply, and increased immediately from the prone to the supine position; there was no difference between the two groups in relation to CVP in the prone position (P>0.05). (C) CO decreased following the postural change to the prone position and also increased in the supine position. There was no difference between the two groups in the prone position (P>0.05). (D) There was no difference in the SVRI between the two groups (P>0.05). Ppeak increased from the supine position to the prone position Cdyn decreased in both groups. MBP, mean blood pressure; PCV, pressure-controlled ventilation; CVP, central venous pressure; CO, cardiac output; SVRI, systemic vascular resistance index; Ppeak, peak airway pressure; Cdyn, dynamic compliance.

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Parameter	VCV group (n=19)	PCV group (n=18)	P value
V <sub>T</sub> (mL)	519.41±14.38	523.39±14.38	0.846
RR (breaths/min)	9.31±0.31	8.42±0.311	0.05
P <sub>ET</sub> CO <sub>2</sub> (mmHg)	34.06±0.79	35.42±0.79	0.232
Ppeak (cmH <sub>2</sub> O)	18.08±0.47	16.13±0.50	0.008
AutoPEEP (cmH <sub>2</sub> O)	3	3	
Cdyn (mL/cmH <sub>2</sub> O)	34.23±1.70	40.74±1.58	0.007
PaO <sub>2</sub> /FiO <sub>2</sub> (mmHg)	435.48±80.54	529.56±120.04	0.006

Table 3 Ventilatory and oxygenation parameters in the prone position

Variables are mean  $\pm$  SD. VCV, volume-controlled ventilation; PCV, pressure-controlled ventilation; V<sub>T</sub>, vital volume; RR, respiratory rate; P<sub>ET</sub>CO<sub>2</sub>, partial pressure of end-tidal carbon dioxide; Ppeak, peak airway pressure; autoPEEP, auto positive end expiratory pressure; Cdyn, dynamic compliance; PaO<sub>2</sub>/FiO<sub>2</sub>, arterial partial pressure of oxygen versus fraction of inspired oxygen.



**Figure 3** Respiratory variables of the two groups. (A) There was an increase in Ppeak in both groups when the patients were placed in the prone position and a decrease in Ppeak the moment the patients were placed in the supine position. The PCV group also had a lower Ppeak than the VCV group across all study time points (P<0.05). (B) There was a decrease in Cdyn in both groups when the postural positions of patients were changed to the prone position, and an immediate increase as soon as the patients were placed in the supine position. The PCV group had a higher Cdyn than the VCV group across all study time points (P<0.05). Ppeak, peak airway pressure; PCV, pressure-controlled ventilation; VCV, volume-controlled ventilation; Cdyn, dynamic compliance.

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Hospitalization and complications	VCV group (n=19)	PCV group (n=18)	P value
Hospital stay (d)	17.6±8.22	15.45±4.48	0.313
Pulmonary complications	0	0	
Extrapulmonary complications			
Surgical site infection	1	0	
Incision inflammation and drainage	6	2	

Variables are mean ± SD. VCV, volume-controlled ventilation; PCV, pressure-controlled ventilation.

commonly applied in the operation room, PCV patients had a lower decrease in MBP, CO, CVP, and Cdyn, also a lower increase in Ppeak in the prone position under general anesthesia. The oxygenation parameters were higher in the VCV group than the PCV group. These results suggest that PCV is optimal in the prone position under general anesthesia.

When a patient is turned to the supine position under general anesthesia while undergoing lumbar spine fusion surgery a frame is needed to prevent crushing injuries in the body. In this study, a Wilson frame was used. The chest and abdomen are partly compressed by the frame, which restricts the movement of the chest-cage and thus compromises pulmonary compliance, increases intrathoracic pressure (2-4) and abdominal pressure (2,5), and compresses the vena cava, which decreases venous return (1). If this leads to a reduction of SV and CO, then hypotension can occur at the moment of postural changing. Similar to the findings of other studies (4,7), in our study, the CO, MAP, and HR of both groups decreased when patients were in the prone position, and increased when their bodies were turned back to the supine position at the end of surgery. Conversely, in Jang's study (20), no differences were observed in terms of MBP, HR, CI, and SVV when patients were placed in either the supine or prone position after general anesthesia. The differences in the results between the two studies may be due to the fact that different body positions and frames were used (21). Jang used a longitudinal bolster frame, and the patient's legs were positioned above the heart. When a patient's upper and lower limbs are positioned lower than the torso, which is what occurred in the present study, the pooling of the intravascular volume occurs in the extremities, which lead to the decrease of preload and SV (4). Our data also demonstrated that PCV provided a lower Ppeak and higher Cdyn in the prone position compared to VCV. Ninety minutes after being placed in the prone position, patients' MBP was also higher in the PCV group than the VCV group. Like Kyhl et al. (14) we also found a negative correlation between Ppeak and CO.

Many studies have described hemodynamic changes with the body postural changed from the supine to the position; however, this was the first study to observe hemodynamic changes continuously in the prone position. In the prone position, Ppeak and Cdyn increased while CVP and MBP decreased with time. Ninety minutes after patients were placed in the prone position, the MBP of patients in the PCV group was significantly higher, compared to VCV group. It may be that for most cases, 90 min was needed to open the spinal canal, the spinal canal was filled with cerebrospinal fluid that bathes the nerves, once the spinal canal was opened, there's loss of cerebrospinal fluid which reduced the intracranial pressure (ICP) immediately, the reduction of ICP caused the reduction of MBP to keep the spine infusion unchanged due to spinal cord pressure autoregulation (22). Alternately, there may have been impaired autonomic nervous function due to the chronic compression of the lumbar spine (23) and the effects of the general anesthesia (8), which prevented compensatory vasoconstriction to hypotension. Besides all mechanisms mentioned above, the cyclic system was vulnerable to pleural pressure changes. The PCV group in this study had a lower Ppeak and higher Cdyn, which led to a higher blood pressure in the PCV group. The cyclic system was less affected by the PCV pattern, compared to VCV pattern in this study settings. We also found that the mean hospital stay of the PCV group was 2 days shorter than that of the VCV group, and incision inflammation and drainage was less in the PCV group then the VCV group; thus, the use of PCV could save medical resources.

Although more novel ventilation mode was available for new generation ventilator, VCV was still the most commonly used ventilation mode in the operating room for most cases (24), but with the popularization of robotic assisted surgery (25) and other situations in which the compliance of the chest wall was decreased, just as the situation in this study, PCV was recommended for its advantages in better Cdyn, lower Ppeak which decreased the ventilation induced lung injury and less influence on cyclic system, maybe beneficial to the stability of the hemodynamics.

A limitation of this study was that there was no measurement of pleural pressure; thus, we do not know if there was any interaction between the respiratory system and the cyclic system in the prone position. As stated above, the mean hospital stay of patients was shorter in the PCV group than the VCV group; however, the sample is too small to draw the conclusion that the PCV pattern is beneficial to the outcomes of patients. Another limitation of this study was that there was no measurement of autonomic nervous function; thus, there is no direct evidence that hypotension occurs due to impaired autonomic nervous function. In conclusion, PCV resulted in lower Ppeak, higher Cdyn, and higher blood pressure than VCV in the prone position.

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## Footnote

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*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by IEC for Zhongda Hospital, Medical School of Southeast University (No.: 2014ZDSYLL076.0) and informed consent was taken from all the patients.

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## Supplementary

Pneumonia was suspected upon the presence of new and/or progressive pulmonary infiltrates on chest radiograph plus two or more of the following criteria:

- Fever  $\geq$  38.5 °C or hypothermia < 36 °C;
- Leukocytosis ≥12,000 white blood cell (WBC)/mm<sup>3</sup> or leukopenia <4,000 WBC/mm<sup>3</sup>;
- Purulent sputum and/or new onset or worsening cough or dyspnea.

Atelectasis was defined as lung opacification with shift of the mediastinum, hilum or hemidiaphragm towards the affected area and compensatory hyperinflation in the adjacent nonatelectatic lung.

Postoperative acute lung injury (PALI) was defined as the presence of: (I) severe oxygenation failure  $(PaO_2/FiO_2 < 300 \text{ mmHg})$ ; (II) diffuse pulmonary infiltrates on chest radiography; and (III) the absence of signs of left heart

failure within the first postoperative week.

The SIRS criteria were (we used the most deranged value recorded after surgery):

- (I) Core temperature >38 °C or <36 °C. (Core temperature was rectal or tympanic). axillary temperatures were used, 0.5 °C were added to the measured value.</p>
- (II) HR >90 beats per minute. If patient had an atrial arrhythmia, record the ventricular rate. If patients have a known medical condition or were receiving treatment that would prevent tachycardia (for example, heart block or beta blockers), they must meet two of the remaining three SIRS criteria.
- (III) RR >20 breaths per minute or a PaCO<sub>2</sub> <32 mmHg (4.3 kPa) or mechanical ventilation for an acute process.
- (IV) WBC count of >12×10 $^{9}$ /L or <4×10 $^{9}$ /L.