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Original Article

Impacts of different ventilation modes on respiratory mechanics, blood gas and hemodynamics in elderly patients with laparoscopic cholecystectomy

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Abstract: In this study, the impacts of different ventilation modes on respiratory mechanics, blood gas and hemodynamics in elderly patients undergoing laparoscopic cholecystectomy (LC) were compared. 60 LC patients were divided into 3 groups: group L (low tidal volume), group L + P (low tidal volume + positive end expiratory pressure) and group C (large tidal volume). Endotracheal intubation was placed immediately after mechanical ventilation. Results showed that the pressure P_{peak} and P_{plat} of the three groups increased after pneumoperitoneum, which increased the most significantly in group C (P<0.05). P_{peak} and P_{plat} further raised with the extension of pneumoperitoneum time in group C (P<0.05). However, alveolar dynamic compliance (Cd) decreased the most significantly in group L + P (P<0.05). $P_{ET}CO_2$ (partial pressure of end-tidal carbon dioxide) increased the most obviously in group L (P<0.05), and it further raised with the extension of pneumoperitoneum time (P<0.05). The pH value was lower after pneumoperitoneumin in group L (P<0.05), and it further decreased with the extension of pneumoperitoneum time (P<0.05). There was significant difference in pH value (P<0.05) and $PaCO_2$ (partial pressure of atrial carbon dioxide) (P<0.05) at the end of surgery compared with that before pneumoperitoneum in group L. It is indicated that the combination of low tidal volume (VT) and low-level PEEP (Positive End Expiratory Pressure) will effectively reduce airway pressure, prevented lung injury and improve the effect of ventilation. Therefore, the combination mode of low tidal volume plus low-level PEEP was considered a safe and effective ventilation method towards elderly patients in laparoscopic surgery.

Keywords: Laparoscopy, elderly, respiratory mechanics, dynamic compliance of lung, blood gas

Introduction

Laparoscopy, a minimally invasive surgery, is the preferred treatment of many diseases currently, the advantages of which such as smaller trauma, fewer complications and quick recovery have been fully recognized [1-3], therefore it has been widely applied in surgery, obstetrics, gynecology, urology, etc. Gallstones and gallbladder polypus are common diseases that frequently occur in patients of all ages. Surgical removal of the gallbladder is an effective clinical treatment. Laparoscopic cholecystectomy has become the preferred surgical treatment for gallstones or gallbladder polypus and is one of the most common surgical worldwide [3]. With the progress of the population aging in our country, more and more elderly patients will be treated under laparoscopy.

Gas is injected into the abdominal cavity to generate artificial pneumoperitoneum, which provides operation space during the procedure. Carbon dioxide (CO_2) is the most commonly used gaseous medium in laparoscopic surgeries for its advantages of cheap, good solubility and easy obtainment [4]. However, the CO_2 pneumoperitoneum could induce a series of impacts on patients [5], such as disrupting the respiratory and circulatory functions, resulting in functional residual capacity reduction, lung compliance decrease, airway pressure increase and alveolar ventilation/perfusion imbalance [6]. It has been reported that the incidence of atelectasis after CO_2 pneumoperitoneum in LC patients increases by 66% averagely than that before pneumoperitoneum [7]. CO_2, which is absorbed by peritoneum, increases $PaCO_2$ (partial pressure of atrial carbon dioxide), followed

Table 1. General information of patients in three groups ($\overline{x}\pm s$, n = 20)

Group	Age	Gender		BMI	Operation time (min)	Pneumoperitoneum time (min)	Intraoperative fluid infusion (ml)
		Male	Female				
L	76.15±4.04	11	9	23.873±2.28	59.15±11.82	47.50±11.05	1013.20±129.80
L + P	75.75±3.89	9	11	24.971±2.45	62.96±11.22	49.15±10.55	1006.50±138.65
C	75.75±3.46	11	9	23.879±2.72	67.60±15.17	52.85±13.60	1026.00±188.08
F (x^2) value	F = 0.074	x^2 = 0534		F = 1.289	F = 2.168	F = 1.076	F = 0.082
P value	0.929	0.766		0.283	0.124	0.348	0.921

Notes: L: low tidal volume, L + P: low tidal volume + positive end expiratory pressure, C: large tidal volume.

by the elevation of $P_{ET}CO_2$ (partial pressure of end-tidal carbon dioxide) and reduction of pH value, thus resulting in the increasing risk of hypercapnia [8].

In order to reduce $P_{ET}CO_2$ and $PaCO_2$, tidal volume is usually large during operation. However, the traditional large tidal volume (VT) ventilation mode may induce mechanical ventilatory lung injury, and can further aggravate lung injury in elderly patients, because lung function and lung compliance in the elderly are declined. Thus, strengthening the lung function protection towards elderly LC patients under general anesthesia is urgently needed. It significantly reduces postoperative pulmonary complications, accelerates postoperative recovery and shortens hospital stay time.

It has been confirmed that alveolar ventilation is better in volume control mode than in pressure control mode in LC [9]. Several meta-analyses have proved that the application of protective lung ventilation strategies such as low VT, low airway pressure and adequate end-expiratory pressure, etc., is able to significantly improve oxygenation and reduce mortality in treatment of respiratory distress syndrome and acute lung injury [10]. Besides, it has been pointed out that in laparoscopic surgeries, the combination of pneumatic re-dilation with PEEP (Positive End Expiratory Pressure) enables the collapsed alveoli to re-dilate and improves the elastic recoil of chest wall and lung [11, 12].

However, the impact of ventilation modes on lung injury and hemodynamic is rarely reported in elderly patients. This study observed the impacts of different ventilation strategies on the respiratory mechanics, blood gas and hemodynamics in elderly patients undergoing laparoscopic cholecystectomy, aiming to seek an ideal clinically safe ventilation model to improve the overall treatment quality, reduce health care costs and improve the prognosis of patients.

Materials and methods

General information

This study was approved by the ethics committee of Gongli Hospital, and the informed consents were signed by patients or relatives. 60 elderly patients aged ≥ 70 years old that experienced elective LC from May 2013 to May 2014 were selected. All subjects had no previous history of chronic lung disease. Preoperative chest images, lung functions and arterial blood gas were normal. Patients receiving immunosuppressive therapy within three months before surgery or with obvious respiratory infection signs were excluded.

60 patients were randomly divided into three groups according to different ventilation modes: group L (low tidal volume), group L + P (low tidal volume + PEEP) and group C (large tidal volume), with 20 patients in each group. The general information of patients in the three groupsis shown in **Table 1**.

Anesthesia

There was no premedication administration in all patients. GE S/5 monitor (GE, Finland) was connected to patients to monitor electrocardiograph (ECG), pulse oxygen saturation (SpO_2) and noninvasive blood pressure (NIBP). Then peripheral vein was opened, and radial artery catheterization was performed to detect blood pressure under local anesthesia, and mean arterial pressure (MAP) was recorded. The induction and maintenance of anesthesia were the same in the three groups. Anesthesia induction: oxygen was provided and nitrogen was eliminated with a mask, followed by intra-

Table 2. Comparison of hemodynamics of the patients among the three groups ($\bar{x}$±s, n = 20)

Variables	Group	T_0	T_1	T_2	T_3	T_4	T_5
HR (beats/min)	L	76.00±8.03	69.85±6.53	72.15±6.08	70.35±4.69	71.20±5.22	84.25±6.25
	L + P	79.00±6.74	71.10±6.91	74.80±5.96	69.95±6.35	70.25±7.26	86.90±6.34
	C	77.20±5.20	69.55±5.06	72.85±4.96	70.10±5.94	70.10±4.86	85.80±5.21
	F	0.998	0.350	1.166	0.025	0.206	1.000
	P	0.375	0.706	0.319	0.975	0.814	0.374
MAP (mmHg)	L	104.47±8.44	92.45±6.59	93.45±5.26	90.33±6.02	91.60±6.30	107.83±8.14
	L + P	103.77±8.59	91.03±6.98	93.85±5.60	91.03±5.70	89.77±7.07	108.82±7.47
	C	102.55±8.24	88.83±6.55	92.12±5.03	87.25±6.32	89.47±7.10	108.05±7.90
	F	0.265	1.476	0.586	2.238	0.572	0.087
	P	0.768	0.237	0.560	0.116	0.568	0.917

Notes: L: low tidal volume, L + P: low tidal volume + positive end expiratory pressure, C: large tidal volume.

venous injection of 0.02~0.03 mg/kg midazolam (Enhua medicine, China), 0.4~0.5 ug/kg sufentanil (YichangRenfu, China), 0.15 mg/kg cis-atracuriumbesylate (Henry medicine, China) and 1~2 mg/kg propofol (Guorui Pharmaceutical Co., Ltd., China). Tracheal intubation was performed when muscles were fully relaxed, and Dräger Primus anesthesia machine (Dräger, Germany) was connected at volume mode to control breathing. Auscultation was performed to confirm that the endotracheal tube was at the correct position. Anesthesia was maintained with continuous pump infusion (Silugao, Beijing, China): 4~10 mg/kg/h propofol, 0.15~0.25 ug/kg/h remifentanil and 0.1~0.2 mg/kg/h cis-atracuriumbesylate. The depth of anesthesia (BIS value) was maintained at 45 to 60.

Settings of ventilation modes

The ventilation parameter settings of the three groups after intubation before pneumoperitoneum were: tidal volume (VT) = 10 ml/kg, respiratory rate (RR) = 12 beats/min, respiratory ratio (I:E) = 1:2. The ventilation parameter settings of the three groups after pneumoperitoneum were: group L: VT = 7 ml/kg, RR = 16 times/min, I:E = 1:2, PEEP = 0 cmH_2O; group L + P: VT = 7 ml/kg, RR = 12 times/min, PEEP = 5 cmH_2O, I:E = 1:2; group C: unchanged.

Observation indexes

Heart rate (HR) and mean arterial pressure (MAP) were recorded at the following time points: before intubation (T0), before pneumoperitoneum (T_1), 15 min after pneumoperitoneum (T_2), at the end of pneumoperitoneum (T_3), at the end of surgery (T_4) and after extubation (T_5). Arterial blood was then collected for the detection of pH value, PaO_2 and $PaCO_2$ using Radiometer ABL-90 blood gas analyzer (Radiometer, Denmark) at all time points. P_{peak} and P_{plat} were monitored and recorded at T_1-T_3, and the alveolar dynamic compliance (Cd) (Cd = VT/(P_{peak}-PEEP)) was calculated. $P_{ET}CO_2$ was monitored and recorded at T_1-T_4 (Supplemental Table).

Statistical analysis

SPSS19.0 software was used for statistical analysis. The measurement data were expressed as mean ± standard deviation. Repeated univariate analysis of variance (ANOVA) was used for intergroup comparison. Least significant difference (LSD) was used for pairwise comparison, and X^2 test was used for comparison of enumeration data. P<0.05 was considered as significant different.

Results

Comparison of hemodynamics among the three groups

There was no significant difference in hemodynamics among the three groups at each time point (P>0.05, **Table 2**).

Comparison of respiratory mechanics

There was no significant difference in P_{peak} and P_{plat} among the three groups before pneumoperitoneum, while it increased after pneumo-

Table 3. Comparison of respiratory mechanics ($\bar{x}\pm s$, n = 20)

Index	Group	T_1	T_2	T_3	*P* value
Ppeak (cmH_2O)	L	19.60±2.35	24.15±1.42$^{\Delta,▲}$	25.10±1.07	0.002
	L + P	18.40±2.74	23.55±2.78$^{\Delta,▲}$	25.05±2.93	0.000
	C	19.80±2.48	27.55±2.63$^{\Delta}$	30.25±2.40*	0.009
Pplat (cmH_2O)	L	18.15±2.01	23.05±1.43$^{\Delta,▲}$	23.85±1.14	0.005
	L + P	17.25±2.61	22.90±2.94$^{\Delta,▲}$	23.90±2.85	0.000
	C	18.70±2.45	26.50±2.54$^{\Delta}$	29.30±2.54*	0.009
Cd (ml/cmH_2O)	L	26.66±4.32	18.51±1.61$^{\Delta,\#}$	17.78±1.41	0.000
	L + P	28.38±4.73	24.46±4.64$^{\Delta}$	22.55±3.90	0.004
	C	25.87±4.33	18.17±2.34$^{\Delta,\#}$	16.49±1.89	0.000
$P_{ET}CO_2$ (mmHg)	L	34.05±2.67	40.65±2.56$^{\Delta}$	45.00±3.56*	0.005
	L + P	34.10±2.10	37.15±2.21$^{\Delta,※}$	37.45±2.35	0.009
	C	33.00±2.18	35.90±1.71$^{\Delta,※}$	36.60±1.82	0.000

Notes: Repeated ANOVA was adopted to compare the indicators of respiratory mechanics at different time points. $^{\Delta}P<0.01$, compared with T_1; $^{▲}P<0.01$, compared with group C; $^{*}P<0.01$, compared with T_2; $^{\#}P<0.01$, compared with group L + P; $^{※}P<0.01$, compared with group L. L: low tidal volume, L + P: low tidal volume + positive end expiratory pressure, C: large tidal volume.

Table 4. Comparison of blood gas indexes ($\bar{x}\pm s$, n = 20)

Index	Group	T_1	T_2	T_3	T_4	*P* value
pH value	L	7.376±0.03	7.346±0.02$^{\Delta}$	7.327±0.02$^{\Delta,▲}$	7.354±0.02$^{\Delta,▲}$	0.001
	L + P	7.378±0.02	7.394±0.04$^{\#}$	7.394±0.03$^{\#}$	7.400±0.03$^{\#}$	0.052
	C	7.384±0.02	7.371±0.02$^{\#}$	7.394±0.03$^{\#}$	7.396±0.03$^{\#}$	0.089
PaO_2 (mmHg)	L	352.85±27.62	353.70±26.95	352.70±28.97	361.90±23.27	0.152
	L + P	345.50±29.15	346.15±24.37	346.05±23.92	358.55±26.35	0.895
	C	347.60±30.55	347.10±29.38	347.25±30.56	355.30±25.96	0.078
$PaCO_2$ (mmHg)	L	39.45±3.47	46.40±2.41$^{\Delta}$	48.50±1.47$^{\Delta,▲}$	44.95±1.32$^{\Delta,▲}$	0.007
	L + P	39.10±3.63	39.55±3.44$^{\#}$	39.50±3.61$^{\#}$	38.00±2.83$^{\#}$	0.289
	C	38.80±2.73	39.55±2.87$^{\#}$	39.50±3.24$^{\#}$	38.55±2.33$^{\#}$	0.486

Notes: Repeated ANOVA was adopted to compare the indicators of blood gas indexes at different time points. $^{\Delta}P<0.01$, compared with T_1; $^{▲}P<0.01$, compared with T_2; $^{\#}P<0.01$, compared with group L. L: low tidal volume, L + P: low tidal volume + positive end expiratory pressure, C: large tidal volume.

peritoneum and elevated the most significantly in group C. With the increase of pneumoperitoneum time, P_{peak} and P_{plat} in group C were further elevated. There was no significant difference in the Cd values of the three groups before pneumoperitoneum, while it decreased significantly after pneumoperitoneum and reduced the most in group L + P. There was no significant difference in $P_{ET}CO_2$ among the three groups before pneumoperitoneum, while it increased after pneumoperitoneum and elevated the most significantly in group L. With the increase of pneumoperitoneum time, the $P_{ET}CO_2$ values in group L were further elevated. Results of repeated measures ANOVA of indicators of respiratory mechanics at different time pointsare shown in **Table 3**.

Comparison of blood gas indexes

There was no significant difference in pH value among the three groups before pneumoperitoneum, while the pH value significantly decreased in group L after pneumoperitoneum. With the extension of pneumoperitoneum time, the PH value in group L was gradually reduced. The pH value before pneumoperitoneum had no significant difference compared with that at the end of surgery. There was no significant difference in PaO_2 among the three groups at all time points and during surgery. $PaCO_2$ among the three groups before pneumoperitoneum had no significant difference, while it significantly increased in group L after pneumoperitoneum, and there was significant difference in $PaCO_2$ between before pneumoperitoneum and at the end of surgery. Results of repeated measures ANOVA of indicators of blood gas parameters at different time points are shown in **Table 4**.

Clinical outcomes

Because of higher postoperative $PaCO_2$, one patient in group L was successfully extubated after prolonged mechanical ventilation with propofol sedated for 15 min in post anesthesia care unit (PACU). While all the rest successfully revived in PACU without any anesthesia related complications within 24 hours of postoperative follow-up. No obvious postoperative agitation, nausea and vomiting was observed in patients of three groups.

Discussion

Minimally invasive surgery is the development direction of surgery, and will gradually replace traditional surgical methods. Therefore, there will be more and more elderly patients treated with minimally invasive surgery. Laparoscopic cholecystectomy (LC) is one of the most common minimally invasive surgeries in general surgery. Compared with traditional open cholecystectomy, LC has a variety of advantages such as small incision, large surgical field, clear explosion and fast postoperative rehabilitation. However, because of the establishment of CO_2 pneumoperitoneum during the operation procedure, respiration and circulation functions of patients may be disturbed, resulting in the decrease of functional residual capacity, reduction of lung compliance, increase of airway pressure and imbalance of the alveolar ventilation/flow ratio. In the process of artificial pneumoperitoneum, CO_2 is absorbed into the bloodstream by peritoneal capillary, resulting in low pH value and high $PaCO_2$ and $P_{ET}CO_2$ [13, 14]. The impact of CO_2 pneumoperitoneum on respiration and circulation functions will lead to higher surgery and anesthesia risk in elderly patients than that in ordinary patients.

8~12 ml/kg tidal volume is generally applied in conventional mechanical ventilation to maintain normal or near-normal pH value, PaO_2 and $PaCO_2$. However, the setting of 8~12 ml/kg tidal volume, which is appropriate for patients in non-pneumoperitoneum with normal bilateral lung ventilation, is relatively large for patients with CO_2 artificial pneumoperitoneum mechanical ventilation, and often leads to significant increase in airway pressure. It has been proved that high tidal volume and high airway pressure are the major risk factors of mechanical ventilation-induced lung injury [15, 16], and pneumoperitoneum will result in the increase of P_{peak} and P_{plat} and the decline of lung dynamic compliance [17]. Higher airway peak pressure caused by CO_2 artificial pneumoperitoneum is more likely to lead to higher mechanical aeration lung injury in elderly patients, which was confirmed in this study. P_{peak} and P_{plat} increased after pneumoperitoneum in patients of three groups, and that in patients of group C (large tidal volume group) raised the most significantly. Meanwhile, lung dynamic compliance decreased the most significantly in group C. Ours results indicated that potential lung damage occurred more frequently in elderly patients.

The essence of low tidal volume mechanical ventilation is to reduce tidal volume and airway pressure. Low tidal volume mechanical ventilation can avoid mechanical aeration lung injury, but unable to cope with the increase of $PaCO_2$, reduction of pH value and hypercapnia caused by CO_2 absorption. In this study, lower pH and higher $PaCO_2$ and $P_{ET}CO_2$ were observed in all patients after pneumoperitoneum, and that were more significant in low tidal volume group. These results demonstrated that though low tidal volume mechanical ventilation reduced the airway pressure and the possibility of lung injury, and it might increase the risk of higher $PaCO_2$ and lower pH value caused by CO_2 accumulation.

It has been found that when patients are in the reverse Trendelenburg position, $PaCO_2$ increases significantly after pneumoperitoneum [18]. The combination application of low tidal volume, high ventilation frequency and PEEP significantly improves analysis parameters of arterial blood gas in patients. In this study, $PaCO_2$ and $P_{ET}CO_2$ increased and the pH value decreased during pneumoperitoneum in group L + P (low tidal volume group + PEEP), but they were still in normal value range. There was no decrease of PaO_2 during operation. A short period of higher arterial blood CO_2 above the normal range is allowed when patients has enough oxygenation during the operation, which leads to the decrease of combination ability of interstitial oxygen and hemoglobin, promotes the release of oxygen and oxygen uptake of tissue, therefore provides oxygen for important viscera [19].

The combination application of low-level PEEP and low tide volume can buffer alveoli at the end of expiratory, so that the interalveolar pressures can be balanced, alveolar collapse can be avoided, and the shear stress between large and small alveoli may be reduced during mechanical ventilation, therefore decreases the occurrence of lung injury. It has been showed that PEEP can effectively prevent alveolar collapse and atelectasis, keep end-expiratory alveolar relatively open, and meanwhile re-expand the collapsed alveoli [20]. Low tidal volume along with low-level PEEP reduces the incidence of perioperative pulmonary complications, while high-level PEEP has no benefit on the incidence of perioperative pulmonary complications [21]. Therefore, in our study, PEEP was set at 5 cmH_2O. There was no significant difference in MAP and HR among the three groups at each time point, indicating that the combination of low tidal volume and PEEP did not affect hemodynamic stability, which was consistent with previous findings [22].

In summary, low tidal volume plus low-level PEEP can effectively reduce airway pressure in elderly patients with LC. Thus lung injury was prevented, ventilation effect was improved, and meantime CO_2 accumulation and hypercapnia were avoided. Therefore, low tidal volume plus low-level PEEP was considered an appropriate and effective ventilation mode for elderly patients.

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Disclosure of conflict of interest

None.

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