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Original Article

Pressure-controlled inverse ratio ventilation improves gas exchange in obese children undergoing laparoscopic surgery: a randomized controlled study

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Abstract: Background: Obese children undergoing laparoscopic surgery frequently experience high end-tidal carbon dioxide partial pressure ($P_{ET}CO_2$) and respiratory acidosis. This study aimed to investigate the effects of pressure-controlled inverse ratio ventilation (IRV) with an inspiratory to expiratory ratio (I:E) of 1.5:1 on obese children undergoing laparoscopic surgery. Methods: Eighty children undergoing laparoscopic surgery were randomly assigned to either the IRV group (I:E=1.5:1) or the control group (I:E=1:1.5). The lungs were mechanically ventilated following tracheal intubation. The children underwent pressure-controlled ventilation with an I:E ratio of 1.5:1 or 1:1.5. Respiratory mechanics, hemodynamic values, and ventilation-related side effects were recorded. Results: Thirty minutes after establishing CO_2 pneumoperitoneum, the IRV group exhibited significantly higher tidal volume (Vt) and arterial partial pressure of oxygen (PaO_2) compared to the control group (97.6 ± 6.6 vs. 93.2 ± 8.0 ml, 283 ± 54 vs. 247 ± 40 mmHg, respectively) ($P < 0.01$). Furthermore, $PaCO_2$ was significantly lower in the IRV group than in the control group (41.4 ± 5.8 vs. 45.5 ± 5.7 mmHg, P=0.002). The incidence of intra-operative hypercapnia was significantly decreased in the IRV group (25% vs. 42.5%, P=0.03). Conclusion: Pressure-controlled IRV can reduce the incidence of hypercapnia, increasing Vt, and thereby improving CO_2 elimination in obese children undergoing laparoscopy. This ventilation technique significantly improves gas exchange in this patient population. (Registration number: ChiCTR2000035589).

Keywords: Inverse ratio ventilation, gas exchange, hypercapnia, laparoscopy, obese children

Introduction

Obesity and pneumoperitoneum significantly affect respiratory mechanics in patients undergoing laparoscopic surgery. The gold standard for assessing the efficacy of mechanical ventilation remains the measurement of partial pressure of carbon dioxide in arterial blood ($PaCO_2$). Obesity reduces functional residual capacity and alters ventilation-perfusion matching [1]. During laparoscopic surgery, obesity and increased intra-abdominal pressure influence CO_2 elimination [2]. Pediatric patients undergoing laparoscopic surgery frequently experience hypercapnia and respiratory acidosis. Maintaining end-tidal carbon dioxide partial pressure ($P_{ET}CO_2$) within the normal range without causing ventilator-related lung injury poses a challenge. Attempting to alleviate hypercapnia by increasing respiratory frequency under pressure-controlled ventilation mode proves difficult. Pressure-controlled ventilation with positive end-expiratory pressure (PEEP) enhances oxygenation while reducing tidal volumes (Vt). Although higher airway pressure under pressure-controlled ventilation increases Vt, it may cause lung barotrauma and volutrauma. The literature suggests that inverse ratio ventilation (IRV) improves oxygenation and reduces peak airway pressure compared to conventional ventilation modes [3-7]. We therefore investigated the effect of pressure-controlled IRV with an inspiratory/expiratory (I:E) ratio of 1.5:1 on gas exchange in obese children undergoing laparoscopic surgery. Pressure-controlled IRV has proven effective in enhancing oxygenation in patients with acute hypoxemic respiratory failure. This study aimed to determine if pressure-controlled IRV can improve ventilation without increasing the levels of $PaCO_2$ in obese children. We hypothesized that pressure-controlled IRV with an I:E ratio of 1.5:1 would enhance gas exchange and facilitate CO_2 elimination in obese children undergoing laparoscopic surgery.

Methods

Children undergoing elective laparoscopy were enrolled in this study. Inclusion criteria: body mass index (BMI) of 28 kg/m^2 or higher, of either sex, aged 2 to 6 years, and American Society of Anesthesiologists (ASA) physical status I and II. The expected surgery duration was more than 30 min. Children with cardiopulmonary diseases were excluded. Eighty children were randomly assigned to the IRV group (I:E=1.5:1) or the control group (I:E=1:1.5) using a computer-generated randomization table.

All children were fasted for 6 hours prior to surgery and received no premedication. Upon entering the operating room, peripheral venous access was established, and routine monitoring including electrocardiogram, noninvasive blood pressure (BP), heart rate (HR), and pulse oxygen saturation (SpO_2) was initiated. Anesthesia was induced with intravenous fentanyl (3 μg/kg), propofol (3 mg/kg), and cis-atracurium (0.1 mg/kg). Anesthesia was maintained with inhalation of 2-3% sevoflurane. After tracheal intubation, both lungs were mechanically ventilated using pressure-controlled mode. Initially, respiratory parameters were set at an airway pressure of 20 cmH_2O, respiratory rate of 20 breaths/min, positive end-expiratory pressure (PEEP) of zero, oxygen flow of 2 L/min, fraction of inspired oxygen of 1.0, and I:E ratio of 1:1.5. In the control group, ventilation continued with an I:E ratio of 1:1.5 when CO_2 pneumoperitoneum (intra-abdominal pressure 10 mmHg) was established, while in the IRV group, I:E ratio was set at 1.5:1. Other respiratory measurements remained consistent between the two groups.

Sevoflurane levels were adjusted to maintain the bispectral index (BIS) value between 40 and 55 (BIS monitor Model A2000, USA) and to control the hemodynamic response to the surgical procedure within a 20% range of the preoperative value. Muscle relaxation was monitored by train-of-four (TOF) stimulation (Organon Corporation, type: TOF-Watch SX, Holland). Cis-atracurium was infused at a rate of 0.08 mg $kg^{-1}h^{-1}$ to maintain TOF value below 5%. Respiratory settings were not adjusted if $P_{ET}CO_2$ did not exceed 50 mmHg within 30 min after establishing CO_2 pneumoperitoneum. The airway pressure was adjusted to maintain $P_{ET}CO_2$ between 35 and 45 mmHg after 30 min of establishing CO_2 pneumoperitoneum. Spirometry readings included inspiratory Vt, mean airway pressure (Pmean), $P_{ET}CO_2$, and total PEEP (PEEPtot) using a side-stream spirometry device (GE company, Taipei, China). Ringer's solution was infused at a rate of 5-6 $ml{\cdot}kg^{-1}{\cdot}h^{-1}$ during the operative period.

After establishing CO_2 pneumoperitoneum, the children were positioned supine with a 20° head-down tilt. Noninvasive systolic blood pressure (SBP), diastolic blood pressure (DBP), and HR were recorded at baseline or before anesthesia (T0), 2 min before establishing CO_2 pneumoperitoneum (T1), 30 min after establishing CO_2 pneumoperitoneum (T2), and the end of surgery (T3). Respiratory mechanics were recorded at T1 and T2. Arterial blood was drawn and analyzed using a blood gas analyzer (Type: ABL8000, Denmark) at T1 and T2, respectively. Hypercapnia was defined as $PaCO_2$ > 45 mmHg. Time to extubation and time to discharge from the post-anesthesia care unit (PACU) were recorded. Post-operative complications, such as post-operative hypoxemia (defined as SpO_2 below 91% while receiving air), pneumothorax, and other pulmonary complications were recorded. Children were discharged from the PACU when the Modified Aldrete Score was 9 or above [8].

Statistical analysis

Data were analyzed using SPSS 17.0 statistical software (SPSS Inc., Chicago, USA). Quantitative variables with a normal distribution were compared using *t*-tests and a one-sided analysis of variance. Data with non-normal distribution were analyzed using a two-sided Mann-Whitney U-test in both groups. Categorical variables were evaluated with the Chi-square test and Fisher's test. All quantitative data were expressed as mean ± standard deviation. A $P < 0.05$ was considered significant.

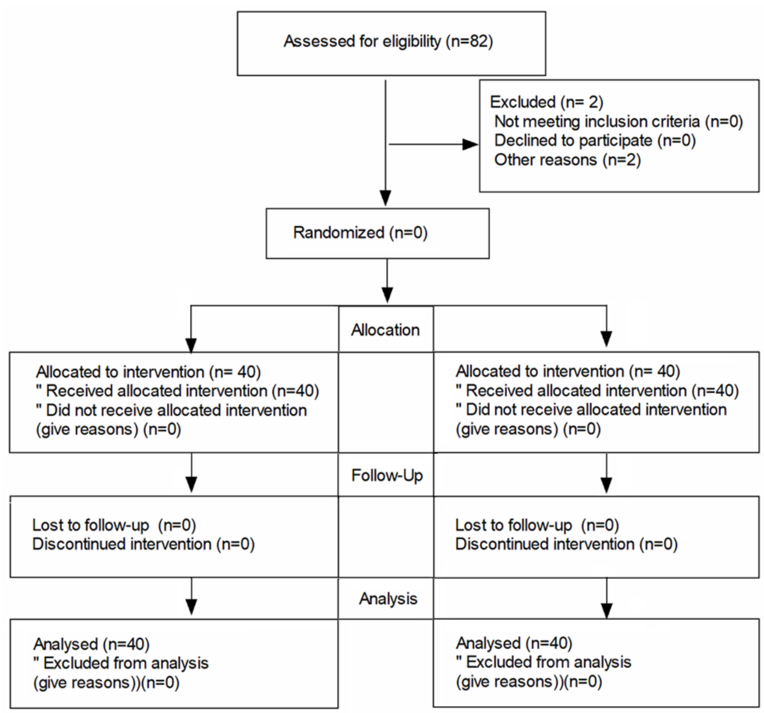

Figure 1. Flow diagram of study.

Sample sizes were determined based on the primary outcome, the levels of $PaCO_2$ in this study. A priori power analysis using two-sided analysis with an α error of 0.05 and a power of 0.8 indicated that 32 patients were needed in each group to detect a difference of 2 mmHg in $PaCO_2$ levels. The sample size was increased to 40 in each group to account for potential dropouts.

Results

Demographic data

Eighty-two children were initially enrolled in the study (**Figure 1**). However, two patients were excluded due to hesitations in participation, leaving a total of eighty children who completed the study. There were no significant differences in BMI, gender, age, or duration of surgery between the two groups (**Table 1**) ($P > 0.05$).

Blood gas analysis

Blood gas analysis at T1 revealed no significant differences in PaO_2, $PaCO_2$, and Ph between the two groups ($P > 0.05$). At T2, PaO_2 and pH values were significantly higher in the IRV group compared to the control group (283 ± 54 vs. 247 ± 40 mmHg, 7.34 ± 0.03 vs. 7.32 ± 0.03) (**Table 2**) ($P < 0.01$), while $PaCO_2$ was significantly lower in the IRV group (41.4 ± 5.8 vs. 44.5 ± 5.7 mmHg) (P=0.002). SaO_2 values were similar in both groups ($P < 0.05$).

Respiratory parameters

At T2, the IRV group exhibited significantly higher Vt, Pmean, and auto-PEEP compared to the control group (97.6 ± 6.6 vs. 93.2 ± 8.0 ml, 16.3 ± 1.0 vs. 15.4 ± 1.4 cmH_2O and 2.65 ± 0.58 vs. 1.98 ± 0.48 cmH_2O, respectively) ($P < 0.01$) (**Figure 2**). $P_{ET}CO_2$ was significantly lower at T2 in the IRV group than in the control group (41.4 ± 5.8 vs. 44.5 ± 5.7 mmHg) (P=0.002). Blood pressure and HR, as shown in **Figure 3**, did not exhibit significant differences between the two groups at T2 ($P > 0.05$).

Adverse events

Within 30 min after initiation of CO_2 pneumoperitoneum, eight cases of hypercapnia occurred in the IRV group, while 17 cases were observed in the control group. The incidence of intra-operative hypercapnia was significantly lower in the IRV group (P=0.03). No postoperative hypoxemia was observed, and there were no significant differences in the incidence of hypercapnia, extubation time, or time to discharge from PACU between the two groups ($P > 0.05$) (**Table 1**). No respiratory complications were observed during the hospital stays.

Discussion

A larger tidal volume leads to increased minute ventilation and higher peak airway pressure when respiratory rates are constant. PEEP can enhance oxygenation but also increase peak or plateau airway pressure. Consequently, we chose not to utilize PEEP in this study.

Our investigation into the effects of pressure-controlled inverse ratio ventilation (IRV)

Table 1. Data of children (n=40)

Index	IRV group	Control group	*P*-value
Age (years)	4.0 ± 1.2	4.2 ± 1.3	0.521
BMI (kg/m²)	30.3 ± 1.6	30.2 ± 1.2	0.617
Gender (Male/Female)	28/12	24/16	0.321
Surgery performed, 1/2 (n)	16/24	18/22	0.723
Duration of pneumoperitoneum (min)	61.4 ± 7.7	62.4 ± 8.2	0.586
Duration of surgery (min)	73.6 ± 6.4	74.4 ± 6.3	0.573
Time to extubation (min)	12.4 ± 2.1	11.5 ± 2.5	0.106
PACU discharge time (min)	39.2 ± 8.2	39.6 ± 11.9	0.870
Intraoperative hypercapnia (n)	8 (25%)	17 (42.5%)	0.030*
Postoperative hypoxemia (n)	0	0	0.999

Data are expressed as the mean (standard deviation) or number. Surgery performed: 1, appendectomy; 2, herniorrhaphy. BMI: body mass index; PACU: post-anesthesia care unit. *$P < 0.05$, compared with the control group.

Table 2. Arterial blood gas of children (n=40)

Index	IRV group	Control group	*P*-value
pH	7.34 ± 0.03	7.32 ± 0.03	0.005*
PaO_2 (mmHg)	283 ± 54	247 ± 40	0.001*
$PaCO_2$ (mmHg)	41.4 ± 5.5	45.5 ± 5.7	0.002*
SaO_2 (%)	99.7 ± 1.5	99.6 ± 1.7	0.782

Data are expressed as mean (standard deviation) or numbers. PaO_2: oxygen partial pressure in arterial blood. $PaCO_2$: partial pressure of carbon dioxide in arterial blood. SaO_2: oxygen saturation in arterial blood. *$P < 0.05$, compared with the control group.

(I:E=1.5:1) ventilation on obese children undergoing laparoscopy revealed significant improvements in CO_2 removal and oxygenation compared to conventional I:E ratio ventilation. IRV, differing from conventional ventilation modes, extends inspiratory time, increases alveolar ventilation and functional residual capacity, and expands collapsed alveoli. Besides, the dead space is decreased, which contributes to the gas distribution in the lungs. Currently, few studies explore IRV in obese children undergoing laparoscopy. In the present study, IRV demonstrated higher Vt and Pmean in the IRV group than in the control group. Prolonged inspiratory time and decreased inspiratory flow velocity increased Vt. Additionally, IRV generated auto-PEEP (endogenous PEEP) [9], which was beneficial for oxygenation. The literature indicates that arterial blood oxygenation is directly related to mean airway pressure [7, 10], highlighting its importance in gas exchange [11]. Our results align with Sinha et al. [12] findings, who reported a significant increase in Vt, P_{mean}, and dynamic lung compliance when pressure-controlled IRV with an I:E ratio of 1.5:1 was used, compared to conventional pressure-controlled ventilation with an I:E ratio of 1:2, during gynecologic laparoscopy with laryngeal mask ventilation.

In the pressure-controlled IRV mode, the prolonged inspiratory time and relatively shorter expiratory time generate endogenous PEEP due to gas delay. Interestingly, our study found no statistical differences in blood pressure and heart rate between the groups, indicating that IRV with an I:E ratio of 1.5:1 did not affect venous return. Beyond an I:E ratio of 2:1, IRV can indeed reduce venous return and cardiac output [4, 13]. When inspiratory time is excessively prolonged and Pmean reaches a certain high level, pressure-controlled IRV might lead to a decrease in cardiac output, affecting hemodynamics [4, 14]. The study by Mercat et al. [6] supports the idea that IRV can increase Pmean and PaO_2 [6]. However, the impact of Pmean on hemodynamics becomes significant only when it reaches a high threshold. Interestingly, despite a significantly higher Pmean in the IRV group compared to the conventional ventilation group, there were no significant differences in hemodynamic measurements between the two groups. This observation aligns with the results reported by *Movassagi, et al.* [14].

At 30 min after establishing CO_2 pneumoperitoneum, the IRV group exhibited significantly higher PaO_2 levels than the conventional ventilation group, indicating that IRV could effectively increase PaO_2 levels and promote oxygenation. This finding resonates with the study by

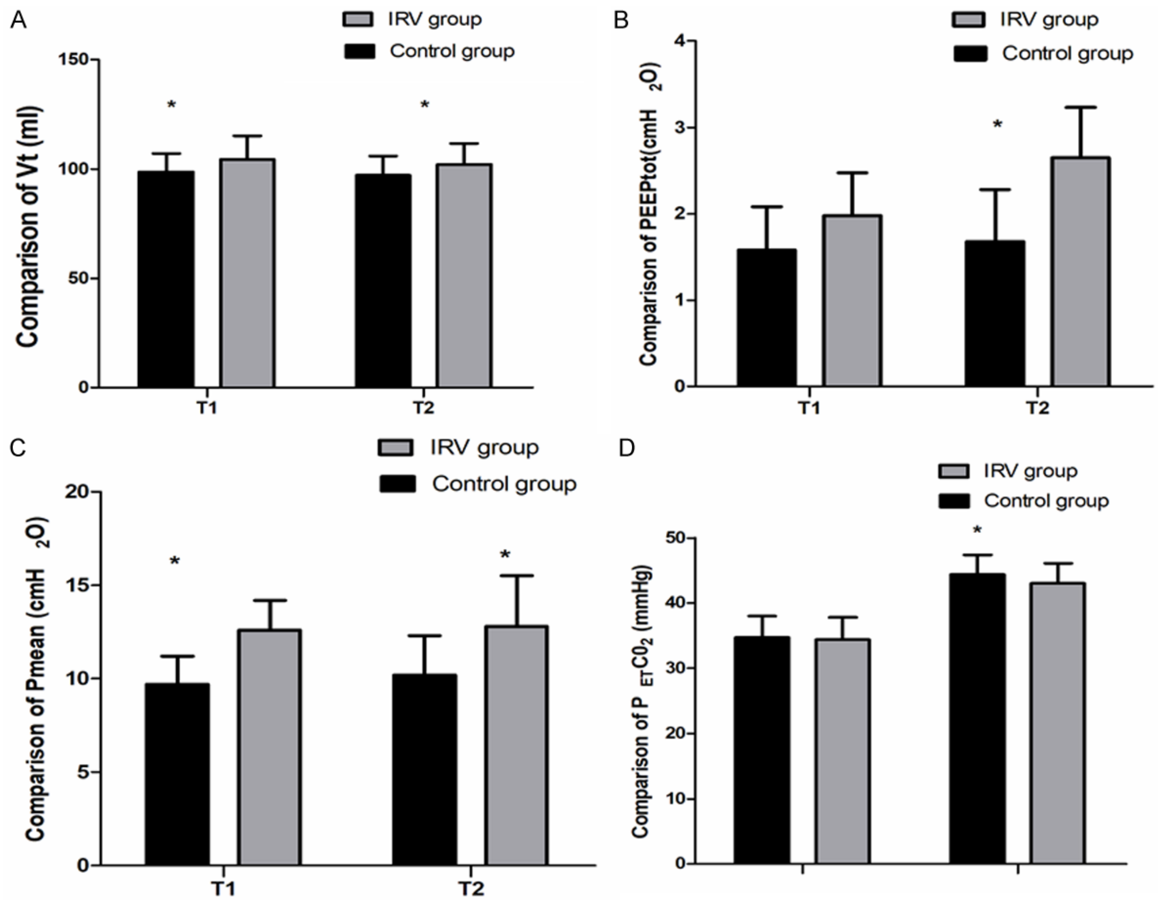

Figure 2. Comparison of respiratory mechanics between the 2 groups. At T1, T2 and T3, there were significant differences in Vt, P_{mean}, $PEEP_{tot}$ and $P_{ET}CO_2$ between the 2 groups (**P* < 0.05). T1: immediately before establishing CO_2 pneumoperitoneum, T2: 30 min after initiation of CO_2 pneumoperitoneum, T3: at the end of surgery. Vt: tidal volume, P_{mean}: mean airway pressure, $PEEP_{tot}$: total positive end expiratory pressure, $P_{ET}CO_2$: end-tidal carbon dioxide partial pressure.

Tweed et al. where arterial oxygenation was superior to pressure-controlled IRV (I:E=2:1) in patients undergoing abdominal gynecologic surgery compared to conventional ventilation [15]. Moreover, $PaCO_2$ levels were lower in the IRV group than in the control group, signifying a significant difference between the two groups. The significant increase in $PaCO_2$ in both groups 30 min after establishing CO_2 pneumoperitoneum in both groups was primarily due to CO_2 absorption in the blood [16]. Notably, IRV did not affect CO_2 removal. Studies have indicated that during mechanical ventilation, changes in tidal volumes per 100 ml led to a 5.3 mmHg decrease in $PaCO_2$ in patients with normal weight, and a 3.6 mmHg decrease in morbidly obese patients [17]. Hence, tidal volumes or minute ventilation volumes played a crucial role in determining CO_2 removal during mechanical ventilation. Additionally, higher CO_2 pneumoperitoneum pressure may influence hemodynamics during laparoscopic surgery [18].

The limitations of this study are as follows: IRV, being distinct from conventional ventilation, presents potential risks, particularly the long-term complications associated with prolonged respiratory time, which require further investigation. Moreover, larger sample sizes should be enrolled in future to comprehensively explore adverse respiratory and hemodynamic effects.

Conclusion

Pressure-controlled IRV emerged as a promising approach to mitigating hypercapnia, increasing Vt, and enhancing CO_2 removal in obese children undergoing laparoscopy when compared to conventional ventilation. Notably,

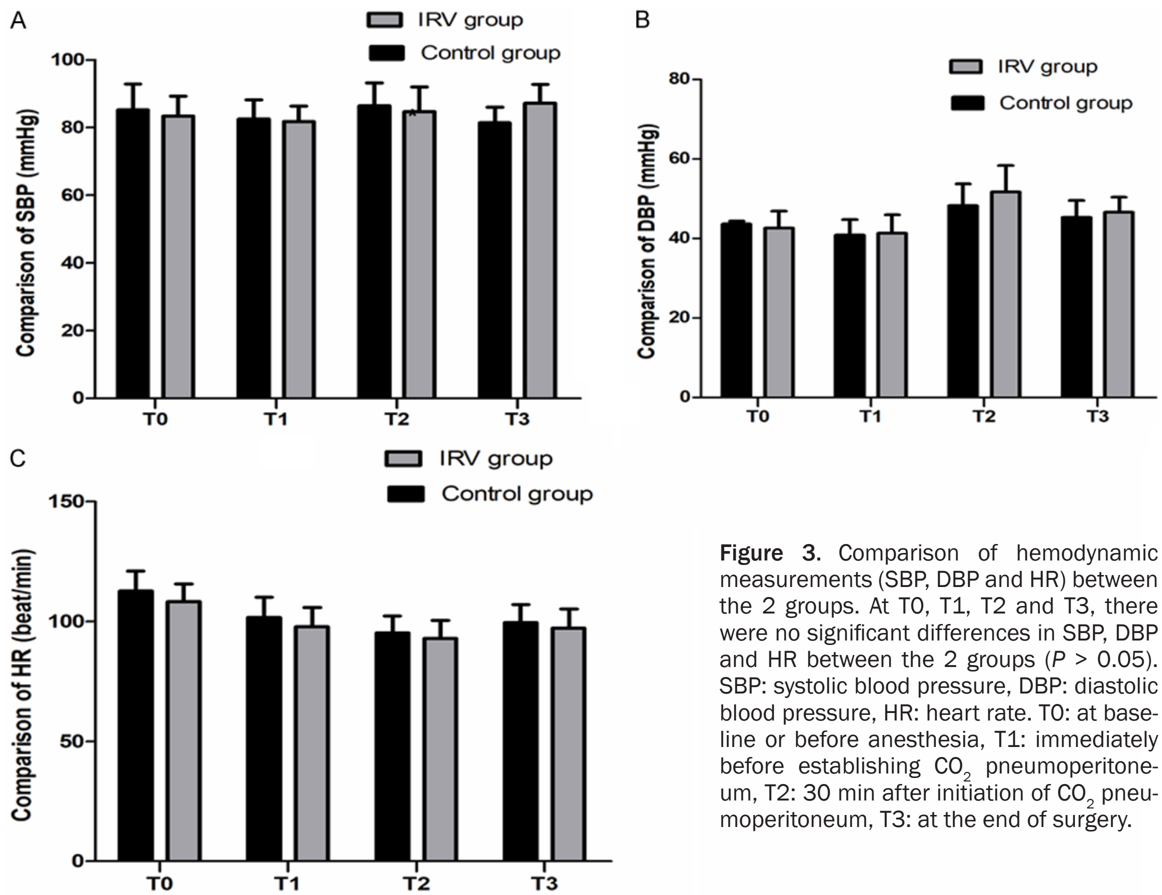

Figure 3. Comparison of hemodynamic measurements (SBP, DBP and HR) between the 2 groups. At T0, T1, T2 and T3, there were no significant differences in SBP, DBP and HR between the 2 groups ($P > 0.05$). SBP: systolic blood pressure, DBP: diastolic blood pressure, HR: heart rate. T0: at baseline or before anesthesia, T1: immediately before establishing CO_2 pneumoperitoneum, T2: 30 min after initiation of CO_2 pneumoperitoneum, T3: at the end of surgery.

IRV outperformed conventional ventilation in terms of CO_2 removal efficiency and respiratory mechanics in children undergoing laparoscopy.

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Disclosure of conflict of interest

None.

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