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Original Article

Method for predicting airway pressure during mechanical ventilation in overweight/obese children undergoing adenotonsillectomy

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Abstract: Overweight/obese children undergoing mechanical ventilation experience elevated airway pressure. The objectives of this study were to investigate the effects of body mass index (BMI) on airway pressure in children and to design a method of estimating airway pressure during intraoperative mechanical ventilation. A total of 180 children aged 2-10 years, who were undergoing adenotonsillectomy, were enrolled. They were allocated to one of three groups based on BMI: normal weight, overweight, or obesity. Peak inspiratory pressure (P_{peak}), plateau inspiratory pressure (P_{plat}), and dynamic pulmonary compliance (C_{dyn}) were measured during mechanical ventilation with a VCV mode. Serious postoperative pulmonary complications were monitored 5 days after the surgery. The results showed that P_{peak} and P_{plat} were significantly increased in overweight/obese patients (p < 0.05). BMI had a significant positive correlation with P_{peak} (r = 0.60, p < 0.001) and P_{plat} (r = 0.52, p < 0.001); age and C_{dyn} were positively correlated (r = 0.69, p < 0.001). The fitted equation for estimating the P_{peak}, P_{plat}, and C_{dyn} were created using linear regression analysis according to the BMI and age: P_{peak} (cmH_2O) = 1.049 × BMI-1.145, with an R^2 of 0.363; P_{plat} (cmH_2O) = 0.929 × BMI-1.211, with an R^2 of 0.274; and C_{dyn} (mL/cmH_2O) = 1.919 × year + 7.418, with an R^2 of 0.472. Those methods used to predict the P_{peak}, P_{plat}, and C_{dyn}, had a sensitivity of 76.3%, 78.9%, and 97.4% and a specificity of 52.6%, 52.6%, and 36.8%, respectively. Youden's index was 0.289, 0.316, and 0.342, respectively. There were no serious postoperative pulmonary complications in any of the children. We concluded that a significant positive correlation was observed between BMI and airway pressure, age, and C_{dyn} in pediatric patients undergoing general anesthesia; thus, the equation to rapidly evaluate the range of airway pressure and C_{dyn} was fitted based on a child's BMI and age.

Keywords: Body mass index, airway pressure, dynamic pulmonary compliance, mechanical ventilation

Introduction

Perioperative respiratory adverse events in children, a major source of all critical incidents, are one of the major causes of morbidity and mortality during pediatric anesthesia [1-3]. The most common threat during anesthesia is high airway pressure, which potentially leads to numerous complications, including pulmonary barotrauma, hypoxemia, hypercapnia, and atelectasis. In our experience of performing general anesthesia in children with obstructive sleep apnea syndrome (OSAS), there was often a large variation in airway pressure and an elevated airway pressure during positive mechanical ventilation, particularly among those who were overweight or obese. The cause of this phenomenon is unclear, even after excluding the common factors [4], including light anesthesia, endobronchial intubation, poor pulmonary compliance, acute bronchospasm, obstruction of the breathing circuit, kinking or obliteration of the endotracheal tube (ETT) lumen by mucous plugs or blood clots, and ETT connector defects; this suggests that this occurrence may be attributed to overweight/obese body conditions [5].

Airway-related perioperative complications during tonsillectomy are more frequent in OSAS children with overweight/obese body conditions than in their healthy weight counterparts, and an overweight or obese body condition is often present in these OSAS patients [6, 7].

Table 1. BMI (kg/m^2) cut-off values for overweight and obesity for children

Age (yr)	Boys		Girls	
	Overweight	Obesity	Overweight	Obesity
2.0	17.5	18.9	17.5	18.9
2.5	17.1	18.4	17.1	18.9
3.0	16.8	18.1	16.9	18.3
3.5	16.6	17.9	16.8	18.2
4.0	16.5	17.8	16.7	18.1
4.5	16.4	17.8	16.6	18.1
5.0	16.5	17.9	16.6	18.2
5.5	16.6	18.1	16.7	18.3
6.0	16.8	18.4	16.7	18.4
6.5	17.0	18.8	16.8	18.6
7.0	17.2	19.2	16.9	18.8
7.5	17.5	19.6	17.1	19.1
8.0	17.8	20.1	17.3	19.5
8.5	18.2	20.6	17.6	19.9
9.0	18.5	21.1	17.9	20.4
9.5	18.9	21.7	18.3	20.9
10.0	19.3	22.2	18.7	21.5
10.5	19.7	22.7	19.1	22.1
11.0	20.1	23.2	19.6	22.7
11.5	20.4	23.7	20.1	23.3
12.0	20.8	24.2	20.5	23.9

Therefore, we aimed to study the effects of body mass index (BMI) on airway pressure and dy namic pulmonary compliance (C_{dyn}), in an effort to develop and validate a simplified evaluation method for predicting the airway pressure and C_{dyn} in pediatric patients with OSAS during intraoperative mechanical ventilation. Additionally, we hope that it can serve as a reference to reduce the risk of airway-related respiratory complications and improve the effectiveness of mechanical ventilation in overweight/obese children.

Material and methods

Approval from the institutional review board (IRB) of Xinhua Hospital Affiliated with Shanghai Jiao Tong University, School of Medicine (Approval No. XHEC-D-2013-023) and written, informed parental consent was obtained; the trial was registered at the Chinese Clinical Trial Registry (ID: ChiCTR-RCH-13004060). The study was conducted at Xinhua Hospital, School of Medicine, Shanghai Jiaotong University in Shanghai, China. The investigators certify that this study did not raise any issues concerning patient risk and that the study was performed in accordance with the Declaration of Helsinki with no ethical complications.

Healthy children (aged 2-10 years and American Society of Anesthesiology Class I) scheduled for adenotonsillectomy surgery in the supine position under general anesthesia from 01/01/2014 to 7/30/2015 were enrolled. The children were diagnosed with OSAS by otolaryngologists and required surgery to alleviate their clinical symptoms. Children with upper respiratory infections, abnormal chest radiographs, or a history of acute or chronic respiratory, pulmonary, major abdominal, chest wall deformities, or neuromuscular disease were excluded. The BMI was designated according to the Working Group on Obesity in China (WGOC) using BMI cutoff values from standardized growth charts for overweight and obese children aged 2-18 years (**Table 1**) [13]. Overweight and obese children were included in the study, and normal weight children were recruited as controls.

Patients underwent an electrocardiogram, followed by continuous monitoring of noninvasive arterial blood pressure, arterial oxygen saturation, and bispectral index (BIS). While patients were administered 100% oxygen through a face mask, anesthesia was induced using intravenous midazolam 0.1 mg/kg, propofol 2 mg/kg, remifentanil 1 μg/kg, and rocuronium 0.6 mg/kg. Thereafter, adequate neuromuscular blockade (train-of-four monitoring) was provided, and anesthesia was maintained (BIS 40-60) with propofol 4-8 mg·kg^{-1}·h^{-1} and remifentanil 0.15-0.3 μg·kg^{-1}·min^{-1}. Two minutes later, orotracheal intubation was performed, and the tube position was verified by auscultation and fiberoptic bronchoscopy by an experienced anesthesiologist. Mechanical ventilation was provided using a standard anesthesia ventilator system (Ohmeda 7810, Modulus 2 Anesthesia system, Madison, WI, USA) and a constant flow ventilator with a TV of 10 mL/kg, positive end expiratory pressure (PEEP) at 4 cmH$_2$O, preset respiratory rate of 18 beats/min, an end tidal CO_2 maintained between 36-45 mmHg by adjusting the respiratory rate, an inhalation-to-exhalation time ratio of 1:2, and 2 L/min of oxygen. All children received a constant TV using a similar circuit and compression volume. Ventilatory settings were kept constant in the

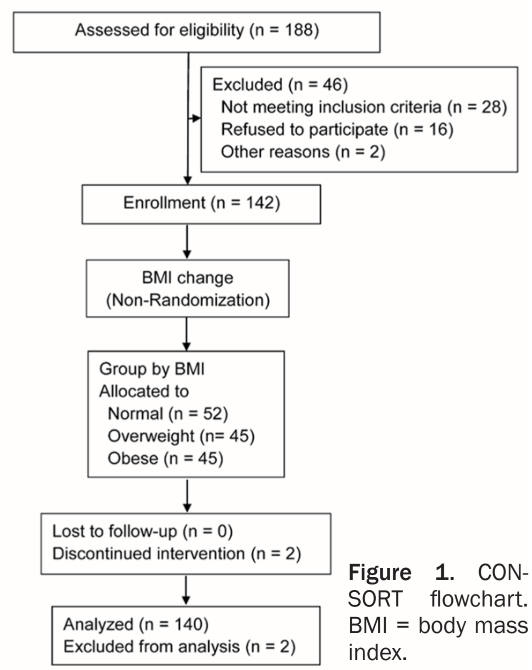

Figure 1. CONSORT flowchart. BMI = body mass index.

VCV mode during the study. The patients were placed in the supine position, and the P_{peak}, P_{plat}, and C_{dyn} values were recorded during positive pressure ventilation using the Datex Capnomac Ultima gas monitor (Datex Ohmeda), with the D-Lite® sensor positioned between the ETT and the Y-piece in the ventilator breathing circuit. After allowing ventilation to stabilize for 3 min (2-3 min following endotracheal intubation, the P_{peak} value varied less than 1 cmH_2O), data were independently recorded at 4-6 min by a different anesthesiologist. All data were recorded during atisfactory muscle relaxation (TOF T4/T1 < 25%). All procedures were performed under a single-blinded protocol.

Serious postoperative pulmonary complications (PPCs), including hypoxemia, pneumothorax, and acute respiratory distress syndrome were followed 5 days after surgery. When serious hypoxemia (SpO_2 < 90% under room air) occurred, chest CT imaging was performed to observe the atelectasis and pneumonia.

Statistical analysis

Data were analyzed using SPSS 19.0 statistical analysis software (SPSS Inc, Chicago, IL, USA). The changes in P_{peak}, P_{plat}, and C_{dyn} were assessed using one-way ANOVA, with p < 0.05 considered significant. The relationship between the P_{peak}, P_{plat}, and C_{dyn} variables and BMI were evaluated using correlation analysis and Pearson correlation coefficient (R). Comparisons of the P_{peak}, P_{plat}, and C_{dyn} variables in both the measured and fitted groups were assessed using paired Student's t test. The sensitivity and specificity of the fitted equation were analyzed with a receiver operator characteristic (ROC) curve, and an area under the curve (AUC) was used to generate and test a nomogram. The optimal criterion value was determined at the point on curve at which the Youden's index was maximal. Statistical significance was defined as p < 0.05. Results are reported as the mean ± standard deviation.

The number of patients in each group required to reveal a statistically significant difference, was determined by one-way ANOVA power analysis using PASS 11 software (NCSS, LLC, Kaysville, UT, USA). For the BMI variable, the airway pressure in normal (n = 7), overweight (n = 8), and obese (n = 7) patients was measured in a preliminary trial. The P_{peak} of normal, overweight, and obese patients was 15.3 ± 3.2 cmH_2O, 17.6 ± 3.2 cmH_2O, and 20.4 ± 3.1 cmH_2O, respectively, and the P_{plat} was 13.3 ± 3.7 cmH_2O, 14.6 ± 4.9 cmH_2O, and 16.6 ± 2.9 cmH_2O, respectively. Based on the difference between the two groups, a two-sided type I error rate of 0.05, a power of 0.90, and a total of 38 patients were required to reveal a statistically significant difference.

Results

A total of 180 patients were included in the study. Any patient with an oxygen saturation (SpO_2) of < 94% for > 60 s during fiberoptic bronchoscopy confirmation of ETT placement was excluded. The details of the CONSORT flowchart are summarized in **Figure 1**.

Effects of being overweight or obese on P_{peak}, P_{plat}, and C_{dyn}

A total of 142 patients were included in the part of this study, and 2 were excluded because the ETTs were distorted due to inappropriate surgical technique. The patient demographics are shown in **Table 2**. The overweight/obese group exhibited significantly increased P_{peak} and P_{plat} (**Table 3**) values compared to that of the normal body group, but there was no significant difference in C_{dyn}.

Table 2. Patient demographics of the normal/overweight/obese group

	Normal	Overweight	Obese
N	52	43	45
Sex (M/F)	32/20	24/19	25/20
Age (yr)	5.65 ± 2.03	5.58 ± 1.73	5.69 ± 1.84
BMI	14.67 ± 1.29	17.42 ± 1.11*	20.73 ± 2.80*,#

Values are mean ± SD. *P < 0.05 versus the normal, #P < 0.05 versus the overweight. BMI = body mass index.

Table 3. Effect of BMI on the P_{peak}, P_{plat} and C_{dyn}

	BMI variable		
	Normal	Overweight	Obese
P_{peak} (cmH_2O)	14.49 ± 2.56	17.85 ± 2.79*	21.84 ± 5.06*,#
P_{plat} (cmH_2O)	12.00 ± 2.91	15.01 ± 2.86*	17.76 ± 4.69*,#
C_{dyn} (mL/cmH_2O)	18.81 ± 4.97	17.91 ± 5.29	18.49 ± 5.34

Values are mean ± SD. *P < 0.05 versus the normal, #P < 0.05 versus the overweight. P_{peak} = peak airway pressure; P_{plat} = plateau airway pressure; C_{dyn} = dynamin pulmonary compliance.

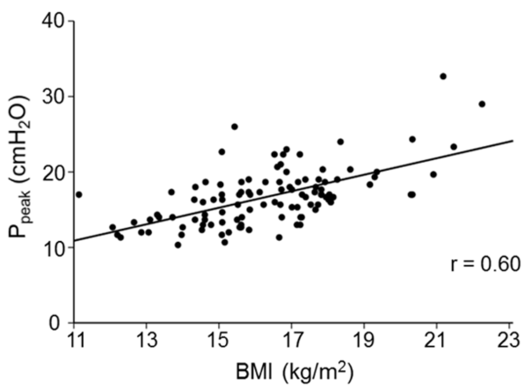

Figure 2. A linear increase in P_{peak} with BMI was observed in children with OSAS. P_{peak} = peak inspiratory pressure, BMI = body mass index.

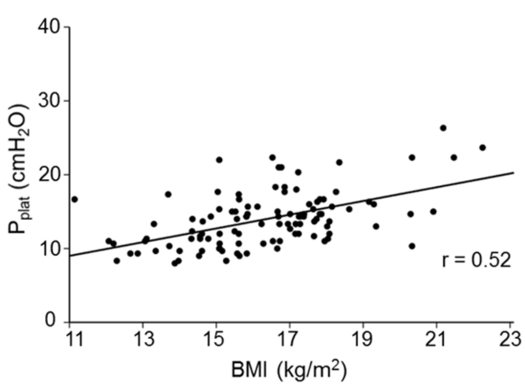

Figure 3. A linear increase in the P_{plat} with BMI was observed in children with OSAS. P_{plat} = plateau inspiratory pressure, BMI = body mass index.

Relationships between BMI and P_{peak}, P_{plat}, and C_{dyn}

For the correlation analys is, age and BMI were chosen as candidate risk factors potentially associated with high P_{peak}, high P_{plat}, and low Cdyn in OSAS children. There were significant positive correlations between BMI and elevated P_{peak} and P_{plat} values, and between age and C_{dyn} in the OSAS patients. Simple linear regression was used to characterize these correlations, and the regression lines were as follows: P_{peak} (cmH_2O) = 1.049 × BMI-1.145, with an R^2 of 0.363 (**Figure 2**); P_{plat} (cmH_2O) = 0.929 × BMI-1.211, with an R^2 of 0.274 (**Figure 3**); and C_{dyn} (mL/cmH_2O) = 1.919 × year + 7.418, with an R^2 of 0.472 (**Figure 4**). No other parameters were significantly associated with P_{peak}, P_{plat}, or C_{dyn}.

Validation of fitted equation

In this part, a total of 38 patients (normal weight, n = 20; overweight, n = 10; obese, n = 8) were included in this analysis; no patients were excluded or withdrew from the study. The childrens' age (yr) was 5.01 ± 2.63, and BMI was 16.17 ± 2.42 in this group. We compared the P_{peak}, P_{plat}, and C_{dyn} from the fitted equation with the measurement, which was used to validate the accuracy of our fitted equation for predicting P_{peak}, P_{plat}, and C_{dyn}. There was no significant difference in the P_{peak}, P_{plat}, and C_{dyn} in both groups (the fitted group vs. the measured group) (**Table 4**). The ability of the fitted equations to predict the respiratory parameters were determined by ROC analysis, and they are shown in **Table 5**.

The incidence of PPCs

There were no episodes of serious hypoxemia (SpO_2 < 90% under room air), pneumothorax, or acute respiratory distress syndrome in either group.

Discussion

In this study, being overweight or obese was significantly associated with increased P_{peak} and P_{plat} values in young OSAS patients, and increased P_{peak} and P_{plat} values were positively correlated with BMI. There was no significant

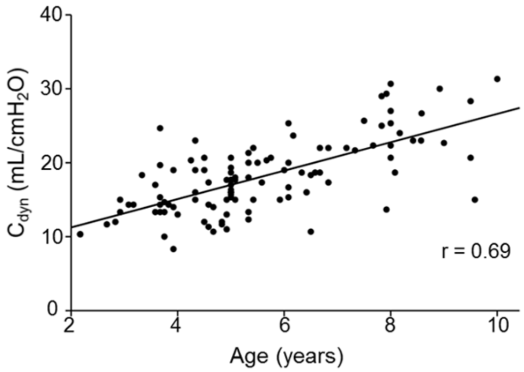

Figure 4. The C_{dyn} showed a linear increased with age in children with OSAS. C_{dyn} = dynamic pulmonary compliance.

relationship between being overweight or obese and C_{dyn}; however, C_{dyn} was positively correlated with age. More importantly, we were able to develop a good model for predicting P_{peak}, P_{plat}, and C_{dyn} based on BMI and age in children undergoing VCV.

It is frequently recommended that ventilation remain at a pressure of < 20 cmH$_2$O. P_{peak} and C_{dyn} should be changed cautiously during endobronchial intubation [8, 9]. In the current study, the mean P_{peak} of 14.4 ± 2.3 cmH$_2$O observed using cuffed ETTs in children aged 2-10 years with a normal BMI was lower than that reported by Campos et al. [9]; they used a similar methodology and reported a mean P_{peak} of 23.6 ± 5.3 cmH$_2$O in children of unknown BMI and aged 0.2-7.0 years, using uncuffed ETTs. The C_{dyn} measured in the present study was also lower than that reported previously by Mahajan et al. [8]. Notably, the P_{peak} values derived using the ETTs utilized in our study were similar with those previously reported in children and adults using laryngeal masks [10, 11]; however, the patients' BMIs were unknown in those prior studies. Given that leak pressure around ETTs is associated with an overestimation of P_{peak} and pulmonary compliance values [12], this discrepancy can be primarily attributed to the difference in leak pressures between the various ETT sizes [8, 13]; cuffed ETTs were used in all patients in the present study, and, thus, there was no leak pressure. The cuffed ETTs, relative to uncuffed ETTs, can minimized the sevoflurane concentrations within the surgeons' operating area during pediatric adenoidectomies, which further suggests that cuffed ETTs can provide a higher airway seal pressure for positive airway pressure ventilation than other airway devices [14]. In addition, the mean BMI was normal in the patients in our study, but the BMI was not measured in the study conducted by Campos et al. [15], which may also contribute to the discrepancy because ventilation strategies used in obese patients differ from those used in normal patients. Differences in the study design and methodology, including BMI, ventilation parameters, leaks, and the final position of the ETT in the bronchus, may have contributed to the observed differences between our study and other studies.

The combined percentage of children who were overweight or obese in a study reported by Nafiu et al. [16] was 20.7%, and they concluded that children with OSAS were more likely to experience perioperative complications [17]. These complications included intraoperative desaturation, difficulties with mask ventilation, and upper airway obstruction, which are closely related to those of a high BMI [17]. However, it is unclear how changes in airway pressure and C_{dyn} are correlated with BMI, as this has not been studied thoroughly in children with OSAS. In the present study, there was a significant increase in P_{peak} and P_{plat} in overweight and obese children, BMI was significantly correlated with P_{peak} and P_{plat}, and there was a significant positive relationship between C_{dyn} and age. Interestingly, some studies report that airway resistance is significantly associated with age [8, 18], while in the present study, P_{peak} and P_{plat} were only significantly associated with BMI. Notably, the children in the aforementioned prior study were anesthetized with sevoflurane, which maintains diaphragm contractility [18], but in the present study, rocuronium was administered in order to reduce muscle tension during intraoperative mechanical ventilation. Therefore, we surmise that the muscle relaxant used was the primary cause of the discrepancy between the results of the two studies.

These results suggest that a relatively high airway pressure may be both safe and necessary to meet the requirements of intraoperative mechanical ventilation in overweight and obese children undergoing mechanical ventilation with VCV mode (setting the target tidal volume at 10 mL/kg), but there is still some risk of lung injury. Although P_{plat} was within 20 cmH$_2$O in our three study groups, the actual driving pressure

Table 4. Comparison of fitted values with measured values of P_{peak}, P_{plat}, and C_{dyn}

	Fitted value	Measured value	P
P_{peak} (cmH_2O)	15.82 ± 2.54	15.21 ± 3.13	0.085
P_{plat} (cmH_2O)	13.81 ± 2.25	13.34 ± 3.11	0.180
C_{dyn} (mL/cmH_2O)	17.03 ± 3.11	16.47 ± 4.85	0.298

Values are mean ± SD. Fitted value: the value come from fitted equation; Measured value: the value come from the actual measurement. P_{peak} = peak airway pressure; P_{plat} = plateau airway pressure; C_{dyn} = dynamin pulmonary compliance.

Table 5. Ability of fitted equations to predicate respiratory parameters

	Sensitivity (%)	Specificity (%)	Youden's index	AUC (95% CI)	P
P_{peak}	76.3%	52.6%	0.289	0.591 (0.461 - 0.722)	0.170
P_{plat}	78.9%	52.6%	0.316	0.605 (0.475 - 0.735)	0.114
C_{dyn}	97.4%	36.8%	0.342	0.570 (0.435 - 0.705)	0.294

AUC: area under the ROC curve; 95% CI: 95% confidence interval; P_{peak} = peak airway pressure; P_{plat} = plateau airway pressure; C_{dyn} = dynamin pulmonary compliance.

(driving pressure = P_{plat}-PEEP), at the range of 8-14 cmH_2O, was at a higher level. Driving pressure, as one of the most critical indicators for evaluating ventilator-induced lung injury, is the increase in airway pressure due to hyperinflation during mechanical ventilation, and a high driving pressure is associated with worse outcome [19, 20]. However, no serious respiratory complications were detected in our present study, which may have been attributed to shorter surgery times and good pulmonary compliance. Therefore, we suggest that the conventional mechanical ventilation setting (VCV with TV at 10 mL/kg), may be not an ideal ventilation strategy, and further investigation is required to determine an optimal lung-protective mechanical ventilation strategy in pediatric patients undergoing general anesthesia, especial in those who are overweight or obese.

There are some limitations in this study. First, P_{peak}, P_{plat}, and C_{dyn} were measured during mechanical ventilation at the position of the Y-piece; however, measuring those parameters at the position of distal end of the ETT (PT) is a relatively more accurate method. In the clinical setting, airway pressure is measured at the ventilator (PV), the Y-piece in the breathing circuit (PY), or the distal end of the ETT (PT) during intraoperative mechanical ventilation. Guttmann et al. [21] proposed monitoring the tracheal pressure by continually calculating ETT resistance via PY. In the present study, we continuously measured P_{peak}, P_{plat}, and C_{dyn} during mechanical ventilation at the Y-piece using the D-Lite all-in-one flow sensor, a small, lightweight, inexpensive sensor that can accurately and reliably measure airway pressures and pulmonary compliance [22]. Measuring PT is a relatively accurate method to calculate lung and airway pressures, but it is not widely employed because a specialized ETT is required. PV, and especially PY, can overestimate the pressures applied to the lungs and airways during positive pressure ventilation [23, 24]. Therefore, measuring PY is an effective, easy, and practical method to evaluate airway resistance during clinical anesthesia. A second limitation is the data from the present study were collected under realistic clinical conditions, and the results were derived from Chinese children diagnosed as being overweight or obese according to the WGOC guidelines [13]. While the methods for generating the standardized BMI growth curve in Chinese children were identical to those described by the World Health Organization (WHO) and US Centers for Disease Control (CDC) in 2000, slightly different BMI cut-off values were found between overweight and obese children [13]. The diagnostic criteria defining overweight and obese children differs by country, which may result in variation in the evaluation of lung and airway resistance in different countries.

In summary, a significant positive correlation was observed between BMI and airway pressure in pediatric patients receiving VCV in the current study. Based on these findings, we were able to formulate an equation that can be used to rapidly determine an appropriate range of airway pressures for VCV based on a child's BMI. Thus, the results of the present study may be used as a reference to reduce the risk of respiratory complications and improve the effectiveness of mechanical ventilation in overweight/obese children undergoing general anesthesia.

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Disclosure of conflict of interest

None.

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