Factors affecting airway compliance and resistance in children receiving general anesthesia during adenotonsillectomy

Jingjie Li, MS\textsuperscript{a}, Siyuan Li, MS\textsuperscript{b}, Hong Jiang, MD\textsuperscript{a,*}, Lai Jiang, MD\textsuperscript{b,*} , Lin Qiu, BS\textsuperscript{a}

Abstract
Airway compliance is an important index in the surgery of pediatric patients. This study aimed to explore factors affecting dynamic airway compliance (Cdyn) and airway resistance (Raw) after general anesthesia endotracheal intubation for adenotonsillectomy of pediatric patients.

A prospective study was undertaken of 107 children who underwent adenotonsillectomy in Xinhua Hospital Affiliated to Shanghai Jiaotong University School of Medicine between January and June 2018. The values of Cdyn and Raw were recorded at 5, 10, and 15 minutes during general anesthesia endotracheal intubation. Univariate analysis and multiple linear regression analysis were performed for factors that affected Cdyn and Raw.

Of the 107 patients aged 56.67 ± 18.28 months, 69 (64%) patients were male, and 26 (24%) and 12 (11%) had an upper respiratory infection in the past week and 1 to 2 weeks, respectively. During anesthesia, Cdyn showed a decreasing trend (P < .001) while Raw showed an increasing trend (P < .001). Multivariate analysis revealed that height (β = 0.177–0.193) had the strongest correlation with Cdyn; rales during preoperative auscultation (β = −2.727 to −1.363) and sputum suction (β = −1.670 to −0.949) were also associated with Cdyn (all P < .05). Height was the factor with the strongest negative correlation with Raw (β = −0.382 to −0.305). Rales during preoperative auscultation (β = 10.063–11.326) and sputum suction (β = 3.863–9.003) were also associated with Raw (All P < .05).

Height, rales during preoperative auscultation and sputum suction were all associated with intraoperative Cdyn and Raw for pediatric patients undergoing adenotonsillectomy and should be considered before the surgery.

Keywords: airway compliance, airway resistance, anesthesia, pediatric, upper respiratory infection

1. Introduction
Lung compliance monitoring is indispensable during general anesthesia to ensure adequate oxygenation and gas exchange.\cite{1} Lung compliance refers to the change of lung volume in unit pressure. Clinically, lung compliance is classified as static and dynamic. Many factors can affect lung compliance during general anesthesia, including personal factors such as age, height, weight, and preoperative respiratory diseases; and intra-operative factors including method of anesthesia and ventilation, anesthesia agents such as muscle relaxants, inhalation drugs and opioids, patient postures, and surgical location.\cite{2,3,4} However, the perioperative factors affecting dynamic airway compliance (Cdyn) and airway resistance (Raw) remain unclear. As the ventilator works continuously during general anesthesia endotracheal intubation (ETI) without interrupting the ventilation air flow, change in Cdyn is mainly monitored in clinical practice. As Cdyn can monitor alveolar changes in a real-time manner, it is primarily important in assessing the intra-operative lung function of the patient.\cite{5,6}

Upper respiratory tract infections (URIs) are associated with an increase in frequency of airway adverse events and airway interventions during general anesthesia.\cite{7} Pediatric patients receiving adenotonsillectomy are often complicated with pharyngeal inflammation, mucosal congestion, and airway hyper-responsiveness.\cite{8} In addition, the secretion of respiratory mucosa is exuberant in children, especially when they are crying and screaming. Surgical stimulation to the oral cavity during...
operation can also increase airway resistance and decrease lung compliance. General anesthesia endotracheal intubation has often been the focus of pediatric anesthesia, especially for pediatric patients combined with URIs before the operation.[9]

While most previous studies on lung compliance in children have focused on single-factor changes and there is a lack of systematic and multi-factorial studies.[10,11] Therefore, we undertook a study to analyze factors that may affect Cdyn and Raw after endotracheal intubation in these patients.

2. Materials and methods

2.1. Study design

This was a prospective study of consecutive patients treated between January 2018 and June 2018 to explore factors affecting Cdyn and Raw after general anesthesia endotracheal intubation for adenotonsillectomy of pediatric patients. The study was approved by the ethics committee of Xinhua hospital. Informed consent was obtained from all patients or their parents before enrollment.

2.2. Patients

This study enrolled pediatric patients according to the following inclusion criteria:

1) patients who were diagnosed as American Society of Anesthesiologists Grade 1 to Grade 2 and were scheduled to receive adenotonsillectomy in our hospital;
2) patients aged between 3 and 6 years;
3) patients without obstructive or restrictive lung diseases.

The exclusion criteria were:

1) children with congenital heart disease or severe liver and kidney dysfunction;
2) children with a known history of allergies to narcotic drugs;
3) children with obvious thoracic deformity and foreseeable difficulty in receiving intubation;
4) children with a history of asthma.

2.3. Anesthesia during surgery

All children received routine general anesthesia induction by intravenous (IV) infusion of midazolam 0.05 mg/kg, propofol 3 mg/kg. The plasma target-controlled concentration of remifentanil was set at 2 ng/mL and 3 minutes after administration of IV 0.15 mg/kg cis-atracurium, ETI was performed (caliber = 4 + age/4) with a reinforced endotracheal tube. Administration of premedicative atropine (0.01 mg/kg IV) was dependent on the chief anesthesiologist’s advice before anesthesia induction.

After anesthesia induction and ETI, anesthesia was maintained by 4 to 8 mg/kg/h propofol, and the plasma concentration of remifentanil was target-controlled at 2 ng/mL. At the same time, respirator-assisted ventilation was applied at a tidal volume of 10 mL/kg, respiratory rate of 18 bpm, an inhalation/exhalation ratio (E/I) of 1.2, air-oxygen mixture ventilation of 1:1, and a ventilation flow rate of 2 L/min. The maintenance dose of IV propofol was adjusted according to the intra-operative BIS between 50 and 60. At the same time, muscle relaxant recovery was monitored by TOF using the muscle relaxation monitor. Additional 0.05 to 0.1 mg/kg cis-atracurium IV was administered when necessary to maintain endotracheal T1 < 10% during the anesthesia period so as to avoid the impact of muscle relaxation on Cdyn and Raw of the pediatric patients.

2.4. Data collection

Detailed information was collected and recorded including the sex, age, height, weight, lung markings in preoperative chest X-ray, preoperative white cell count, data of preoperative auscultation, sputum suction after the operation, the presence, or absence of crying and screaming, and length of URI in days. URI were reported by their parents and was defined as if at least 2 of the following symptoms were present: rhinorrhea, sore or scratchy throat, sneezing, nasal congestion, malaise, cough, or fever > 38°C.

Cdyn and Raw were observed and recorded at three time points: 5, 10, and 15 minutes after intubation.

2.5. Statistical analysis

The SPSS 21.0 software package (IBM Corp., Amonk, New York, USA) was used for statistical analysis. Continuous data were represented by mean ± standard deviation. Analysis of variance was used to compare continuous data among multiple groups. Factors affecting continuous data were analyzed by multivariate regression analysis, and variable screening was performed by stepwise regression. Repeated measurements were analyzed by analysis of variance for repeated measurements, and least significant difference t test was performed for group-wise comparison at different time points. P < .05 was considered to be statistically significant.

3. Results

3.1. Baseline characteristics of children

This study evaluated data from 107 pediatric patients scheduled to receive adenotonsillectomy. The baseline data for the patients are listed in Table 1. The patients were aged 56.67 ± 18.28 months, with 110.18 ± 11.66 cm height, and 19.72 ± 5.57 kg weight. Sixty-nine of (64%) patients were boys, 26 (24%) had a URI in the past week and 12 (11%) had a URI between 1 and 2 weeks.

3.2. Data of Cdyn and raw

Table 2 shows the Cdyn and Raw mean values at each time point during anesthesia. Cdyn of the pediatric patients showed a...
Table 2

| Variables                  | 5 min       | 10 min      | 15 min      | P      |
|----------------------------|-------------|-------------|-------------|--------|
| Cdyn                       | 13.27 ± 3.32| 12.86 ± 3.23| 12.45 ± 3.12| < .001 |
| Raw                        | 32.63 ± 9.40| 34.96 ± 12.09| 36.58 ± 13.83| < .001 |

Cdyn = dynamic airway compliance, Raw = airway resistance.

Cdyn and Raw during anesthesia.

Table 3

Multiple linear regression analysis of factors related to Cdyn and Raw at each time point during anesthesia.

| Variables                               | β        | SE       | S.E.B.     | P      |
|-----------------------------------------|----------|----------|------------|--------|
| Cdyn at 5 min                           |          |          |            |        |
| Height                                  | 0.192    | 0.017    | 0.675      | < .001 |
| Rates during pulmonary auscultation     | -2.727   | 0.505    | -0.322     | < .001 |
| Sputum suction                          | -0.549   | 0.399    | -0.144     | 0.016  |
| Cdyn at 10 min                          | 0.193    | 0.017    | 0.605      | < .001 |
| Rates during pulmonary auscultation     | -2.006   | 0.517    | -0.243     | < .001 |
| Sputum suction                          | -1.051   | 0.398    | -0.163     | 0.010  |
| Cdyn at 15 min                          | 0.177    | 0.018    | 0.660      | < .001 |
| Rates during pulmonary auscultation     | -1.363   | 0.540    | -0.171     | 0.013  |
| Sputum suction                          | -1.670   | 0.415    | -0.268     | < .001 |
| Raw at 5 min                            | -0.305   | 0.056    | -0.378     | < .001 |
| Rates during pulmonary auscultation     | 11.326   | 1.589    | 0.472      | < .001 |
| Sputum suction                          | 3.863    | 1.249    | 0.206      | 0.003  |
| Crying and screaming                    | 3.579    | 1.694    | 0.243      | 0.003  |
| Raw at 10 min                           | -0.382   | 0.083    | -0.369     | < .001 |
| Rates during pulmonary auscultation     | 10.132   | 2.506    | 0.328      | < .001 |
| Sputum suction                          | 6.337    | 1.928    | 0.263      | < .001 |
| Raw at 15 min                           | -0.364   | 0.098    | -0.307     | < .001 |
| Rates during pulmonary auscultation     | 10.063   | 2.961    | 0.285      | < .001 |
| Sputum suction                          | 9.003    | 2.278    | 0.327      | < .001 |

Cdyn = dynamic airway compliance, Raw = airway resistance.

decreasing trend (P < .001) while Raw showed an increasing trend (P < .001).

3.3. Factors influencing Cdyn and raw

Multivariate analysis of factors related to Cdyn and Raw is shown in Table 3. This revealed that height was positively correlated with Cdyn and had the strongest correlation with Cdyn (P < .001 at 5, 10, and 15 minutes). Moreover, rates during pulmonary auscultation (P < .001 at 5 and 10 minutes and P = .013 at 15 minutes) and sputum suction (P = .016 at 5 minutes, P = .010 at 10 minutes, and P < .001 at 15 minutes) were also associated with Cdyn. Among the various factors affecting Raw of the pediatric patients, height was also the factor with the strongest correlation, which was negatively correlated with Raw (P < .001 at 5, 10, and 15 minutes). Moreover, rates during pulmonary auscultation and sputum suction were also associated with Raw (P < .001 at 5 and 10 minutes, and P = .001 at 15 minutes).

4. Discussion

Good lung compliance is necessary for maintaining perioperative respiratory function. The aim of this study was to explore factors affecting Cdyn and Raw after general anesthesia endotracheal intubation for adenotonsillectomy of pediatric patients. The results showed that Cdyn showed a decreasing trend and Raw an increasing trend during anesthesia. Multivariate analysis revealed that height had the strongest correlation with Cdyn but that rates during preoperative auscultation and sputum suction were also associated with Cdyn. Height also had the strongest negative correlation with Raw and rates during pulmonary auscultation and sputum suction were also associated with Raw.

Previous studies found that Raw tended to increase while Cdyn tended to decrease after general anesthesia ETI. In addition, stimulation of the endotracheal tube on the air passage and tracheal carina may induce reflexive bronchoconstriction and thereby increase the airway resistance and reduce lung compliance. However, these studies focused on post-ETI lung compliance in adult patients, and all the data were recorded within 15 minutes. In the present study, we only included children undergoing adenotonsillectomy, knowing that the duration of such an operation is relatively short. To avoid incomplete data collection, we only recorded data until 15 minutes after ETI. It was found that Cdyn decreased and Raw increased with time after ETI in this group of patients.

Although multiple factors may affect lung compliance during the process of anesthesia, there are few studies in children, so there is no consensus about whether their physique and other intrinsic factors of children may affect lung compliance. One study on factors affecting compliance of the respiratory system in 32 children aged 3 to 54 months showed that compliance of the respiratory system was correlated with age, height, and weight, with height showing predominating influence. However, Greenough et al. reported that age had the strongest correlation with the overall compliance of the respiratory system in their 63 pediatric patients aged 2 to 7 years (R = 0.83), followed by height (R = 0.73). Such a difference may be attributed to multiple reasons. Marsh et al. and Greenough et al. reported that the compliance of the respiratory system was calculated after pulmonary function monitoring when the children were conscious. However, crying, disrupting, and other uncooperative factors may all have great impact on respiratory compliance. In our study, 107 children aged 3 to 6 years received the same selective operation under ETI general anesthesia, thus maximally avoiding the interference of other factors during measurement of lung compliance. In addition, Marsh et al. and Greenough et al. reported the overall compliance of the respiratory system based on the data of pulmonary function monitoring, including the impact from both the lung, and the bony thorax. Our data were directly obtained from real-time monitoring during continuous working of the respirator after ETI and therefore can more directly reflect the pulmonary function of the pediatric patients. It should be noted that elevated eosinophil cationic protein in the bronchoalveolar lavage fluid are related to irritable airways, likely following airway inflammation, indicating that eosinophil cationic protein could help detect respiratory adverse events perioperatively.

The results of this study highlight the importance of rates during pulmonary auscultation. Rates are abnormal lung sounds of popping and crackling that can identify patients with problems such as pneumonia. However, their analysis is very subjective and reliant upon the treating physician’s experience. Because
tulobuterol patch is associated with reduced Raw and elevated recovery of the heart rate. However, as shown in our study, no demonstrated that treatment with the transdermal decrease in Cdyn and increase in Raw with time. However, it was such as ketamine, because these narcotics apparently increase use of atropine is especially important after the use of narcotics it can reduce saliva secretion and inhibit the vagus re.

anticholinergic agent atropine to see whether it could reduce Raw thus increasing the airway secretion. So sometimes we used the anticholinergic effect of prolonged anesthesia on lung compliance. In the present study, we selected children aged 3 to 6 years, knowing that children of this age group are more likely to undergo tonsillectomy due to adenoid hyperplasia, tonsillar hyperplasia, and chronic tonsillitis. In addition, the secretion of respiratory mucosa is exuberant in children, especially when they are crying, and disrupting. Intrairal operation also increases stimulation on the respiratory tract, thus increasing the airway secretion. So sometimes we used the anticholinergic agent atropine to see whether it could reduce Raw and improve Cdyn.

Atropine is an anticholinergic drug commonly used by anesthesiologists for general anesthesia induction, knowing that it can reduce saliva secretion and inhibit the vagus reflex. It is often used for its antispasmodic effects. However, in our study, no significant atropine effect on Cdyn or Raw was observed in the multivariate analysis. And there was only a tendency of slight decrease in Cdyn and increase in Raw with time. However, it was demonstrated that treatment with the transdermal β2-agonist tulobuterol patch is associated with reduced Raw and elevated Cdyn.

Several limitations of this study should be raised. The sample size in our study was relatively small, which might increase the inability to detect a significant difference. Whether a different conclusion could be made in larger sample of children needs more study. In addition, included in our study were pediatric patients who were scheduled to receive adenotonsillectomy, and all the data were recorded within 15 minutes. Hence, our study does not elucidate the effects of prolonged anesthesia on lung compliance.

In summary, the present study demonstrated that no significant correlations were found between days of preoperative URI and Cdyn. Height, rates during preoperative auscultation and postoperative sputum sucking were the main influencing factors for Cdyn and Raw respectively in pediatric patients.

**Author contributions**

Hong Jiang and Lai Jiang: study concept and design. Jingjie Li and Siyuan Li: acquisition of the data. Jingjie Li and Lin Qui: analysis and interpretation of the data. Jingjie Li and Lai Jiang: draft the manuscript, obtain funding, technical, and material support. All authors have read and approved the manuscript.

**References**

[1] McCollum ED, Park DE, Watson NL, et al. Listening panel agreement and characteristics of lung sounds digitally recorded from children aged 1-59 months enrolled in the Pneumonia Enology Research for Child Health (PERCH) case-control study. BMJ Open Respir Res 2017;4:e000193.

[2] Grisco DL, Russo A, Romano R, et al. Lung volumes, respiratory mechanics and dynamic strain during general anaesthesia. Br J Anaesth 2018;121:1156–65.

[3] Tomescu DR, Popescu M, Dima SO, et al. Obesity is associated with decreased lung compliance and hypercapnia during robotic assisted surgery. J Clin Monit Comput 2017;31:85–92.

[4] Paliu FM, Sinha P, Liu KD, et al. Influence of clinical factors and exclusion criteria on mortality in ARDS observational studies and randomized controlled trials. Respir Care 2018;63:1060–9.

[5] Mahajan A, Hoffman N, Hsu A, et al. Continuous monitoring of dynamic pulmonary compliance enables detection of endobronchial intubation in infants and children. Anesth Analg 2007;105:51–6.

[6] Kaskinen AK, Kirjavainen T, Raumann P, et al. Ventilator-derived dynamic respiratory system compliance: comparison with static compliance in children. Respir Physiol Neurobiol 2018;249:32–4.

[7] Mallory MD, Travers C, McCracken CE, et al. Upper respiratory infections and airway adverse events in pediatric procedural sedation. Pediatrics 2017;140:e20170009.

[8] Carapagnano LF, Laedonita D, Foschino-Barbaro MP. Non-invasive study of airways inflammation in sleep apnea patients. Sleep Med Rev 2011;15:317–26.

[9] de Carvalho ALR, Vital RB, de Lira CCS, et al. Laryngeal mask airway versus other airway devices for anesthesia in children with an upper respiratory tract infection: a systematic review and meta-analysis of respiratory complications. Anesth Analg 2018;127:941–50.

[10] Sun R, Wang G, Hao X, et al. Flumazenil reduces respiratory complications during anesthesia emergence in children with preoperative upper respiratory tract infections. Medicine (Baltimore) 2018;97:e05316.

[11] Serafini G, Cavalloro F, Mori A, et al. Upper respiratory tract infections and pediatric anesthesia. Minerva Anestesiol 2003;69:457–9.

[12] Kil HK, Roko GA, Ryan-Dykes MA, et al. Effect of prophylactic bronchodilator treatment on lung resistance after tracheal intubation. Anesthesiology 1994;81:43–8.

[13] Eames Wo, Roko GA, Wu RS, et al. Comparison of the effects of etomate, propofo, and thiopental on respiratory resistance after tracheal intubation. Anesthesiology 1996;84:1037–11.

[14] Kim ES, Bishop MJ. Endotracheal intubation, but not laryngeal mask airway insertion, produces reversible bronchoconstriction. Anesthesiol 1999;90:391–4.

[15] Mahdavi A, Razavi SS, Malekianzadeh B, et al. Comparison of the peak inspiratory pressure and lung dynamic compliance between a classic laryngeal mask airway and an endotracheal tube in children under mechanical ventilation. Tanaffos 2017;16:289–94.

[16] Montravers P, Dureuil B, Moliex S, et al. Effects of intravenous midazolam on the work of breathing. Anesth Analg 1994;79:538–62.

[17] Sevin SO, Barreto G, Martins LC, et al. Traumatic endotracheal tube for mechanical ventilation. Rev Bras Anestesiol 2011;61:311–9.

[18] Marchal F, Crance JP. Measurement of ventilatory system compliance in infants and young children. Respir Physiol 1987;68:311–8.

[19] Greenough A, Stocks J, Nothen U, et al. Total respiratory compliance and functional residual capacity in young children. Pediatr Pulmonol 1986;2:321–6.

[20] von Ungern-Sternberg BS, Sly PD, Loh RK, et al. Value of cosinophil cationic protein and tryptase levels in bronchoalveolar lavage fluid for predicting lung function impairment in anasthesed, asthmatic children. Anaesth 2006;61:1149–54.

[21] Cox RG. Anesthetic management of pediatric adenotonsillactomy. Can J Anaesth 2007;54:1021–5.

[22] Tait AR, Malviya S, Veepol-Lewis T, et al. Risk factors for perioperative adverse respiratory events in children with upper respiratory tract infections. Anesthesiology 2001;95:299–306.

[23] Tait AR, Malviya S. Anaesthesia for the child with an upper respiratory tract infection: still a dilemma? Anesth Analg 2005;100:39–65.

[24] Regli A, Becke K, von Ungern-Sternberg BS. An update on the perioperative management of children with upper respiratory tract infections. Curr Opin Anaesthesiol 2017;30:362–7.
[25] Mirakhur RK, Dundee JW, Connolly JD. Studies of drugs given before anaesthesia. XVII: anticholinergic premedicants. Br J Anaesth 1979; 51:339–45.

[26] Heinz P, Geelhoed GC, Wee C, et al. Is atropine needed with ketamine sedation? A prospective, randomised, double blind study. Emerg Med J 2006;23:206–9.

[27] Kye YC, Rhee JE, Kim K, et al. Clinical effects of adjunctive atropine during ketamine sedation in pediatric emergency patients. Am J Emerg Med 2012;30:1981–5.

[28] Lee DW, Kim ES, Do WS, et al. The effect of tulobuterol patches on the respiratory system after endotracheal intubation. J Dent Anesth Pain Med 2017;17:265–70.