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# Factors Causing Post-Anesthetic High Respiratory Resistance in Patients Undergoing Transurethral Resection of Bladder Tumors

Junko Nakahira,<sup>1,\*</sup> Shoko Nakano,<sup>1</sup> Toshiyuki Sawai,<sup>1</sup> Junichi Ishio,<sup>1</sup> Naomi Ono,<sup>1</sup> and Toshiaki Minami<sup>1</sup> <sup>1</sup>Department of Anesthesiology, Osaka Medical College, Takatsuki, Japan

<sup>\*</sup> *Corresponding author*: Junko Nakahira, MD, PhD, Department of Anesthesiology, Osaka Medical College, 2-7 Daigaku-machi, Takatsuki, Osaka 569-8686, Japan. Tel: +81-726831221, Fax: +81-726846552, E-mail: ane052@osaka-med.ac.jp

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#### Abstract

**Background:** In this study, we investigated the causes of high respiratory resistance that is observed after general anesthesia. We focused on respiratory resistance at 5 Hz (R5), which were measured preoperatively and postoperatively.

**Methods:** Our prospective observational study enrolled 68 patients who underwent transurethral resection of bladder tumors from April to October 2015. Respiratory impedance was measured the day before surgery and immediately after general anesthesia. Participants were divided into 2 groups: Group L (postoperative R5 values < 4.0 cmH<sub>2</sub>O/L/sec; n = 33) and Group H (postoperative R5 values  $\geq$  4.0 cmH<sub>2</sub>O/L/sec; n = 35). Patient background, preoperative R5 values, endotracheal tube or subglottic devices, anaesthetic period, desflurane or sevoflurane, and endotracheal suctioning were compared.

**Results:** Significant parameters were height, inhalation of desflurane, endotracheal suctioning, and preoperative R5 value. Logistic regression showed that endotracheal suctioning and a higher preoperative R5 level increased postoperative respiratory resistance (>  $4 \text{ cmH}_2\text{O}/\text{L/sec}$ ).

**Conclusions:** The endotracheal suctioning at the end of anesthesia influenced respiratory resistance more than use of the endotracheal tube and desflurane.

*Keywords*: Forced Oscillation Technique, Respiratory Impedance, Ventilator-Induced Lung Injury, Mechanical Ventilation, General Anesthesia

#### 1. Background

Spirometry is an established method to measure respiratory function, and it requires maximal patient effort to complete the measurements. However, postoperative respiratory evaluation using spirometry may not be accurate. The forced oscillation technique (FOT) is a non-invasive method of measuring respiratory impedance, the spectral relationship between pressure and airflow (1). FOT measurements require no special breathing manoeuvres or interference with normal breathing (2), and clinical use of FOT has increased as more FOT devices have become commercially available, such as the MostGraph-01® impulse oscillation system (Chest MI, Tokyo, Japan) (3). The evidence base for the clinical utility of FOT has expanded, especially for the evaluation and management of obstructive pulmonary diseases, including asthma and chronic obstructive pulmonary disease. However, changes in the respiratory impedance that occur as a result of airway inflammation and pulmonary function are not fully understood. Impedance is determined by 2 components: respiratory resistance (Rrs) and respiratory reactance (Xrs). Xrs reflects the elastic and inertial properties of the lung (4) and its meaning and clinical usefulness are not well established.

Rrs, however, is a good parameter to determine narrowing or obstruction of the airway. We used the FOT and investigated the factors contributing to higher postoperative respiratory resistance in patients who received general anesthesia.

# 2. Methods

This prospective study was approved by the ethics committee of Osaka Medical College, Japan. Written informed consent was obtained from all participants. The study was registered with the Japan medical association center for clinical trials on September 2, 2013 (reference JMA-IIA00136). We enrolled 68 patients who had the American society of anesthesiologists physical status classification 1 or 2 and who underwent general anesthesia for transurethral resection of bladder tumors. We excluded patients with a history or symptoms of asthma, such as coughing or wheezing at rest, patients diagnosed with chronic obstructive pulmonary disease according to the global initiative for chronic obstructive lung disease guidelines (5), and patients who had taken oral steroids, had had a respiratory tract infection, or exacerbation within the previous 3 months. Patient background

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information was collected by reviewing patient records. Spirometry was performed the day before surgery.

The participants were divided into 2 groups as follows: Group L included 33 patients whose postoperative R5 values were less than 4.0 cmH<sub>2</sub>O/L/sec, and Group H included 35 patients whose postoperative R5 values greater than or equal to 4.0 cmH<sub>2</sub>O/L/sec.

## 2.1. Measurements

Forced oscillation was measured with standard techniques, using a MostGraph-O1<sup>®</sup> device (Chest, Tokyo, Japan) (4, 6), the day before surgery and immediately after removal of the airway adjunct. Rrs and Xrs were recorded in the sitting position with participants breathing normally through a mouthpiece while wearing a nose clip. To minimize artefacts from vibrations, an investigator supported the patient's cheeks. For preoperative measurements, patients sat unsupported in a chair. Postoperative measurements were recorded on the operating with with the patients sitting at 45-50° with their legs straight.

#### 2.2. Anesthetic Management

On the day of surgery, anesthesia was induced using intravenous propofol (2 mg/kg), rocuronium (0.8 mg/kg), an infusion of remifertanil (0.5  $\mu$ g/kg/min), and inhaled sevoflurane (3.0%) or desflurane (5.0% - 6.0%). The urologist determined the need for neuromuscular blockade during surgery, according to the location of the tumor. A cuffed endotracheal tube (Portex Soft Seal<sup>®</sup>, Smiths Medical, Kent, UK) with an internal diameter 7.0 mm for women and 8.0 mm for men was used for patients who needed a neuromuscular blocker; a subglottic device (i-gel®, Intersurgical, Wokingham, UK) of size 3 for women or size 4 for men was inserted for the other patients. Anesthesia was maintained using inhaled sevoflurane 1.0% - 1.5% or desflurane 4.0% -5.0% and intravenous remifentanil 0.25 - 0.5  $\mu$ g/kg/min in a fraction of inspired oxygen ( $FiO_2$ ) of 0.4. We used high fresh gas flow for sevoflurane anesthesia with 1L/min of oxygen and 2L/min of air, and low fresh gas flow for desflurane anesthesia with 0.5L/min of oxygen and 1L/min of air. Patients were mechanically ventilated using volumecontrolled ventilation at 8 mL/kg predicted body weight without positive end-expiratory pressure. For postoperative analgesia, acetaminophen (1000 mg) was administered intravenously at the end of the surgery. Anaesthetic agents were stopped immediately after the operation. After spontaneous breathing had returned, the FiO<sub>2</sub> was increased to 1.0 and sugammadex (1.5 mg/kg) was administered intravenously to those who had received rocuronium. Extubation or removal of the subglottic device occurred when the patient responded to their name, body

temperature was >  $35.5^{\circ}$ C, peripheral oxygen saturation was > 97%, and there was stable breathing at a rate of 10 - 20 breaths/min. Open suctioning with a 14 Fr catheter at -20 kPa through the endotracheal tube was performed to remove sputum, depending on the anaesthesiologist in charge. In patients whose airway pressure during mechanical ventilation was greater than 20 cmH<sub>2</sub>O, suctioning was mandatory. After the airway adjunct had been removed, oxygen was administered by facemask at a rate of 4 L/min for 4 hours. All participants were encouraged to walk on the first postoperative day.

#### 2.3. Statistical Analysis

All results are presented as the mean  $\pm$  standard deviation or number. The Student's t-test with unequal variance (Welch's method), the Chi-square test or Fisher's exact test was used to compare the 2 groups when appropriate. After the univariate analyses, the variables with P < 0.2 were used in logistic regression analysis. Statistical significance in the logistic regression was defined as P < 0.05. All statistical analyses were performed using SPSS Statistics (version 22, IBM, Armonk, NY).

## 3. Results

Data from 33 patients in Group L and 35 patients in Group H were obtained. The average R5 of all patients was  $4.45 \pm 1.89$  cmH<sub>2</sub>O/L/sec (mean  $\pm$  standard deviation). There were no patients who showed emphysema examined by preoperative computed tomography or abnormal oxygen saturation. There was no difficult airway management in the patient with an endotracheal tube or subglottic device, and no patients who had gastro-esophageal reflux. There were no patients in whom endotracheal suctioning or alveolar recruitment were performed during mechanical ventilation. There were also no patients who fought with the mechanical ventilation due to spontaneous breathing and in whom sonorous rhonchi were head during mechanical ventilation. There were no patients whose airway pressure during mechanical ventilation was greater than 20 cmH<sub>2</sub>O, in whom tracheal suction was mandatory. All patients with endotracheal suctioning, just before extubation, had a cough reflex after the suctioning. There were no patients who had tracheal bleeding or tracheal stenosis. There was no use of broncho-active drugs during anesthesia, such as ephedrine. There were no laryngospasm incidences after extubation.

There were no significant differences in the spirometry results or in the effects of the patients' smoking habits (Table 1). We compared the 2 groups, and parameters with P < 0.2 in the univariate analysis were height, inhalation of desflurane, endotracheal suctioning, and preoperative R5 value, which is the respiratory resistance at 5 Hz (Table 1). After logistic regression, endotracheal suctioning (P = 0.014; odds ratio, 5.4; 95% confidence interval, 1.4 - 20.8) and preoperative R5 value (P = 0.001; odds ratio, 6.6; 95% confidence interval, 2.1 - 20.6) were significant (Table 2). There was a correlation between preoperative R5 and postoperative R5 (r = 0.323, P = 0.007).

Variables	Group L	Group H	P Value	
Patient background				
Age, y	$65\pm11$	$65\pm12$	0.970	
Age, y; minimum - maximum	40 - 84	43 - 85	-	
Male/Female	31/2	30/5	0.429	
Height, cm	$166.4\pm8.3$	$163.5\pm7.4$	0.133	
Body weight, kg	$63.6 \pm 14.6$	$64.0\pm9.4$	0.893	
Body mass index	$22.9\pm4.3$	$24.0\pm3.3$	0.243	
Body surface area, m <sup>2</sup>	$1.7\pm0.2$	$1.9\pm0.4$	0.746	
Current smoker	7	7	0.902	
Current and previous smoker	28	29	0.824	
Brinkman index	$735\pm 699$	$673\pm 641$	0.705	
VC,% predicted	$108\pm14$	$105\pm18$	0.477	
FVC, % predicted	$106\pm14$	$102\pm17$	0.338	
FEV1.0, % predicted	$95\pm14$	$92\pm16$	0.356	
FEV1.0/FVC $\times$ 100, %	$75\pm 6$	$75\pm7$	0.909	
Intraoperative data				
Sevoflurane/Desflurane	31/2	28/7	0.151	
Endotracheal tube/Subglottic device	24/9	27/8	0.674	
Endotracheal suctioning	9	22	0.003	
Anaesthetic time, min	$85\pm22$	$83 \pm 18$	0.666	
Operation time, min	$42\pm18$	$41\pm15$	0.811	
Infusion volume, ml	$646 \pm 208$	$604 \pm 137$	0.342	
Respiratory resistance				
Preoperative R5, cmH <sub>2</sub> O/L/min	$1.9\pm0.4$	$2.5\pm0.9$	< 0.00	
Postoperative R5, cmH <sub>2</sub> O/L/min	$3.1\pm0.7$	$5.7\pm1.7$	< 0.00	
Preoperative R20, cmH <sub>2</sub> O/L/min	$1.5\pm0.4$	$1.9\pm0.6$	< 0.00	
Postoperative R20, cmH <sub>2</sub> O/L/min	$2.4 \pm 0.6$	4.1±1.3	< 0.00	
Preoperative R5 - R20. cmH <sub>2</sub> O/L/min	$0.4 \pm 0.2$	$0.6\pm0.5$	0.058	
Postoperative R5 - R20, cmH <sub>2</sub> O/L/min	$0.7\pm0.5$	$1.5\pm0.8$	< 0.00	

Abbreviations: FEV1.0, Forced Expiratory Volume in the First Second; FVC, Forced Vital Capacity; VC, Vital Capac-

 $^{\rm ITY.}_{\rm a}$  Data are expressed as the mean  $\pm$  standard deviation or number.

#### 4. Discussion

Our results showed that the factors increasing postoperative respiratory resistance were relatively greater than preoperative R5 value and endotracheal suctioning. Endotracheal suctioning at the end of anesthesia influenced respiratory resistance more than the use of the endotracheal tube and desflurane.

R5 is representative of the respiratory resistance at low frequency and it indicates the respiratory resistance of the whole respiratory system including the peripheral airways, while R20 shows respiratory resistance of relatively larger airways (7). The normal respiratory resistance value has not been established. The normal limit of R5 in patients without respiratory difficulty or disorders is generally assessed to be less than 2 cmH<sub>2</sub>O/L/min and 2 - 3 cmH<sub>2</sub>O/L/min is the cut off. Initially, an R5 greater than 3 cmH<sub>2</sub>O/L/min is determined to be a high respiratory resistance (8, 9). An increase in respiratory resistance is caused by increased resistance to the airway flow, increased tissue resistance, and increased thoracic resistance. For respiratory abnormalities, the respiratory resistance increases with bronchial restriction in asthma and airway collapse in chronic obstructive pulmonary disease (1, 8, 10, 11). Previously, we reported that a long duration of general anesthesia with endotracheal intubation caused a greater amount of respiratory resistance (4). The cut-off value in our study was set as 4cmH<sub>2</sub>O/L/sec, considering the previous study and the postoperative results of all patients in this study.

According to the guidelines for extubation, endotracheal suctioning is an invasive procedure, and therefore, suctioning and extubation should be performed under general anesthesia if they are necessary in critical asthmatic patients (12). Possible complications of endotracheal suctioning include hypoxia, tracheal spasm, atelectasis, tracheal tissue injury, arrhythmia, and elevation of intracranial pressure (13). To reduce the occurrence rate of these complications, tracheal suctioning should be performed only when it is needed. There are 2 methods for endotracheal suctioning: open and closed suctioning. We performed open suctioning in all cases. There are fewer tissue injuries with open suctioning (14), however, both methods can cause tracheal stimulation and cough reflex. Endotracheal suctioning is recommended only when the patient has secretions in the airway or the mouth (13). In this study, the surgical procedure was transurethral resection of the prostate, which was relatively short, less invasive, and less influential on respiratory systems. The anesthesiologist in charge determined the need for endotracheal suctioning, without hearing lung sounds before the extubation for all patients.

Rales heard during auscultation of the lungs are the only way to detect the presence of airway secretions. Auscultation with manual ventilation through the endotracheal tube is performed with a higher airway pressure than that set for mechanical ventilation. If there is sputum in Table 2. Results of Logistic Regression<sup>a</sup>

Factors	P Value	Odds Ratio	Confidence Interval		
Preoperative R5	0.001	6.598	2.114	to	20.591
Endotracheal suctioning	0.014	5.436	1.418	to	20.834
Height	0.396	2.407	0.893	to	1.046
Desflurane inhalation	0.610	1.656	0.238	to	11.502

<sup>a</sup>Accuracy: 76.5%, Hosmer-Lemshow, P = 0.436.

the trachea and the relatively central bronchi, sonorous rhonchi (low and continuous rales) are heard through the stethoscope as the sputum moves due to the changing diameter and shape of the airway. To achieve more accuracy in this study, entry criteria for the participants should include the presence of rales. There are many studies on the effect of shallow and deep suctioning, where the suction catheter is inserted. However, the effect is still controversial in adult patients (15, 16). In this study, shallow suctioning was performed, where the catheter tip did not go into the bronchus.

Desflurane is an inhaled agent that stimulates the upper airway (17, 18). However, desflurane is controversial because it reduces bronchoconstriction (19) and has no effect on basal (20) and elevated airway tone (21). However, it irritates the airways, manifesting as an elevated respiratory resistance (19, 22). It increases respiratory resistance with 2 MAC (minimum alveolar concentration), while sevoflurane continues to have a bronchodilator effect (19). Contrary to our expectations, desflurane was not a factor that increased the postoperative respiratory resistance.

In paediatric patients, height is an important parameter that has a correlation to respiratory resistance (23). In our study, there were no significant differences in BSA (body surface area) between the 2 groups. We included height in the logistic regression analysis, which was significant (P < 0.2) when the 2 groups were compared. Finally, height was not a factor for increasing the postoperative respiratory resistance.

Unnecessary endotracheal suctioning should be prevented to avoid postoperative respiratory complications caused by endotracheal injury, however, the reason for this is not known. Our study indicated that the measurement of respiratory resistance could be a means to evaluate postoperative respiratory status. Spirometry, an established measurement to evaluate respiratory function, is used to evaluate respiratory function in many studies; however, we suggest that patients' postoperative condition affects the spirometry results in any kind of surgery because spirometry requires a patient's maximum for inspiration and expiration. Although patients are forced to breathe through a mouthpiece while wearing a nose clip during the FOT, patients only breathe normally in the sitting position (24). The FOT is a more reliable method to evaluate the comparison between pre- and post-operative status.

## 4.1. Conclusions

The factors that increase postoperative respiratory resistance higher than 4 cmH<sub>2</sub>O/L/sec were relatively greater preoperative R5 value and endotracheal suctioning. The endotracheal suctioning at the end of anesthesia influenced respiratory resistance more than the use of an endotracheal tube and desflurane.

#### Footnotes

Authors' Contribution: Junko Nakahira participated in the design, coordination of the study, and helped draft the manuscript. Shoko Nakano made substantial contributions to the conception, design of the study, the acquisition of data, and drafted the manuscript. Toshiyuki Sawai performed the statistical analyses and revised the manuscript critically for important intellectual content. Naomi Ono and Junichi Ishio made substantial contributions to the conception of the study and helped correct the manuscript. Toshiaki Minami made substantial contributions to the conception of the study and helped draft the manuscript. All authors have read and approved the final manuscript.

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**Competing Interests:** The authors declare that they have no competing interests.

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