

# Laryngeal Reflex before and after Placement of Airway Interventions: Endotracheal Tube and Laryngeal Mask Airway™

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**Background:** Previous reports indicate that detrimental laryngeal function persists over several hours after tracheal extubation even in patients who have regained full consciousness from anesthesia. The authors hypothesize that even after minor surgery, the presence of an endotracheal tube (ETT) impairs the receptors at the vocal cord and diminishes the defensive laryngeal function. The hypothesis was tested by comparing types of experimentally induced laryngeal airway reflexes before and after surgery in anesthetized patients with use of either an ETT or a Laryngeal Mask Airway™.

**Methods:** Twenty adult patients undergoing elective minor surgeries were randomly allocated into two groups, the ETT and Laryngeal Mask Airway™ groups, depending on the airway management method used during surgery. While maintaining sevoflurane at 1 minimum alveolar concentration, laryngeal and respiratory responses were elicited by instillation of distilled water on the vocal cords immediately before and after surgery. Furthermore, the vocal cord angles were endoscopically measured under complete paralysis.

**Results:** Some laryngeal reflex responses of both groups, particularly the cough reflex, were significantly attenuated after minor surgery. Significant narrowing of the glottic aperture was evident in patients with ETT placement but not in patients with Laryngeal Mask Airway™ placement.

**Conclusions:** With either airway intervention, laryngeal defensive reflexes are depressed immediately after surgery even without visible laryngeal swelling. The sensory impairment attributable to the presence of an ETT cannot be the solo factor responsible for the modification of the defensive airway reflexes elicited from the larynx.

LARYNGEAL reflexes such as the cough reflex, expiration reflexes, and laryngeal closure with apnea protect the airways from aspiration.<sup>1</sup> It is well-established knowledge that general anesthetics modify these reflexes, and the impairment of upper airway protective reflexes has been demonstrated.<sup>2-4</sup> However, previous clinical reports have indicated that detrimental laryngeal function persists over several hours after prolonged tracheal intubation even when these patients have regained full consciousness from anesthesia,<sup>5,6</sup> suggesting possible involvement of mechanisms other than influence of anesthetic drugs, such as mechanical damage of the

larynx caused by endotracheal tube (ETT) placement and noxious stimuli evoked from surgery.

Our previous study, we found that in surgical patients anesthetized with sevoflurane, postoperative airway reflex responses differed from those occurred before surgery in patients with ETT placement.<sup>7</sup> Consequently, sensory impairment of the larynx where the ETT directly touches the vocal cords was suggested to occur during placement of an ETT and to modify laryngeal reflexes. In contrast, because the Laryngeal Mask Airway™ (LMA™) (LMA-Classic™; Laryngeal Mask Company, Nicosia, Cyprus) does not directly touch the vocal cords, it is believed to be less traumatic on the reflexogenic area of the larynx and to preserve laryngeal reflexes. In fact, our previous study demonstrated that LMA™ placement was capable of preserving postoperative laryngeal patency more than ETT placement.<sup>8</sup> We therefore hypothesized that the short-term use of an ETT impairs the receptors at the vocal cords and diminishes the laryngeal reflexes, whereas the use of an LMA™ preserves the laryngeal reflexes. The hypothesis was tested by evaluating the types and durations of laryngeal airway reflexes elicited by instillation of distilled water on the vocal cords of anesthetized patients who were randomly allocated to be placed with either ETT or LMA™ before and after minor surgery.

## Materials and Methods

### Subjects

After obtaining approval of the Hospital Ethics Committee of Chiba University Hospital, informed consents were obtained from 20 patients (American Society of Anesthesiologists physical status I-II) who were to undergo general anesthesia for elective minor surgeries such as partial mastectomy and minor urological or otolaryngological procedures. None had clinical evidence of respiratory, cardiovascular, or neuromuscular disorders. Random allocation of the patients was conducted through selection of sealed envelopes, assigning patients to one of two groups (ETT or LMA™ group) of ten subjects each.

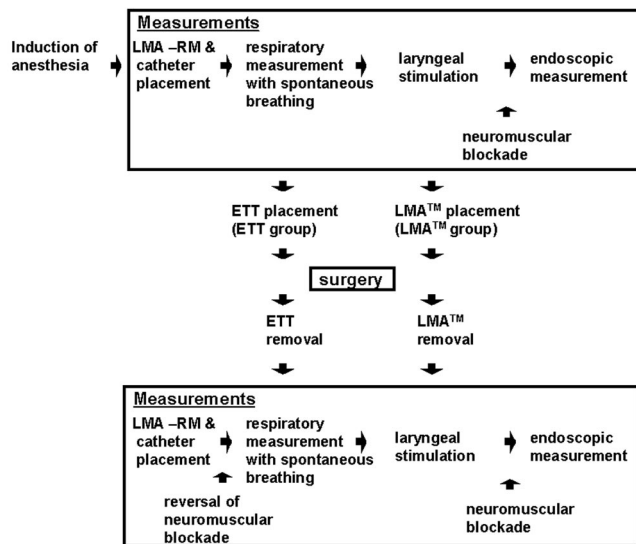
### Preparation of the Subject

The experimental protocol is schematically shown in figure 1. All patients were premedicated with intramuscular injection of atropine 0.5 mg and midazolam 3-4 mg 30 min before induction of anesthesia. Anesthesia was induced through inhalation of sevoflurane by the

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**Fig. 1.** Experimental protocol of this study. ETT = endotracheal tube; LMA™ = Laryngeal Mask Airway™; LMA-RM = Laryngeal Mask Airway™ for respiratory measurements.

single breath technique.<sup>9</sup> After administration of succinylcholine (1 mg/kg), a polyethylene catheter was inserted into the trachea just below the vocal cords for measurement of subglottic pressure, followed by placement of a LMA™ (size 3 or 4) for respiratory measurements (LMA-RM) before surgery. Anesthesia was maintained by sevoflurane in oxygen. End-tidal sevoflurane concentration was monitored with a respiratory gas analyzer (AS/3; Datex, Helsinki, Finland) and kept constant (1.7% sevoflurane: 1.0 minimum alveolar anesthetic concentration). Airflow was measured by a pneumotachograph connected to a differential pressure transducer (TP-602T; Nihon Koden, Tokyo, Japan). End-tidal carbon dioxide tension was measured by a side-stream capnometer (CAPNOX; Colin, Aichi, Japan). The airway pressure at the proximal end of the LMA-RM and subglottic pressure were measured by pressure transducers (23NB005G; IC sensors, Silicon Valley, CA). Airflow, the airway pressure at the proximal end of the LMA-RM, subglottic pressure, and end-tidal carbon dioxide tension were recorded on an eight-channel thermal recorder (WS-682G; Nihon Koden, Tokyo, Japan), and stored simultaneously in a personal computer with a sample frequency of 50 Hz by a data logging software package (LABDAT 5.2 RHT-Infodat, Montreal, Quebec) for later analysis. A fiberoptic endoscope (FB15H or FB10H, Pentax, Tokyo, Japan) connected to a camera (ETV8; Nisco, Saitama, Japan) was passed through a self-sealing diaphragm of the elbow connector down to the end of the LMA-RM to visualize the laryngeal aperture. The glottic aperture images were recorded on videotapes for later analysis.

### Laryngeal Stimulation

An epidural catheter was inserted through a suction channel of the endoscope to lodge the tip of the catheter

just above the glottis. It was assumed that the effect of succinylcholine administered at the time of anesthesia induction had worn off at the time of measurement, as the breathing stabilization time was more than 15 min after completion of the experimental setting. After stability of all respiratory variables and sevoflurane concentration were obtained for at least 5 min, 0.5 ml distilled water was injected through the catheter at end-expiratory phase, and the laryngeal and respiratory responses were measured. After subsequent intravenous administration of 8–10 mg vecuronium, complete paralysis was visually confirmed by loss of train-of-four electrical stimulation of the ulnar nerve (NS252; Fisher & Paykel Healthcare, Auckland, New Zealand). The glottic aperture image during apnea at atmospheric pressure was videotaped for later analysis of glottic aperture angle.

On completion of the preoperative respiratory measurements, both LMA-RM and polyethylene catheter were removed, followed by insertion of either a cuffed ETT (ID 7.0 mm for female patients and 8.0 mm for male patients) or a new LMA™ (size #3 or #4) for surgery. During surgery, anesthesia was maintained by sevoflurane (end-tidal concentration 1–2%) and nitrous oxide (60–66%), and vecuronium was administered as necessary. Patients received no narcotics and were hemodynamically stable throughout anesthesia. Patients were mechanically ventilated by intermittent positive pressure ventilation mode with 8–10 breaths/min and a tidal volume of 10 ml/kg during surgery without air leak. Measurement or control of intracuff pressure was not conducted.

### Respiratory Measurements and Laryngeal Stimulation after Surgery

On completion of the surgery, the ETT or LMA™ used during surgery was removed, followed by reinsertion of a subglottic catheter and a LMA-RM. The residual effect of the muscle relaxant was fully reversed by an intravenous administration of 1.0 mg atropine and 2.0 mg neostigmine, and subsequent confirmation of successive neuromuscular blockade reversal was conducted by ulnar nerve electric stimulation with a train-of-four responses. The same laryngeal stimulation performed immediately before surgery was repeated after confirmation of stable respiratory variables and sevoflurane concentration (1.7%). Endoscopic measurements of the vocal cord angle were also repeated under complete paralysis achieved by administration of succinylcholine (1 mg/kg). The complete paralysis was confirmed by total loss of responses to train-of-four stimulations of the ulnar nerve. We continued to carefully monitor the extent of neuromuscular block before removal of LMA on awakening from anesthesia because the effects of succinylcholine have been reported to be enhanced after neostigmine administration.

**Table 1. Anthropometric Characteristics and Duration of ETT or LMA™ Placement**

	ETT group (n = 10)	LMA™ group (n = 10)
Age (yr)	48.5 (33–72)	43.0 (28–68)
Sex (male/female)	2/8	2/8
Height (cm)	156 (145–166)	157 (154–175)
Weight (kg)	55 (48–76)	63 (40–90)
Volume of infusion (ml · kg <sup>-1</sup> · h <sup>-1</sup> )	6.2 (2.7–7.4)	5.0 (2.7–6.7)
Duration of airway device placement (min)	150 (95–230)	202 (65–240)

Values are expressed as median (range).

ETT = endotracheal tube; LMA™ = Laryngeal Mask Airway™.

### Data Analysis

Each laryngeal image was printed on paper for the purpose of vocal cord angle measurement, defined as the angle produced by lines connecting the anterior and posterior commissures. The glottic aperture angle under complete paralysis was considered to be an index for vocal cord swelling. The glottic aperture angle was measured by an investigator (S. I.) blinded to the airway management procedure.

In accordance with our previous categorization of laryngeal reflexes,<sup>2–4,7</sup> the following were identified: 1) expiration reflex, defined as forceful expiration without preceding inspiration, 2) spasmodic panting, defined as rapid shallow breathing (respiratory frequency >60/min) lasting >10 s, 3) cough reflex, defined as forceful expiration with prior inspiration, and 4) apnea with laryngospasm, defined as complete closure of glottis lasting >10 s on video image. Using computer software (ANADAT 5.1&5.2; RHT-Infodat Inc., Montreal, Quebec, Canada), respiratory frequency, tidal volume, and minute volume were determined from the flow signal. To evaluate the duration of laryngeal responses, the time intervals between the beginning of laryngeal reflexes and reestablishment of stable breathing ( $T_{LR}$ ) when tidal volume recovered to 80% of prestimulation levels were measured. When the duration of laryngeal responses exceeded 3 min, the measurements were terminated and the patients were mechanically ventilated after administration of a muscle relaxant.

**Table 2. Ventilatory Variables During Spontaneous Breathing, the Time Requiring Re-establishment of Stable Breathing and Changes in the Angle of the Glottic Aperture Under Complete Paralysis Before and After Placement of Each Device**

	ETT group		LMA™ group	
	Before	After	Before	After
$V_T$ (ml)	237 (205–583)	227 (170–573)	275 (191–467)	237 (171–435)*
f (/min)	20.4 (10.3–24.2)	21.1 (10.3–28.0)*	21.5 (13.2–29.2)	23.5 (14.1–30.5)
MV (l/min)	5.03 (3.86–6.17)	5.30 (3.72–6.24)	5.56 (3.95–9.08)	5.70 (3.96–7.83)
PETCO <sub>2</sub> (mmHg)	41.0 (36.0–44.5)	43.0 (37.5–46.0)	38.0 (36.0–43.5)	39.0 (35.0–43.0)
$T_{LR}$ (sec)	110 (78.0–233.0)	49.5 (14.0–76.5)*	115 (67.0–173.0)	67.0 (41.0–141.0)
Angle (degree)	28.5 (22.5–35.0)	20.5 (17.3–31.5)*	33.0 (29.4–39.2)	33.0 (25.0–38.0)

Values are expressed as median (10–90%).

\*  $P < 0.05$  versus before surgeries.

Angle = the angle of the glottic aperture under complete paralysis; ETT = endotracheal tube; f = respiratory frequency; LMA™ = laryngeal mask airway; MV = minute volume; PETCO<sub>2</sub> = end-tidal carbon dioxide tension;  $T_{LR}$  = time requiring re-establishment of stable breathing;  $V_T$  = tidal volume.

### Statistical Analysis

Mann-Whitney rank sum test was used to compare patient characteristics between groups. We did not compare respiratory variables and reflex patterns between the groups because of the small number of subjects. Wilcoxon signed rank test was used to determine the difference of variables between before and after surgery. Fisher exact probability test evaluated differences of the incidences of reflexes between before and after surgery. All values are given as median (10th–90th percentiles). In all analyses,  $P < 0.05$  was considered significant.

### Results

Table 1 demonstrates anthropometric characteristics of the patients, volume of intravenous infusion, and duration of ETT or LMA™ placement for each group. No significant differences of the parameters were evident between the groups. In one patient of the LMA™ group, measurements of vocal cord angle both before and after surgery were not completed for technical reasons.

#### Spontaneous Breathing Pattern before and after Surgery

Table 2 demonstrates the changes in spontaneous breathing patterns before and after surgery for each group. The postoperative breathing pattern was characterized by an increase in respiratory frequency and decrease in tidal volume in both groups and both minute volume and end-tidal carbon dioxide tension did not change before and after surgery.

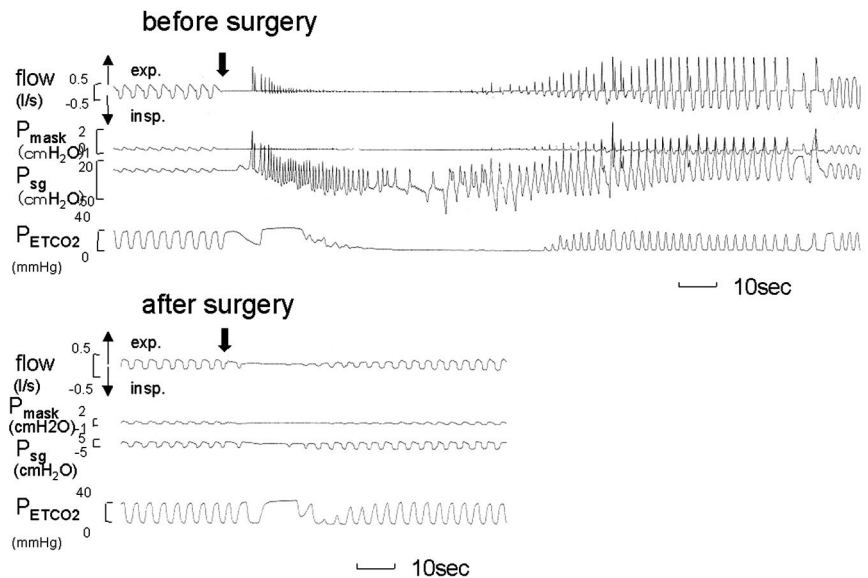
#### Vocal Cord Angle before and after Surgery

In the ETT group, a significant reduction of the vocal cord angle was observed after surgery ( $P = 0.004$ ) (table 2). In contrast, the glottic angle did not change after surgery in patients of the LMA™ group ( $P = 0.547$ ).

#### Responses to Laryngeal Stimulation in the ETT Group

Figure 2 demonstrates typical responses to laryngeal stimulation observed in a patient of the ETT group.

**Fig. 2.** Experimental records illustrating responses to laryngeal stimulation observed in a patient managed by an endotracheal tube. At the points indicated by the arrows, 0.5 ml distilled water was injected onto the vocal cords. flow = airflow;  $P_{mask}$  = mask pressure;  $P_{sg}$  = subglottic pressure;  $P_{ETCO_2}$  = end-tidal carbon dioxide tension; exp. = expiration; insp. = inspiration. Note disappearance of the cough reflex after surgery.



Before surgery, injection of distilled water elicited apnea with laryngeal closure, followed by a series of expiration reflexes, and subsequent re-elicitation of apnea with long duration despite the presence of vigorous inspiratory efforts, indicated by negative deflections in the subglottic pressure tracing. The airway protective reflexes continued for approximately 3 min before restoration of regular breathing pattern. In contrast, after surgery, the same stimulation produced only a short period of apnea followed by immediate restoration of breathing airflow (fig. 3). Figure 3A summarizes the types and incidences of various reflex responses observed before and after surgery. After surgery, the incidence of cough reflex and spasmodic panting significantly reduced the duration of laryngeal reflex responses evaluated by  $T_{LR}$  significantly decreased ( $P = 0.002$ ) (table 2).

*Responses to Laryngeal Stimulation in the LMA™ Group*

Figure 4 demonstrates the typical responses to laryngeal stimulation observed in a patient of the LMA™ group before and after surgery. Although expiration reflex, spasmodic panting, apnea with laryngeal closure, and cough reflexes were all observed before surgery, spasmodic panting and cough reflexes did not occur and long apnea with laryngeal closure after expiration reflexes was observed after surgery. In addition to significant suppression of cough and expiration reflexes after surgery as shown in figure 3B,  $T_{LR}$  tended to decrease, although this difference was not significant ( $P = 0.098$ ).

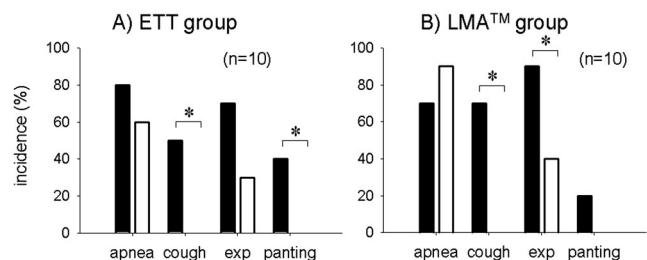
**Discussion**

The major findings of this study are as follows: 1) some laryngeal reflex responses elicited by laryngeal stimula-

tion, particularly the cough reflex, were significantly attenuated immediately after minor surgery in both ETT and LMA™ groups, 2) duration of laryngeal reflex ( $T_{LR}$ ) was shortened significantly by ETT placement, 3) a significant narrowing of the glottic aperture was evident in patients with ETT placement but not in patients with LMA™ placement. Contrary to our expectations, not all but some laryngeal reflex responses significantly attenuated immediately after surgery even in patients with LMA™ placement.

*Changes in Laryngeal Reflexes after ETT Placement*

Previous studies showed that after tracheal extubation, radiopaque dye, which the patients were instructed to swallow, was identified in the subglottic region even in alert patients who had apparently fully recovered from general anesthesia, indicating depression of airway protective function at the larynx.<sup>5,6</sup> Burgess *et al.*<sup>6</sup> demonstrated that in cardiac surgical patients with prolonged intubations, laryngeal incompetence persisted within 8 h after extubation. It is worthy to note that coughing was not observed in any of their patients with laryngeal



**Fig. 3.** The incidence of various types of airway reflexes in response to laryngeal stimulation before (black bars) and after (open bars) surgeries. apnea = apnea with laryngospasm; cough = cough reflex; exp = expiration reflex; panting = spasmodic panting. ETT = endotracheal tube, LMA™ = Laryngeal Mask Airway™. \* $P < 0.05$  between before and after surgery.

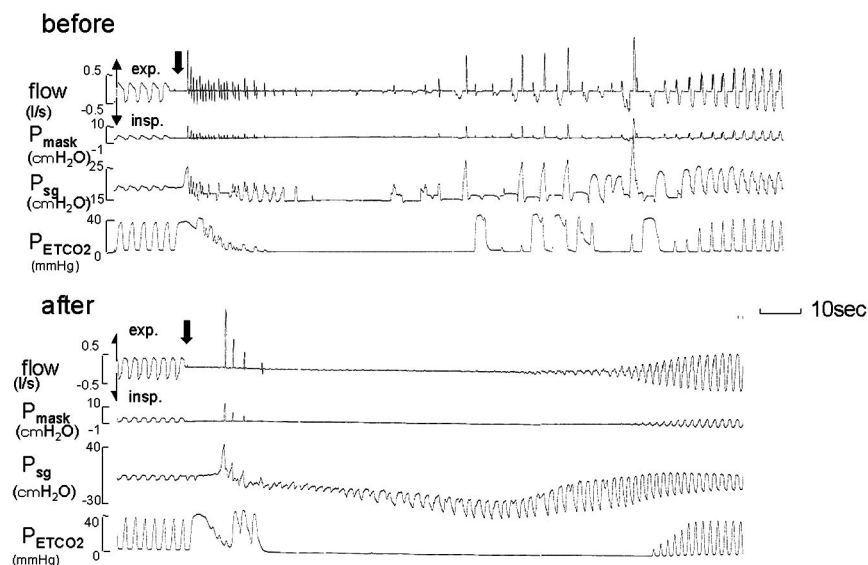


Fig. 4. Experimental records illustrating responses to laryngeal stimulation observed in a patient managed by a Laryngeal Mask Airway™. At the points indicated by the arrows, 0.5 ml distilled water was injected onto the vocal cords. flow = airflow;  $P_{\text{mask}}$  = mask pressure;  $P_{\text{sg}}$  = subglottic pressure;  $P_{\text{ETCO}_2}$  = end-tidal carbon dioxide tension; exp. = expiration; insp. = inspiration. Note depression of the cough reflexes after surgery.

incompetence, suggesting that aspiration may have been silent without the occurrence of laryngeal irritation. Moreover, silent pulmonary aspiration after tracheal extubation was observed not only in surgical patients but also in nonsedated critically ill patients,<sup>10</sup> indicating the contribution of ETT placement itself, rather than consciousness level, to the development of laryngeal incompetence. Although this study was performed under anesthesia, our results agree with these observations, and provide physiologic explanation for possible development of the postoperative laryngeal incompetence.

#### Changes in Laryngeal Reflexes after LMA™ Placement

At the planning stages of our study, the use of LMA™ was not considered to impair the laryngeal reflexes for the reason that LMA™ placement would be less traumatic to the larynx. Supportive of this consideration was a report by Lee *et al.* that demonstrated the advantages of LMA™ to vocal function,<sup>11</sup> moreover, our previous study demonstrated that postoperative laryngeal patency was preserved after LMA™ placement.<sup>8</sup> However, contrary to our expectations, cough reflex was found to be significantly depressed after surgery even in the LMA™ group. Although postoperative  $T_{\text{LR}}$  did not significantly decrease in the LMA™ group, influences of the LMA™ placement were essentially similar to those observed in the ETT group. Our result was in accord with the finding of Caranza *et al.*<sup>12</sup> that upper airway reflex sensitivity as assessed by ammonia vapor threshold concentration was impaired 2 h after general anesthesia with LMA™ placement and with ETT placement.

#### Mechanisms of Changes of Laryngeal Reflexes after Airway Interventions

Laryngeal reflex depression may result from impairment of any part of the laryngeal reflex arc, including the

afferent neural pathway, neuromuscular effectors, and central modulators. Significant reduction of the vocal cord angle in association with postoperative vocal cord swelling of the ETT group indicates a possibility that the presence of an ETT may directly cause pathologic changes to the epithelium where the irritant receptor was located, depressing afferent input from the laryngeal mucosa. Although no study has systematically examined causal effects of laryngeal edema on functional impairment of the receptors responsible for the laryngeal reflexes, Kimoff *et al.*<sup>13</sup> indicated possible association between sensory impairment of upper airway receptors and upper airway mucosal edema in obstructive sleep apnea patients.<sup>14</sup> Accordingly, peripheral modification of the laryngeal reflex arc is one possible explanation of the observed laryngeal dysfunction in patients with ETT placement.

Because significant narrowing of the glottic aperture of the vocal cords was not observed in the LMA™ group, our results can not be solely explained by the apparent laryngeal swelling. Immeasurable minor injuries or slight edema of the receptors at the peripheral site could be caused by placement of a LMA™ and impaired the afferent reflex arc. Reports in support of this speculation have indicated that the vocal cords of patients with LMA™ placement may develop microtrauma.<sup>15</sup> Figueredo *et al.*<sup>15</sup> reported that the incidence of postoperative discomfort after LMA™ placement was higher in patients with positive pressure ventilation than those with spontaneous breathing. It was their speculation that the laryngopharyngeal complaints was attributable to the incidence of microtrauma contributed by shear stress between flowing gas and the vocal cords during mechanical ventilation.

Brimacombe *et al.*<sup>16</sup> reported increased intracuff pressure of LMA™ by use of nitrous oxide has a possibility of influencing the laryngeal soft tissue. Furthermore, con-

stant exposure of the larynx in the LMA™ group to a volatile anesthetic, such as sevoflurane, during surgery may have an effect on the laryngeal receptors. Although a study by Nishino *et al.* showed that volatile anesthetics cause various instantaneous effects on different types of laryngeal receptors,<sup>17</sup> the effects of continuous sevoflurane exposure during surgery on laryngeal receptors have not been studied. Even without injuries of the peripheral receptors, the receptor function could accommodate to these noxious stimuli, depressing laryngeal reflexes.<sup>17</sup>

In addition to these peripheral mechanisms, continuous mechanical stimulation of laryngeal irritant receptors by an ETT or continuous mechanical oppression of the pharynx by LMA™ placement could induce adaptation mechanisms in the central nervous system responsible for the laryngeal reflex, resulting in depression of the reflex.<sup>7</sup> Surgical stress, such as continuous noxious stimuli evoked from the surgical site, is another possible mechanism that may influence the upper airway reflex program in the brainstem.<sup>7</sup>

#### *Clinical Implications*

Because our study was conducted under general anesthesia, the results of this study do not necessarily apply to the postoperative laryngeal function during wakefulness or recovery from anesthesia in the postanesthesia care unit. The depressed laryngeal reflexes, therefore, may be compensated by alertness after surgery, and silent aspiration previously reported would not occur in patients with normal laryngeal function preoperatively. However, it should be also noted that depression of upper airway reflex after surgery was reported in awake persons despite complete recovery of auditory reaction time,<sup>12</sup> suggesting that alertness does not assure prevention of silent aspiration even in normal patients. Needless to say, our results may be particularly important in patients with compromised upper airway protective functions and those with a history of aspiration pneumonia. In addition, because deteriorated laryngeal reflexes were evident in patients with LMA™ and ETT placement, it is important to note that postoperative impairment of the airway protective mechanism may result regardless of the choice of airway interventions. Future studies should be directed to elucidate consequences and clinical significance of laryngeal protective function impairment after airway interventions.

In our study, it was found that laryngeal defensive reflexes after minor surgery are depressed with either ETT or LMA™ placement. Significant postoperative alteration of the laryngeal reflex responses even in patients with LMA™ placement indicates that sensory impairment resulting from the presence of an ETT is not the sole factor responsible for the modification of the defensive airway reflexes.

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