

Effect of Increasing Depth of Propofol Anesthesia on Upper Airway Configuration in Children

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Background: The upper airway tends to be obstructed during anesthesia in spontaneously breathing patients. The purpose of the current study was to determine the effect of increasing depth of propofol anesthesia on airway size and configuration in children.

Methods: Magnetic resonance images of the upper airway were obtained in 15 children, aged 2–6 yr. Cross-sectional area, anteroposterior dimension, and transverse dimension were measured at the level of the soft palate, dorsum of the tongue, and tip of the epiglottis. Images were obtained during infusion of propofol at a rate of $50\text{--}80\ \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ and after increasing the depth of anesthesia by administering a bolus dose of propofol and increasing the infusion rate to $240\ \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$.

Results: Overall, the cross-sectional area of the entire pharyngeal airway decreased with increasing depth of anesthesia. The reduction in cross-sectional area was greatest at the level of the epiglottis ($24.5\ \text{mm}^2$, 95% confidence interval = $16.9\text{--}32.2\ \text{mm}^2$; $P < 0.0001$), intermediate at the level of the tongue ($19.3\ \text{mm}^2$, 95% confidence interval = $9.2\text{--}29.3\ \text{mm}^2$; $P < 0.0001$), and least at the level of the soft palate ($12.6\ \text{mm}^2$, 95% confidence interval = $2.7\text{--}22.6\ \text{mm}^2$; $P < 0.005$) in expiration and resulted predominantly from a reduction in anteroposterior dimension. The airway cross-sectional area decreased further in inspiration at the level of the epiglottis. The narrowest portion of the airway resided at the level of the soft palate or epiglottis in the majority of children.

Conclusion: Increasing depth of propofol anesthesia in children is associated with upper airway narrowing that occurs throughout the entire upper airway and is most pronounced in the hypopharynx at the level of the epiglottis.

GENERAL anesthetics dose-dependently attenuate upper airway muscle activity, thereby rendering the upper airway vulnerable to obstruction in spontaneously breathing patients.^{1–5} Despite research spanning decades, the anatomic site of anesthesia-induced airway obstruction is controversial.^{1,6–11} The traditional view, supported by radiologic studies, is that posterior movement of the tongue, resulting in apposition with the pharyngeal wall, is the predominant cause of airway obstruction.¹ More recent studies using a variety of imaging techniques in adults have challenged this view, suggesting that airway

obstruction occurs at other sites, such as at the level of the epiglottis or soft palate.^{6–11}

Magnetic resonance imaging (MRI) can accurately determine upper airway cross-sectional area (CSA) and has been used to assess the effects of general anesthesia on upper airway configuration.^{10–14} In adults undergoing MRI, upper airway anteroposterior dimension decreased at the level of the soft palate but remained unchanged at the level of the dorsum of the tongue and tip of the epiglottis during propofol anesthesia.¹¹ The configurational changes leading to obstruction in the upper airway during anesthesia in children are unknown. Experimental studies in animals demonstrated that anesthesia-induced depression of upper airway muscle activity is more pronounced in developing than in adult animals at equipotent anesthetic concentrations.^{15,16} The hypothesis of the current study was that increasing depth of propofol anesthesia narrows the entire pharyngeal airway in children. To test this hypothesis, we studied the effect of propofol anesthesia on upper airway size and configuration in spontaneously breathing children undergoing MRI.

Materials and Methods

With approval from the research ethics board and written informed parental consent, 15 children with American Society of Anesthesiologists physical status class I or II, aged 2–6 yr, scheduled for elective MRI of the brain or spine, were studied. Excluded were children who had a history of obstructive sleep apnea, prematurity, pathology of the upper airway, gastroesophageal reflux, moderate or severe developmental delay, craniofacial anomalies, suspected raised intracranial pressure, or a body weight of at least 20% more than ideal.

No premedication was given. Nitrous oxide (70%) in oxygen was administered, and a 22-gauge intravenous catheter was inserted. Immediately after insertion of the catheter, nitrous oxide was discontinued. Anesthesia was induced using $2.0\ \text{mg/kg}$ propofol and $10\ \mu\text{g/kg}$ glycopyrrolate, and a continuous infusion of propofol was started at a rate of $50\ \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ using a syringe pump. The patients breathed spontaneously throughout the imaging while oxygen was administered ($2\ \text{l/min}$) via a nasal catheter. An MRI-compatible device was used to monitor arterial oxygen saturation, exhaled carbon dioxide tension (via the nasal catheter), respiratory rate, heart rate, and arterial blood pressure. A respiratory bellows was placed around the chest to obtain a

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waveform of the respiratory cycle. The head position was standardized such that the angle between the horizontal plane of the MRI table and a line connecting the tragus of the ear and the lateral corner of the eye was 110° .¹²

Magnetic resonance images were acquired using a GE 1.5 Tesla cardiovascular imaging MRI scanner with maximal gradient strength of 4 G/cm (CV/i system; General Electric Medical Systems, Milwaukee, WI) and a quadrature head coil or phased array spine coil. A T1-weighted three-plane gradient echo localizer image (echo time = 1.6 ms; repetition time = 4.5 ms; 30° flip angle; 5-mm slice thickness; number of excitations = 1; 5 slices/plane; and 256×128 matrix) was obtained to identify the midline and allow selection of subsequent axial images. An axial/oblique T1-weighted single-shot fast-spin echo pulse sequence (echo time = 30 ms; variable repetition time; 3-mm slice thickness; number of excitations = 0.5; field of view = 16×9.6 cm; echo train length = 16; and 192×192 matrix) was used to acquire images at the level of the soft palate, base of the tongue, and tip of the epiglottis. The image acquisitions were triggered manually by the same investigator in early expiration. To determine whether airway caliber changed during the respiratory cycle, image acquisitions were also triggered in early inspiration. The waveform generated by the respiratory bellows was used to determine the phase of the respiratory cycle. Images were taken at each anatomic level during three successive respiratory cycles. The acquisition time was 1 s for each image.

The rate of propofol infusion was set initially at $50 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ and, if the child moved when placed in the scanner, was increased to $80 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$. Baseline images of the upper airway were acquired after the child had been motionless for approximately 5 min. After this initial set of images was obtained, the depth of anesthesia was increased by administering a bolus dose of 2 mg/kg propofol and increasing the rate of infusion to $240 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$. Image acquisitions were repeated approximately 5 min after the increase in propofol infusion rate. The infusion rates of propofol were chosen to encompass the dose range required for pediatric patients undergoing ambulatory procedures.¹⁷ After the second set of images was obtained, the infusion rate was set at $50 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ for the imaging of the brain or spine. To determine whether the duration of propofol infusion affected upper airway CSA, we studied an additional six control subjects in whom the propofol infusion rate was kept constant at $50\text{--}80 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ for both sets of image acquisitions. These six patients were selected using the same inclusion criteria described in the first paragraph of the Methods.

All images were stored on an optical disc and subsequently analyzed by a single investigator without knowledge of the depth of anesthesia or the phase of the respiratory cycle at which the image was obtained. After image

Table 1. Demographics

Patient	Sex	Age, yr	Weight, kg	Diagnosis
1	M	4.9	18.0	Pontocerebellar hypoplasia
2	M	3.5	17.1	Acute leukemia
3	F	6.5	29.8	Mild developmental delay
4	F	2.3	14.3	Vein of Galen malformation
5	M	5.5	23.0	Glioma
6	F	2.3	11.9	Vein of Galen malformation
7	F	6.5	17.3	Mild developmental delay
8	F	4.0	18.0	Neurofibromatosis
9	M	6.5	23.4	Scoliosis
10	F	6.5	25.0	Neurofibromatosis
11	M	4	14.5	Seizure disorder
12	F	6.3	18.9	Fourth ventricle ependyoma
13	M	3.2	16.9	Thoracic neuroblastoma
14	M	2.6	12.8	Thoracocervical dislocation
15	F	6.5	20.1	Pineoblastoma

magnification ($\times 3$), the upper airway CSA, anteroposterior dimension, and transverse dimension were determined using Functool software of a GE Advantage Windows Workstation (AW 3.0; SUN Microsystems, Ontario, Canada). To prevent observer bias, each image was assigned a random code number using a random number table and presented for analysis in random order. At each anatomic level, measurements were obtained from three successive respiratory cycles, and average values were calculated.

Statistical Analysis

Data are presented as mean \pm SD. Two-way repeated-measures analysis of variance was used to compare upper airway CSA and dimensions. $P < 0.05$ was considered statistically significant.

Results

The demographics and diagnoses of the 15 study children, comprising 8 girls and 7 boys, are shown in table 1. The mean age and weight were 4.7 ± 1.7 yr and 18.7 ± 4.9 kg, respectively. In lightly anesthetized children, overall CSA was least at the level of the soft palate and greatest at the level of the tongue in expiration (fig. 1) and inspiration (fig. 2). With increasing depth of propofol anesthesia, the overall CSA of the entire pharyngeal airway decreased significantly (figs. 1–3). The magnitude of the reduction in CSA differed at each anatomic level. The reduction in pharyngeal CSA in expiration was greatest at the level of the epiglottis (mean overall difference in area = 24.5 mm^2 , 95% confidence interval [CI] of the difference = $16.9\text{--}32.2 \text{ mm}^2$; $P < 0.0001$), intermediate at the level of the tongue (mean overall difference in area = 19.3 mm^2 , 95% CI = $9.2\text{--}29.3 \text{ mm}^2$; $P < 0.0001$), and least at the level of the soft palate (mean overall difference in area = 12.6 mm^2 , 95% CI = $2.7\text{--}22.6 \text{ mm}^2$; $P < 0.005$) (fig. 1). Similarly, the reduction in pharyngeal CSA in inspiration at the level of

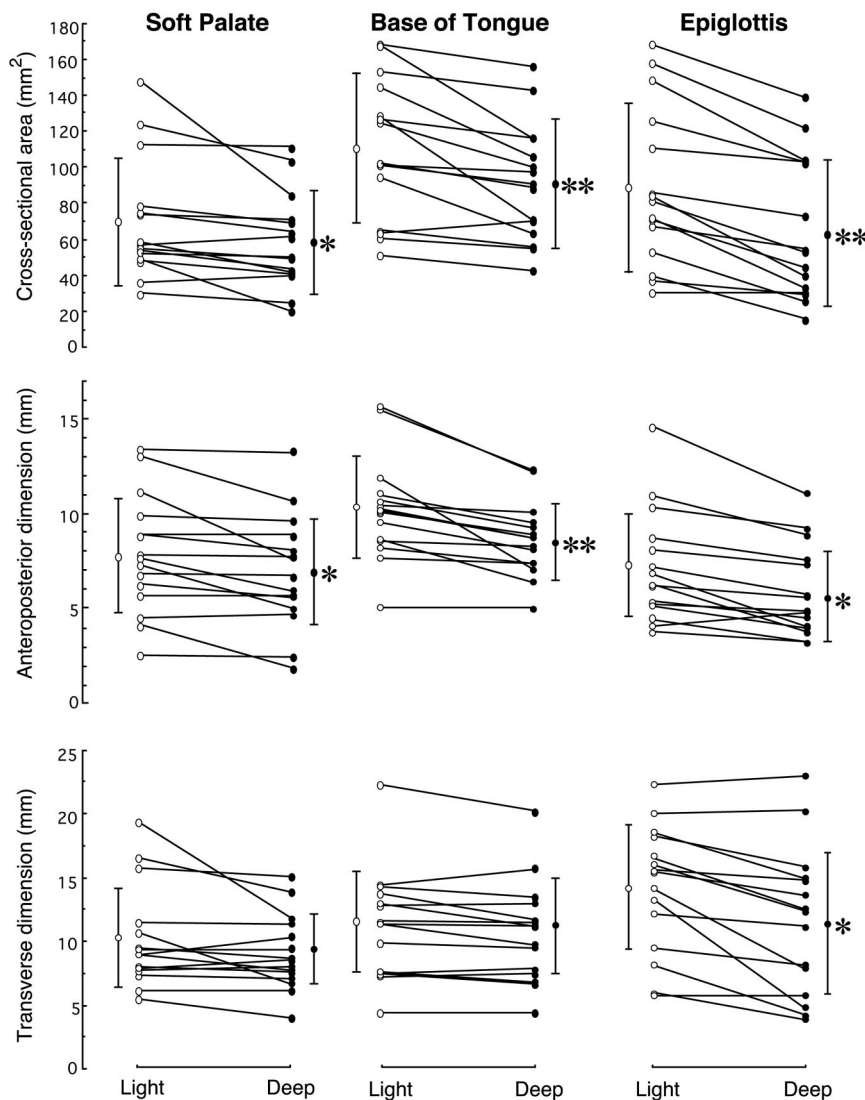


Fig. 1. Individual and mean (\pm SD) values for upper airway cross-sectional area, anteroposterior dimension, and transverse dimension at the level of the soft palate, base of the tongue, and tip of the epiglottis in expiration. Baseline images of the airway were acquired during infusion of propofol at a rate of $50\text{--}80 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ (light anesthesia). Image acquisitions were repeated after the depth of anesthesia was increased by administering a bolus dose of propofol and increasing the rate of infusion to $240 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ (deep anesthesia). * $P < 0.005$ compared with light anesthesia. ** $P < 0.0001$ compared with light anesthesia.

the epiglottis (mean overall difference in area = 15.7 mm^2 , 95% CI of the difference = $8.9\text{--}22.4 \text{ mm}^2$; $P < 0.0001$) and at the base of tongue (mean overall difference in area = 15.1 mm^2 , 95% CI of the difference = $6.1\text{--}24.1 \text{ mm}^2$; $P < 0.0001$) exceeded that at the soft palate (mean overall difference in area = 4.2 mm^2 ; $P = \text{NS}$) (fig. 2). During deep anesthesia, overall CSA at the level of the tip of the epiglottis was similar to that at the level of the soft palate (figs. 1 and 2).

The reduction in the CSA at each anatomic level resulted predominantly from a decrease in the anteroposterior dimension (figs. 1 and 2). The transverse dimension of the airway decreased only at the level of the epiglottis (figs. 1 and 2; $P < 0.005$). The minimum airway was located at the level of the soft palate or tip of epiglottis in the majority of children (fig. 4). In addition, there was a significant decrease in overall CSA in inspiration compared with expiration at the level of the epiglottis during light ($P < 0.0005$) and deep anesthesia ($P < 0.05$) (fig. 2). This inspiratory reduction in CSA at

the level of the epiglottis resulted primarily from a reduction in anteroposterior dimension ($P < 0.05$) (fig. 2).

Mean arterial oxygen saturation remained unchanged with increasing depth of anesthesia ($98 \pm 1\%$). The mean respiratory rate was 15 breaths/min (range, 10–24 breaths/min) during light anesthesia and 12 breaths/min (range, 8–20 breaths/min) during deep anesthesia. There was a small increase in exhaled carbon dioxide tension with increasing depth of anesthesia (39 ± 5 vs. $43 \pm 4 \text{ mmHg}$). CSA and pharyngeal dimensions remained unchanged in the six control patients in whom the rate of propofol infusion was kept constant (table 2). No child demonstrated paradoxical chest wall motion or other clinical evidence of airway obstruction during the study or subsequent imaging of the brain or spine.

Discussion

In the current study, the overall minimum CSA of the upper airway was located in the retropalatal area in

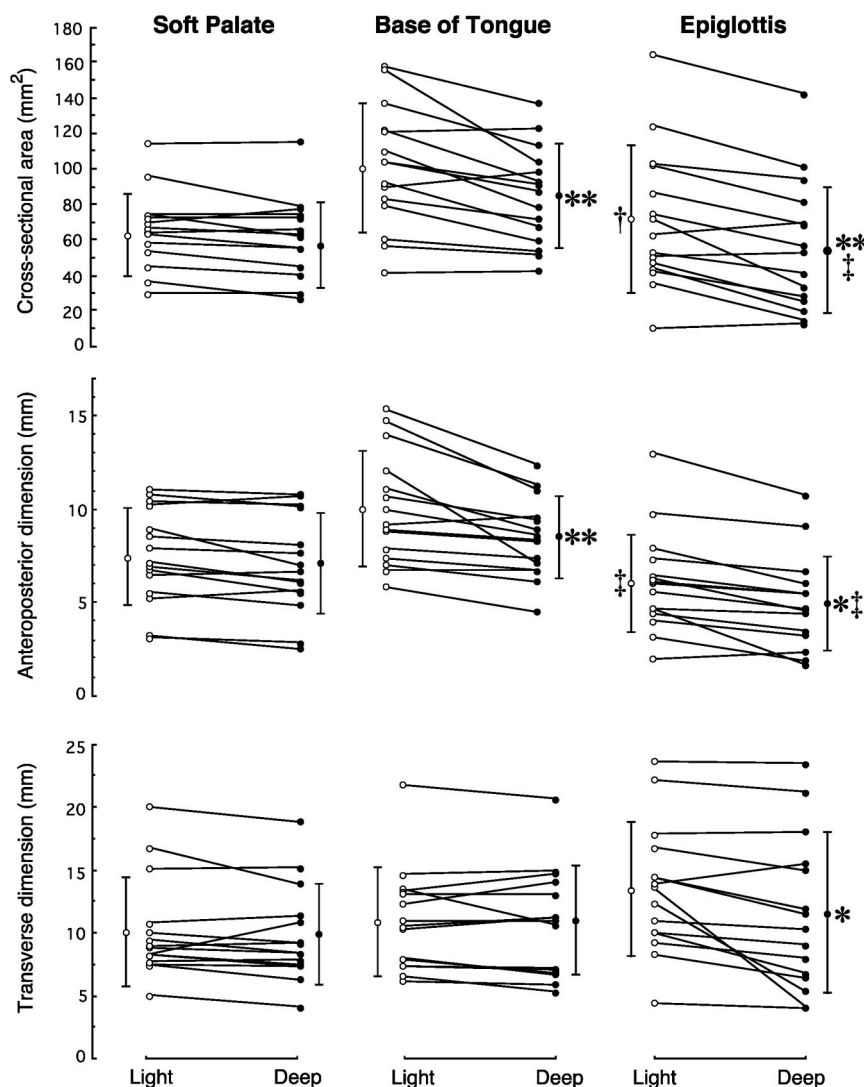


Fig. 2. Individual and mean (\pm SD) values for upper airway cross-sectional area, anteroposterior dimension, and transverse dimension at the level of the soft palate, base of the tongue, and tip of the epiglottis in inspiration during light and deep propofol anesthesia. * $P < 0.005$ compared with light anesthesia. ** $P < 0.0001$ compared with light anesthesia. † $P < 0.0005$ compared with corresponding value in expiration. ‡ $P < 0.05$ compared with corresponding value in expiration.

lightly anesthetized children, in agreement with studies in adults during wakefulness and in children.^{14,18} With increasing depth of propofol anesthesia, the reduction in upper airway caliber was not limited to a specific location within the airway but involved the entire upper airway. In addition, the overall reduction in upper airway caliber resulted predominantly from a reduction in anteroposterior dimension and was greatest at the level of the tip of the epiglottis and least at the level of the soft palate. Consequently, overall CSA at the level of the epiglottis was comparable to that at the level of the soft palate in deeply anesthetized children.

Previous studies using MRI in adults have demonstrated that the minimum anteroposterior dimension at the level of the tongue remained unchanged, whereas that at the level of the soft palate decreased significantly after induction of propofol anesthesia.¹¹ These investigators concluded that posterior displacement of the tongue does not occur and that airway obstruction occurs primarily at the level of the soft palate. However, because they did not image the airway at a specific point

in the respiratory cycle, the contribution of the respiratory cycle to these findings in adults is unclear.¹⁹ Other investigators have drawn similar conclusions from studies involving a variety of anesthetic agents and imaging techniques in adults.⁶⁻¹⁰ Real-time ultrasonography demonstrated that movement of the tongue after induction of anesthesia with thiopentone was inconsistent in direction and insufficient to result in contact with the posterior pharyngeal wall.⁷ Flexible bronchoscopy revealed the epiglottis to be the main site of airway obstruction during halothane anesthesia—the epiglottis moving caudally in inspiration, resulting in contact with the posterior pharyngeal wall and occlusion of the tracheal inlet in a valve-like fashion.⁶ Shorten *et al.*¹⁰ showed that sedation with midazolam and propofol caused a greater reduction in pharyngeal anteroposterior dimension at the level of the epiglottis and soft palate than at the level of the tongue in adults. Similarly, Nandi *et al.*⁸ demonstrated radiographically that the upper airway was obstructed either at the level of the epiglottis or soft palate, and that manual traction on the tongue failed

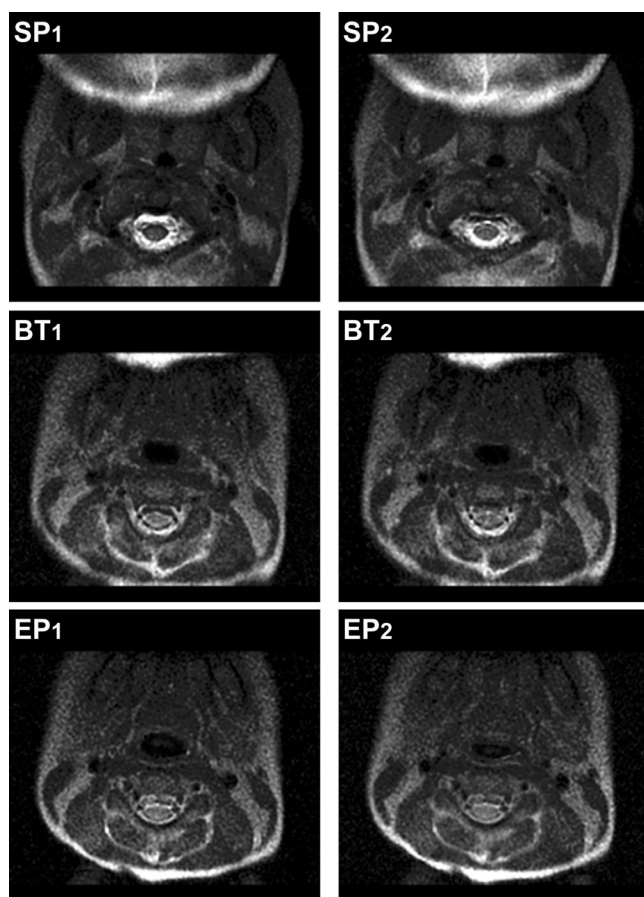


Fig. 3. Representative T1-weighted axial/oblique magnetic resonance images at the level of the soft palate (SP), base of the tongue (BT), and tip of the epiglottis (EP) during light (1) and deep (2) propofol anesthesia demonstrating a reduction in cross-sectional area at each anatomic level with increasing depth of propofol anesthesia. The reduction in cross-sectional area resulted predominantly from a reduction in anteroposterior dimension and was most pronounced in the hypopharynx at the level of the epiglottis.

to relieve the obstruction in elderly thiopentone-anesthetized adults. Indeed, complete upper airway obstruction was possible even when the tongue was surgically removed in cadavers and resulted from an airtight seal between the epiglottis and the pharyngeal wall.⁶ These findings, however, do not exclude the tongue as a potential cause of airway obstruction in some patients.

The mechanism underlying these anesthesia-induced changes in upper airway patency remains speculative. General anesthesia dose-dependently attenuates phasic respiratory activity of upper airway muscles and, to a lesser extent, the activity of intercostal muscles and the diaphragm.^{4,5,15,16} The resulting muscle imbalance is presumed to be an important factor predisposing the upper airway to collapse. Alternatively, general anesthesia might compromise reflexes associated with upper airway intraluminal pressure, air flow, or lung volume, thereby affecting feedback processes involved in syn-

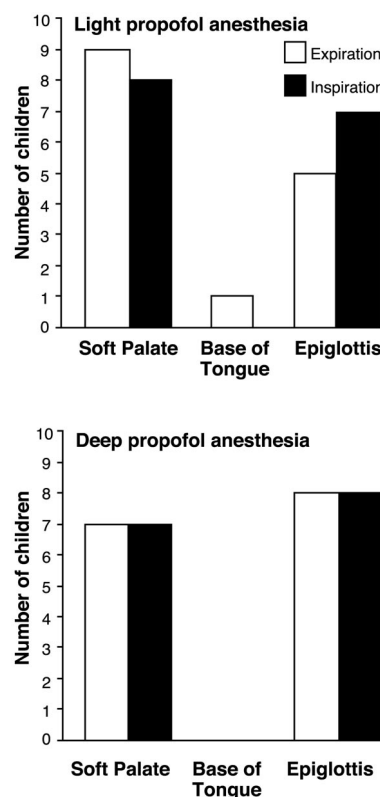


Fig. 4. Frequency histogram showing the site of the narrowest portion of the upper airway during light and deep propofol anesthesia in spontaneously breathing children.

chronizing pharyngeal, chest wall, and diaphragmatic muscle activity.²⁰⁻²³

The degree of pharyngeal narrowing induced by propofol varied considerably among children in the current study. Factors that could explain this variation include differences among patients in the pharmacokinetic and pharmacodynamic properties of propofol, in the inherent compliance of pharyngeal tissues, in the baseline upper airway size, and in the resistive load upstream to the collapsible section of pharyngeal airway, *e.g.*, in the nasopharynx. Because the degree of cervical or atlantooccipital flexion might influence neural activation of upper airway muscles and the susceptibility of the upper airway to obstruction,^{6,24} we used a standardized head position in the current study.

In the current study, inspiratory narrowing of the airway occurred at the level of the epiglottis. In wakefulness, upper airway size changes dynamically throughout the respiratory cycle.^{25,26} Phasic activation of upper airway dilator muscles in inspiration opposes the collapsing effect of negative intraluminal pressure produced by contraction of thoracic muscles, resulting in a small increase in upper airway size toward the end of inspiration. In early expiration, the upper airway expands as a result of positive intraluminal pressure and then decreases in size toward the end of expiration as the positive intraluminal pressure abates. In the current

Table 2. Upper Airway Cross-sectional Areas and Dimensions in Control Subjects

	Cross-sectional Area, mm ²		Anteroposterior Dimension, mm		Transverse Dimension, mm	
	Baseline	Repeat	Baseline	Repeat	Baseline	Repeat
Soft palate						
Expiration	62.7 ± 29.7	64.3 ± 22.5	8.1 ± 2.8	8.0 ± 2.5	9.3 ± 3.8	9.0 ± 4.0
Inspiration	67.0 ± 18.0	65.1 ± 20.0	7.9 ± 2.3	8.1 ± 2.7	9.1 ± 3.8	8.8 ± 4.0
Base of tongue						
Expiration	115 ± 49.2	117 ± 52.0	11.3 ± 3.9	11.5 ± 4.1	10.2 ± 4.2	10.0 ± 4.3
Inspiration	112 ± 46.7	117 ± 50.5	10.7 ± 3.7	11.0 ± 4.0	10.6 ± 3.7	10.5 ± 4.2
Tip of epiglottis						
Expiration	69.7 ± 48.0	72.3 ± 45.7	6.4 ± 3.6	6.2 ± 3.9	12.9 ± 7.0	12.0 ± 7.2
Inspiration	60.0 ± 44.0	64.1 ± 49.1	5.3 ± 3.7*	5.5 ± 4.0	13.5 ± 6.5	12.9 ± 6.2

Data are mean ± SD.

* $P < 0.05$ compared with corresponding value in expiration.

study, the smaller respiratory variation in airway size during deep anesthesia at the level of the epiglottis could be attributed in part to a greater depressive effect of deep anesthesia on upper airway and thoracic inspiratory muscle activity. Further studies are warranted to elucidate the effect of propofol on the dynamic changes that occur in the upper airway during the respiratory cycle.

Our finding that anesthesia with propofol decreased the patency of the entire pharyngeal airway contrasts with observations in adult patients with obstructive sleep apnea. Fast-scanning computerized tomography demonstrated that airway obstruction in patients with sleep apnea is limited to a specific location within the upper airway and that different patients with obstructive sleep apnea have obstruction at different sites.²⁷ Approximately half of the patients had obstruction in the retro-palatal area and half in the hypopharynx, but in none did the obstruction involve the entire upper airway.^{28,29} Although the physiologic mechanisms underlying airway obstruction during anesthesia and in obstructive sleep apnea may be similar,^{15,30} the anatomic factors causing obstruction appear to differ.

We used spin echo magnetic resonance imaging to accurately determine upper airway CSA. This imaging technique yields high-resolution images of the upper airway structures without exposure to ionizing radiation.^{24,25} Spin echo MRI, unlike ultrasonography,⁷ is unaffected by the presence of an air-tissue interface or surrounding structures such as the hyoid bone. Recent advances in MRI technology allowed us to apply this technique to obtain images at specific points in the respiratory cycle, in contrast to previous studies.¹⁰⁻¹⁴ Although techniques such as fast computed tomography scanning and acoustic reflection yield dynamic measurements of pharyngeal caliber at different phases of the respiratory cycle, these techniques are constrained by radiation exposure or limited resolving power.^{27,31} Because the acquisition time for each image was 1 s in our study, respiratory rates greater than 30 breaths/min would have precluded image acquisition at different

phases of the respiratory cycle. The overall mean respiratory rate in our study was 14 breaths/min, and no child had a respiratory rate greater than 24 breaths/min.

The aim of the current study was to investigate the effect of propofol on upper airway caliber without the influence of any type of airway instrumentation or mechanical stimuli. Consequently, a limitation of our study is the potential for different degrees of hypercapnia at the different depths of anesthesia. In animal experiments, hypercapnia was associated with an increase in upper airway muscle activity that could attenuate any suppression caused by general anesthesia.⁴ However, it is likely that any increase in arterial carbon dioxide tension in the current study was small relative to the level required to influence upper airway muscle activity.⁴ A second limitation of our study is the fact that control baseline measurements were obtained in lightly anesthetized patients, rather than in awake subjects, because most children will not remain motionless for the duration of imaging. We hypothesize that even more notable differences in airway caliber would have been observed had we obtained baseline images in awake patients.

In preliminary studies, we noted that mucous secretions accumulated on the pharyngeal walls after induction of anesthesia, showing up on the scan as a bright image that made interpretation of the tissue-airway interface difficult. The contribution of pharyngeal secretions in reducing airway dimension is disproportionately large as airway size decreases.³² Moreover, mucosal surface adhesive forces can modulate the susceptibility of the upper airway to collapse.³³ For these reasons, glycopyrrolate was given to all children immediately after placing the intravenous catheter.

In summary, configurational changes affecting the entire upper airway lead to narrowing with increasing depth of propofol anesthesia in spontaneously breathing children. Whereas the overall minimum airway resided at the level of the soft palate in lightly anesthetized children, overall airway caliber at the level of the epiglottis was comparable to that at the soft palate in deeply

anesthetized children, suggesting that deep anesthesia may render the airway susceptible to collapse at more than one anatomic site.

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