

## Feasibility and safety of transglottic bronchoscopy in mechanically ventilated sheep

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### Abstract

**Purpose** Although bronchoscopy can be safely performed through endotracheal tube in most intubated critically ill patients, sometimes it could lead to complications such as hypoxia and high airway pressures. Theoretically, transglottic bronchoscopy (TGB) does not interfere with mechanical ventilation and could avoid these complications. In a two-period crossover study, we compared this technique with trans-endotracheal tube bronchoscopy (TEB) in normal anesthetized sheep.

**Methods** In five sheep, we did TGB first. The bronchoscope was introduced through the nasal nares and passed into the trachea via space between endotracheal tube and vocal folds. Heart rate,  $V_T$ ,  $P_{\text{peak}}$ , and  $O_2$  saturation were recorded. One week later, we did TEB. In another five sheep, we did TEB first and TGB later.

**Results**  $P_{\text{peak}}$  increased and  $V_T$  and  $O_2$  saturation decreased during TEB ( $53.2 \pm 5.7$  vs.  $27.6 \pm 0.6$ ,  $P = 0.002$ ;  $210 \pm 32$  vs.  $285 \pm 26$ ,  $P = 0.002$ ;  $94.3 \pm 1.3$  vs.  $97.5\% \pm 0.5$ ,  $P = 0.041$ , respectively), but not during TGB. The only statistically significant abnormal finding during TGB was a mild tachycardia ( $96.7 \pm 5.7$  vs.  $94.7 \pm 5.5$ ,  $P = 0.034$ ).

**Conclusion** Although TGB is time consuming and less convenient than TEB, it has minimal interference with mechanical ventilation. Expertise with this technique could be useful in patients with anticipated significant hypoxia and high airway pressures during bronchoscopy.

**Keywords** Transglottic bronchoscopy · Trans-endotracheal tube bronchoscopy · Mechanical ventilation · Sheep

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### Introduction

Bronchoscopy is an important diagnostic and therapeutic modality in the intensive care unit (ICU). It could be safely performed via an endotracheal tube (ETT) in most intubated patients [1–3]. However, complications such as elevated airway pressures, hypoxia and hypercapnia, and hemodynamic instability have been reported, especially in patients with underlying cardiopulmonary disease and small-bore ETT [1, 4, 5]. Theoretically, passing the bronchoscope through the glottis into the trachea in intubated patients does not interfere with mechanical ventilation and could avoid the foregoing complications. The feasibility and possible complications of this transglottic bronchoscopy (TGB) have not been systematically studied. We conducted this study to:

1. Determine whether TGB is feasible in intubated sheep.
2. Compare the rate of high airway peak pressure ( $P_{\text{peak}}$ ) and hypoxia during TGB in comparison with traditional trans-endotracheal tube bronchoscopy (TEB) in this animal model.

## Materials and methods

### Animals

The study was performed in ten healthy female mixed-breed sheep weighing 21–51 kg and aged 2–12 months. The logic of selection of such an age range was to provide the assessment of different sizes of ETT, i.e., 6.5 mm in two sheep, 7 mm in four sheep, and 8 mm in four sheep comparable to the smallest endotracheal tubes that are used in human adolescent, female, and male patients, respectively (Table 1). The sheep were fed with a balanced diet, and water was offered ad libitum throughout the study period.

### Anesthesia and bronchoscopy preparation

The study was designed as a two-period crossover study. In the first part, five randomly chosen sheep were examined via TGB. A 16-gauge catheter was introduced in the left external jugular vein for fluid administration. After premedication with intramuscular xylazine hydrochloride (0.5 mg/kg), anaesthesia was induced with intravenous thiopental (7 mg/kg) without use of any neuromuscular relaxant and maintained with 1–3% halothane. ETT was

inserted through the vocal folds under direct laryngoscopy after applying 2% lidocaine spray. The depth of insertion of the endotracheal tube was 24–26 cm.

The animals were ventilated with controlled mandatory ventilation (CMV) mode with following parameters:  $V_T \approx 8$  ml/kg, rate = 15/min,  $I/E = 1/3$ , positive end-expiratory pressure (PEEP) = 3 cmH<sub>2</sub>O, and  $FiO_2 = 50\%$ . The  $FiO_2$  was not changed throughout the procedures to study the effect of bronchoscopy on arterial O<sub>2</sub> saturation (SaO<sub>2</sub>).

### Bronchoscope

We used a BF40 bronchoscope (Olympus Company; 5.7 mm external diameter, 2.2 mm working channel) as a prototype of an appropriate bronchoscope for common procedures in the adult ICUs.

When bronchoscopy was not feasible with BF40, we used an LF-GP bronchoscope (Olympus Company; 3.2 mm external diameter) as prototype of a portable battery-powered bronchoscope available in ICUs for fiberoptic intubation that could also be used for tracheobronchial inspection. It was used during TEB when the peak pressure “ $P_{\text{peak}}$ ” was greater than 70 cmH<sub>2</sub>O in the first minute of bronchoscopy and during TGB, when there is not enough space for passing the BF40 through the vocal folds.

### Method of bronchoscopy

The fiberoptic bronchoscope was introduced through the nasal nares and passed into the trachea through the space between the endotracheal tube and the vocal folds. After carefully suctioning any secretions above the tube cuff, we

**Table 1**  $P_{\text{peak}}$ ,  $V_T$ , and O<sub>2</sub> saturation at  $T_5$  (and baseline) of trans-endotracheal tube (TEB) and transglottic (TGB) bronchoscopy

No.	Weight (kg)	ETT size	TEB				TGB			
			FOB size	$P_{\text{peak}}$ (cmH <sub>2</sub> O)	$V_T$ (ml)	SaO <sub>2</sub> (%)	FOB size	$P_{\text{peak}}$ (cmH <sub>2</sub> O)	$V_T$ (cc)	SaO <sub>2</sub> (%)
101	21	6.5	3.2	43 (29) <sup>a</sup>	135 (175) <sup>a</sup>	95	3.2	30 (26) <sup>a</sup>	165 <sup>b</sup>	97
102	23	6.5	3.2	41 (29)	165 (200)	99	5.7	26 (24)	195	97
103	25	7.0	5.7	77 (26)	75 (200)	92	5.7	19 (20)	190	98
104	30	7.0 <sup>c</sup>	5.7	76 (26)	155 (250)	94	5.7	28 (30)	245	99
105	31	7.0	5.7	74 (26)	80 (250)	89	5.7	28 (28)	240	98
106	35	7.0	3.2	31 (24)	285 (300)	99	5.7	19 (18)	295	99
107	42	8.0 <sup>c</sup>	5.7	39 (29)	300 (350)	95	5.7	23 (23)	345	97
108	43	8.0	5.7	41 (29)	310 (350)	97	5.7	23 (22)	340	97
109	45	8.0	5.7	68 (28)	250 (375)	86	5.7	25 (23)	370	96
110	51	8.0	5.7	42 (30)	345 (400)	97	5.7	22 (23)	390	98

See text for expansion of the abbreviations

<sup>a</sup> Numbers in parentheses show parameter values at the baseline

<sup>b</sup> TGB  $V_T$  baseline values were the same as TEB  $V_T$

<sup>c</sup> Tracheal diameter (measured as shown in Fig. 1) in sheep 104 = 17 mm and in sheep 107 = 19 mm

temporarily deflated the ETT cuff and passed the bronchoscope alongside the ETT into distal trachea and right bronchi (Fig. 1). For establishing ventilation while permitting easy handling of the bronchoscope, we reinflated the ETT cuff to a pressure of 15–20 cmH<sub>2</sub>O, while allowing minimal leakage [ $<5\%$  of tidal volume ( $V_T$ )] around the cuff. During the procedure electrocardiogram, heart rate (HR), expiratory  $V_T$ ,  $P_{\text{peak}}$ , and SaO<sub>2</sub> were monitored and recorded at the beginning of the bronchoscopy ( $T_0$ ) and at first, second, third, ... minute ( $T_1, T_2, T_3, \dots$ ) after initiation of bronchoscopy by an observer who was unaware of the aim of the study. Vocal folds were examined for any gross injury at the end of bronchoscopy, and animals were monitored up to 1 week after bronchoscopy to assess for possible complications. After 1 week, we did TEB in this group. In another five sheep, we did TEB first and TGB 1 week later.

All procedures involved in this study were approved by the Ethical Committee of Tehran University of Medical Sciences.

#### Statistical analysis of data

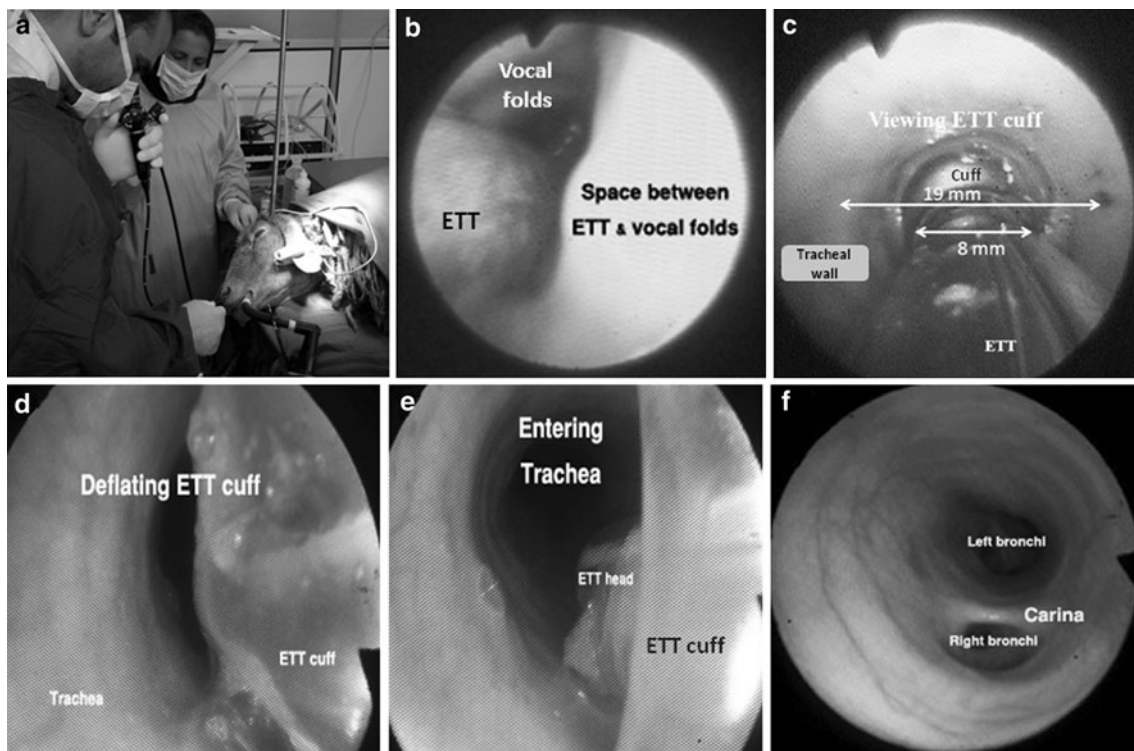
Data were analyzed by SPSS (version 18.0). A paired  $t$  test was used to compare between two techniques. Repeated-measures analysis of variance (ANOVA) followed by the Bonferroni–Dunn test was used for comparing parametric

changes overtime. Results were presented as mean  $\pm$  standard error of mean.

#### Results

TEB could be done with BF40 in seven sheep and with LF-GP in three other sheep (two sheep with 6.5-mm and one sheep with 7-mm internal diameter ETT; Table 1). TGB was feasible with the BF40 bronchoscope in nine sheep. In the smallest sheep (weight, 21 kg; ETT internal diameter, 6.5 mm), we could not pass the BF40, and we used LF-GP in this sheep (Table 1). The mean time for passing the bronchoscope transglottically through the vocal folds was  $2.9 \pm 1.2$  min (range, 2–6 min).

$P_{\text{peak}}$  had a significant increase and  $V_T$  had a significant decrease throughout TEB (Tables 1, 2).  $P_{\text{peak}}$  reached 78 and 93% of its peak value at  $T_1$  and  $T_2$  of TEB, respectively; 81% of  $V_T$  reduction occurred at  $T_2$  (Table 2).  $P_{\text{peak}}$  reached 68 cmH<sub>2</sub>O and  $V_T$  decreased to 67% of its baseline values at  $T_5$  in sheep 109 during TEB via 8-mm ETT (Table 1).  $P_{\text{peak}}$  reached 77, 76, and 74 cmH<sub>2</sub>O and  $V_T$  decreased to 38, 62, and 32% of its baseline values at  $T_5$  in sheep 103–105 during TEB with BF40 via 7-mm ETT (Table 1).  $P_{\text{peak}}$  and  $V_T$  did not change during TGB. The differences in  $P_{\text{peak}}$  and  $V_T$  between the two groups in all time points were statistically significant (Table 2).



**Fig. 1** Transglottic bronchoscopy in sheep 107. ETT endotracheal tube

**Table 2** Changes in cardiopulmonary parameters (mean  $\pm$  SE) during trans-endotracheal tube (TEB) and transglottic (TGB) bronchoscopy

Variables	Baseline	1 min	2 min	3 min	4 min	5 min
<b>TEB</b>						
HR (beats/min)	90.6 $\pm$ 4.4	90.5 $\pm$ 4.2	90.5 $\pm$ 4.2	90.5 $\pm$ 4.3	90.4 $\pm$ 4.3	88.9 $\pm$ 3.7
$P_{\text{peak}}$ (cmH <sub>2</sub> O)	27.6 $\pm$ 0.6	41.5 $\pm$ 3.5 <sup>†,*</sup>	49.3 $\pm$ 5.5 <sup>†,*</sup>	51.0 $\pm$ 5.2 <sup>†,*</sup>	52.4 $\pm$ 5.5 <sup>†,*</sup>	53.2 $\pm$ 5.7 <sup>†,*</sup>
SaO <sub>2</sub> (%)	97.5 $\pm$ 0.5	96.5 $\pm$ 0.7	95.9 $\pm$ 1.1	95.7 $\pm$ 1.0	94.8 $\pm$ 1.4	94.3 $\pm$ 1.3 <sup>‡,*</sup>
$V_T$ (ml)	285 $\pm$ 26	253 $\pm$ 27 <sup>†,*</sup>	224 $\pm$ 29 <sup>†,*</sup>	222 $\pm$ 30 <sup>†,*</sup>	215 $\pm$ 30 <sup>†,*</sup>	210 $\pm$ 32 <sup>†,*</sup>
<b>TGB</b>						
HR (beats/min)	94.7 $\pm$ 5.5	95.3 $\pm$ 5.6	95.9 $\pm$ 5.6	96.5 $\pm$ 5.8 <sup>‡</sup>	96.6 $\pm$ 5.8 <sup>‡</sup>	97.0 $\pm$ 6.3 <sup>‡</sup>
$P_{\text{peak}}$ (cmH <sub>2</sub> O)	23.7 $\pm$ 1.1	23.7 $\pm$ 1.2	23.8 $\pm$ 1.2	24.0 $\pm$ 1.2	24.0 $\pm$ 1.3	24.3 $\pm$ 1.2
SaO <sub>2</sub> (%)	98.2 $\pm$ 0.3	98.0 $\pm$ 0.5	97.8 $\pm$ 0.4	97.9 $\pm$ 0.4	97.4 $\pm$ 0.5	97.6 $\pm$ 0.4
$V_T$ (ml)	285 $\pm$ 26	279 $\pm$ 26	278 $\pm$ 27	276 $\pm$ 26	278 $\pm$ 26	278 $\pm$ 26

See text for expansion of abbreviations

\*  $P < 0.05$  compared to TGB

†  $P < 0.01$  compared to baseline

‡  $P < 0.05$  compared to baseline

The SaO<sub>2</sub> did not decrease during TGB for up to the sixth minute. There was a significant decrease in SaO<sub>2</sub> during TEB (94.4  $\pm$  1.4% at  $T_5$  vs. 97.5  $\pm$  0.5% at baseline,  $P = 0.048$ ; Table 2). The SaO<sub>2</sub> in TEB group was significantly lower compared to TGB group at  $T_5$  (94.4  $\pm$  1.4% vs. 97.6  $\pm$  0.4%,  $P = 0.042$ ; Table 2).

The SaO<sub>2</sub> was decreased in TEB to 86, 89, 87, and 90% at  $T_6$  in the above four sheep (103, 104, 105, and 109) with high  $P_{\text{peak}}$ . In the other six sheep (two with 6.5-mm ETT and one with 7-mm ETT using LF-GP; three with 8-mm ETT using BF40),  $P_{\text{peak}}$  ranged from 31 to 43 cmH<sub>2</sub>O and  $V_T$  reduction was from 5 to 23% at  $T_5$  without any significant change in O<sub>2</sub> saturation.

In seven sheep in which the BF40 bronchoscope was used,  $P_{\text{peak}}$  was significantly higher and SaO<sub>2</sub> and  $V_T$  were significantly lower at  $T_5$  in the TEB group compared to the TGB group (59.6  $\pm$  6.8 vs. 24.0  $\pm$  1.2,  $P = 0.002$ ; 92.9  $\pm$  1.6% vs. 97.6  $\pm$  0.4%,  $P = 0.019$ ; 216.4  $\pm$  42.5 vs. 302.9  $\pm$  29.0,  $P = 0.003$ , respectively).

There was mild tachycardia without significant EKG changes during TGB (96.7  $\pm$  5.7 at  $T_5$  vs. 94.7  $\pm$  5.5 at baseline,  $P = 0.034$ ), but not TEB (Table 2), although the heart rate changes with time during TGB compared to TEB were not statistically significant. No gross vocal fold injury occurred during TGB.

## Discussion

### Feasibility

Tracheal diameter in sheep is very close to that of humans, ranging from 15 to 23 mm [6]. Owing to different shapes of the vocal folds and ETT cross section (V-shape vs. circle), a

posterolateral space appears that permits passage of the bronchoscope through the vocal folds during TGB (Fig. 1). The vocal folds are the narrowest part of the laryngotracheal passage in sheep. Thus, if the bronchoscope could be introduced into the trachea thorough the space between ETT and vocal folds, there is enough space for passing it alongside the ETT into the distal trachea (Table 1; Fig. 1). After passing the ETT cuff, easy maneuvering of the bronchoscope under mechanical ventilation could be attained by reinflating the cuff to a pressure of 15–20 cmH<sub>2</sub>O while leaving minimal leakage around the cuff.

Using BF40, transglottic bronchoscopy was feasible in nine and TEB only in seven sheep.

In the smallest sheep, bronchoscopy could be done with both techniques with LF-GP.

$P_{\text{peak}}$ , tidal volume, and oxygen saturation

During bronchoscopy through the endotracheal tube, the bronchoscope occupies a considerable portion of the lumen of the tube [4, 7]. Using pressure monitoring at the distal tip of the bronchoscope, Lindholm [4] studied  $P_{\text{peak}}$  and intra-tracheal pressure changes during TEB. He showed that the major part of the  $P_{\text{peak}}$  increase was caused by the intra-tracheal pressure increase. High tracheal pressures rapidly induced an intrinsic PEEP effect, and expiratory  $V_T$  decreased. With an 8.0-mm ETT, intrinsic PEEP usually remains below 20 cmH<sub>2</sub>O, but a PEEP value of 35 cmH<sub>2</sub>O was reported in a patient carrying a 7.0-mm ETT [4].

An average PaO<sub>2</sub> decline of 10–20 mmHg during TEB has been reported [1, 5]. In our study, TEB was feasible with BF40 in seven sheep with 7- and 8-mm internal diameter ETTs, although high  $P_{\text{peak}}$ , low  $V_T$ , and hypoxia caused us to abort TEB in four of them before  $T_7$ .

This study corroborates with clinical reports that show that TEB could be performed even with small-bore ETT (<8 mm) in most critically ill patients if done quickly [1–3]. High airway pressure and hypoxia are rapidly reversible after bronchoscopy in most of the patients, although they may be severe and prolonged in patients with coexisting cardiopulmonary diseases [5].

During TGB, none of the sheep experienced hypoxia or an increase in  $P_{\text{peak}}$  regardless of the ETT size, which suggests that this method has minimal interference with mechanical ventilation. Thus, we could expect that with this method we could avoid high airway pressure and gas-exchange abnormality during bronchoscopy in mechanically ventilated patients. In our earlier report, no hypoxia and change in  $P_{\text{peak}}$  occurred in 32 critically ill intubated patients during TGB [8].

#### Other considerations

In 1975, Feldman and Sanders [9] reported passing the bronchoscope through the glottis alongside endotracheal tubes less than 8 mm in two intubated patients. In Feldman's report of these two cases, one of the limitations of this method was the time needed for passing the bronchoscope through the vocal cords [9]. In our study, the mean time for passing the bronchoscope was less than 3 min.

The risk of ventilator-associated pneumonia (VAP) after bronchoscopy in intubated patients has not been systematically studied. Based on current understanding of VAP pathogenesis, bacteria usually enter the lower respiratory tract by leakage around the endotracheal tube cuff or are dislodged from the endotracheal tube intraluminal biofilm [10, 11]. Theoretically, TEB, by dislodging the biofilm particles and TGB, by temporary deflation of the ETT cuff and translocating nasopharyngeal flora into the lower airways, could increase VAP risk. Bronchoscopic-related pneumonia is estimated to occur in fewer than 5% of cases during TEB [3]. The risk is increased up to 47% if re-intubation with a wide-bore ETT was needed for TEB [12]. Careful suctioning of any secretions above the ETT cuff before its deflation during TGB could minimize VAP rate by reducing the amount of bacteria entering the lower airways. None of our previously reported 32 patients completed the VAP criteria after TGB for up to 48 h [8]. Furthermore, in some critically ill patients who need bronchoscopy, TEB may not be feasible because of very high airway pressure or severe hypoxia and TGB is the only feasible method.

There was a mild tachycardia during TGB. The anesthesia provider was blind to the aim of the study, and we did not adjust the anesthesia depth during the procedure. This rise in heart rate could possibly be the result of the

lesser amount of anesthetic drugs used during this method owing to the nonexistence of high  $P_{\text{peak}}$  and hypoxia.

#### Limitations of the study

We compared feasibility and rate of high  $P_{\text{peak}}$  and hypoxia in TGB and TEB in this animal model. We did not measure other parameters such as arterial  $p\text{CO}_2$ , intracranial pressure, or cardiac indices (except HR), although we do not expect significant changes in these parameters in TGB. TGB would be not feasible in some critically ill patients because of vocal cord inflammation or subglottic stenosis. The model was not appropriate for examining the VAP rate between the two methods.

#### Conclusion

Bronchoscopy could be performed through an endotracheal tube in most intubated critically ill patients. However,  $P_{\text{peak}}$  increased and  $V_T$  decreased, especially with a small-bore ETT, leading to hypoxia as TEB proceeded even in this normal animal model.

Although TGB is time consuming and less convenient, it has minimal interference with mechanical ventilation. Expertise with this alternative technique could be useful in patients with anticipated significant hypoxia and high airway pressures during bronchoscopy.

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