The Role of the Cuff Leak Test in Predicting the Effects of Corticosteroid Treatment on Postextubation Stridor

Chih-Liang Wang, MD; Ying-Huang Tsai, MD; Chung-Chi Huang, MD; Yau-Kwang Wu, MD; Ming-Zhu Ye, RT; Hsiu-Min Chou, RT; Shih-Chun Shu, RT; Meng-Chih Lin, MD

Background: There is not enough evidence to determine the most appropriate treatment of postextubation stridor. Although the cuff leak test is a simple method to predict postextubation stridor, little is known about its use in monitoring the effects of steroid treatment for this complication. The aim of this study was to evaluate the effects of steroids on postextubation stridor based on the clinical response and the cuff leak test.

Methods: A cohort of 110 translaryngeal intubated patients in the medical intensive care unit (ICU) were enrolled. A cuff leak test was conducted before extubation. Patients developing postextubation stridor were intravenously given 5 mg of dexamethasone every 8 hours for 3 days. The clinical response and cuff leak volume before and after steroid treatment were gathered for analysis.

Results: The incidence of postextubation stridor was 18.2% (20/110). Fifty-five percent of patients (11/20) with stridor needed reintubation. Overall, 80% of patients (16/20) with postextubation stridor improved with steroid treatment. The leak volume significantly increased after treatment (152.4 ± 109.6 ml vs. 29.9 ± 35.7 ml, \( p = 0.012 \)); stridor did not recur in 64% of reintubated patients (7/11). A threshold leak volume of less than 88 ml predicted the occurrence of stridor (positive predictive value, 54.5%; negative predictive value, 90.9%). Postextubation stridor was associated with the female gender and lower leak volumes (\( p = 0.007 \) and 0.003, respectively).

Conclusion: Corticosteroids improve postextubation stridor. The cuff leak test accurately predicts the absence of stridor and is a non-invasive method of monitoring for regression of laryngeal edema after steroid treatment. Steroid treatment should be considered for patients developing postextubation stridor.


Key words: postextubation stridor, laryngeal edema, endotracheal intubation, corticosteroid, extubation failure, cuff leak test.

Postextubation laryngeal edema is one of the major complications of tracheal intubation. The incidence of postextubation stridor has been reported to range from 3.5% to 22%. Early reintubation is
necessary in 46% to 80% of patients who develop postextubation stridor; this prolongs the duration of mechanical ventilation and increases morbidity in intensive care unit (ICU) patients.

Laryngeal damage is assumed to occur because the endotracheal tube exerts pressure on the posterior larynx and injures the medial surface of the arytenoid cartilage and the vocal cords. A cuff leak test is an easily performed test to assess laryngotracheal patency before extubation, given that the presence of an endotracheal tube makes direct visualization by laryngoscope difficult. The test is useful for identifying patients who are at risk of stridor and indirectly reflects the severity of laryngeal edema.

Non-invasive positive pressure ventilation, aerosolized epinephrine, helium-oxygen therapy and inhaled or injected corticosteroids have been used to treat the laryngeal complications that occur following extubation in sporadic case reports. Corticosteroids have been shown to effectively reduce laryngeal inflammation and edema formation in an animal study and to successfully treat croup and reduce postextubation stridor in pediatric patients.

To our knowledge, there has been no study dealing with the outcome of steroid treatment in adult patients with postextubation stridor. Therefore, we designed this study to (1) evaluate steroid treatment in patients who had developed postextubation stridor and measure the change of the leak volume with a cuff leak test in patients who were reintubated to objectively evaluate improvement in the edematous upper airway after steroid treatment and (2) determine the threshold value of a cuff leak test and the risk factors for postextubation stridor.

METHODS

Patients

All patients admitted to the medical ICU between May 2002 and Dec 2003 who were intubated and in whom extubation was planned were included in this study. Patients who were intubated primarily due to upper airway obstruction or vocal cord paralysis who clinically presented with stridor were excluded. The study was approved by the institutional review board. Informed consent was obtained from patients or their families. Each patient was intubated via the oral route with a 7.5 mm internal diameter endotracheal tube with a low-pressure, high-volume cuff (Kendall Curity® tracheal tube, MA, USA). As part of routine daily airway care, the cuff pressure was checked and kept at 25-30 cm H2O by the respiratory therapists.

Protocol

A cuff-leak test was performed immediately before each extubation while the patient was using any of the following ventilators: Adult Star (Infrasonics; San Diego, CA, USA), or Bird 8400 Sti (Bird; Palm Springs, CA, USA). The test was performed as described by Miller and Cole. All oral and endotracheal secretions were suctioned, and the ventilators were placed on the assist-control mode with the tidal volume (Vt) set at 10 ml/kg of ideal body weight. The initial displayed expiratory tidal volume was measured with the cuff inflated. Then the cuff was deflated and the expiratory tidal volume was recorded after the elimination of artifacts caused by coughing. Six subsequent breath cycles were measured and the average value calculated. The leak volume was defined as the difference between the expiratory Vts with the cuff inflated and deflated. The leak percentage was the leak volume divided by the expiratory Vt when the cuff was inflated.

All patients were evaluated immediately after extubation for signs and symptoms of respiratory distress. Stridor was defined as an inspiratory crowing sound heard in the upper airway. Respiratory distress was defined as tachypnea associated with tachycardia, cold sweating or irritable appearance with or without oxygen desaturation. Dexamethasone 5 mg was intravenously given immediately and every 8 hours for 3 days whenever stridor was noted.

All assessments of stridor, respiratory distress, and the need for reintubation were made by the ICU physicians who were blinded to the leak volume measurements obtained by the respiratory therapists. In those patients reintubated due to postextubation stridor, another cuff leak test was done after 3 days of corticosteroid treatment before extubation if no contraindication for extubation was noted.

Statistical analysis

The results are expressed as mean ± standard deviation (SD) for continuous variables and frequency (%) for categorical variables. The data for the patients with and without stridor were compared. For
continuous variables, the unpaired Student’s t-test was performed to compare the means; the Mann-Whitney U test was used if the samples were not normally distributed. For the categorical variables, the data was analyzed using the chi-square test or Fisher’s exact test when the expected frequency counts were less than 5 in any category. The Wilcoxon signed rank test was used for analysis of paired small sample sizes. A two-tailed p value less than 0.05 was considered statistically significant. A receiver operating characteristic (ROC) plot was used to identify the threshold leak volume and the percentage that predicted the occurrence of stridor. The ROC plot graphed the true-positive rate on the vertical axis against the false-positive rate on the horizontal axis for the various leak volumes and percentages.21 The optimum cut-off point correlated with the best Youden index (sensitivity + specificity - 1).22 All statistical analyses were performed using SPSS 10.0 software (Chicago, IL, USA). The sensitivity, specificity, positive predictive value, and negative predictive value were used to determine the accuracy of the cuff leak test. We defined a positive test as a leak volume or percentage less than the cut-off value.

RESULTS

A total of 130 intubations were conducted in 110 patients with a mean age of 71 ± 13 years (range, 24 to 96). There were 52 men and 58 women. Only the first extubation was used for the analysis of the differences between patients with and without stridor. Overall, 24.5% (27/110) of the patients had been intubated in the previous 6 months. The duration of intubation was 13 ± 14 days (range, 1 to 65). The incidence of postextubation stridor was 18.2% (20/110); stridor usually occurred immediately after extubation. Of the 20 patients who developed stridor, 11 (55%) needed to be reintubated within one hour due to severe respiratory distress caused by upper airway obstruction (Fig. 1). Women had a significantly higher incidence of stridor than men (27.6% vs. 7.6%, p = 0.007; odds ratio = 4.6). Patients with stridor had lower leak values (present as absolute volume or relative percentage) than those without

### Fig. 1

stridor (leak volume: 146.6 ± 158.7 ml vs. 271.2 ± 148.5 ml, \( p = 0.003 \); leak percentage: 28.7% ± 31.5% vs. 51.8% ± 26.6%, \( p = 0.005 \)). There was no significant difference in age, body weight, albumin level, previous intubations, indications for intubation, or chronic morbidities (Table 1).

Steroids were given immediately to the 20 patients who developed stridor; 9 of these patients recovered spontaneously within 24 hours. Three of the remaining eleven patients who needed to be reintubated had a large leak volume; two of them were found to have vocal cord paralysis on fiberoptic bronchoscopy and required a tracheostomy. The other one died due to airway obstruction from a blood clot noted on laryngoscopy examination. In 8 patients reintubated due to stridor, another cuff leak test and re-extubation were done after 3 days of steroid treatment. After steroid treatment, there was a significant increase in the leak volume (29.9 ± 35.7 ml, before vs. 152.4 ± 109.6 ml, after; \( p = 0.012 \)) and percentage (7.2% ± 9.7%, before vs. 33.4% ± 21.1%, after; \( p = 0.012 \)) (Fig. 2). Of the 8 patients, 7

| Table 1. Patient Demographic Data and Clinical Characteristics |
|------------------|-----------------|-----------------|----------|
|                  | All patients (n = 110) | Stridor (n = 20) | No stridor (n = 90) | \( p \) |
| Age (years)      | 71 ± 13           | 67 ± 14          | 72 ± 13          | 0.199  |
| Gender (M/F)     | 52/58             | 4/16             | 48/42             | 0.007  |
| Body weight (kgw)| 56.6 ± 14.7       | 56.1 ± 8.7       | 56.7 ± 15.8      | 0.822  |
| Duration of intubation (days) | 13 ± 14         | 10 ± 14          | 14 ± 14          | 0.331  |
| Intubation history (yes/no) | 27/83           | 4/16             | 23/67             | 0.776  |
| Albumin (g/L)    | 2.8 ± 0.6         | 3.0 ± 0.4        | 2.8 ± 0.7        | 0.173  |
| COPD (yes/no)    | 30/80             | 5/15             | 25/65             | 0.801  |
| Heart failure (yes/no) | 20/90           | 2/18             | 28/62             | 0.055  |
| Renal insufficiency* (yes/no) | 38/72          | 9/11             | 29/61             | 0.277  |
| Liver cirrhosis (yes/no) | 5/105           | 1/19             | 4/86              | 1.000  |
| Sepsis (yes/no)  | 78/32             | 15/5             | 63/27             | 0.656  |
| Shock (yes/no)   | 10/100            | 1/19             | 9/81              | 0.686  |
| DM (yes/no)      | 43/67             | 9/11             | 34/56             | 0.549  |
| Cerebrovascular insult (yes/no) | 36/74           | 7/13             | 29/61             | 0.811  |
| Neuromuscular disorder (yes/no) | 6/104           | 2/18             | 4/86              | 0.299  |
| Leak volume (ml) | 248.5 ± 157.3     | 146.6 ± 158.7    | 271.2 ± 148.5    | 0.003  |
| Leak percentage (%) | 47.6 ± 28.8     | 28.7 ± 31.5      | 51.8 ± 26.6      | 0.005  |

Abbreviations: M: male; F: female; COPD: chronic obstructive pulmonary disease; DM: diabetes mellitus

* serum creatinine > 1.5 mg/dL.

Fig. 2 Change of leak volume and percentage after steroid treatment in eight reintubated patients due to postextubation stridor. (A) leak volume change after steroid treatment. (B) leak percentage change after steroid treatment. Wilcoxon signed-rank test for paired small sample sizes.
were successfully re-extubated without stridor, while one patient developed persistent stridor and needed a tracheostomy due to vocal cord paralysis seen on bronchoscopy. Cut-off leak threshold values of less than 88 ml and less than 18% were identified by the ROC curve to predict the occurrence of stridor with sensitivities of 60% and 55%, respectively, and specificities of 88.9% and 88.9%, respectively (Fig. 3). The positive and negative predictive values for a cut-off leak threshold of less than 88 ml were 54.5% and 90.9% respectively; for a percentage of less than 18%, the positive and negative predictive values were 52.4% and 89.9%, respectively (Table 2). The areas under the ROC curves for leak volume and percentage were 0.731 and 0.726, respectively.

**DISCUSSION**

Postextubation stridor occurred in 20 of 110 patients (18.2%) in our study, and 11 patients (55%) needed to be reintubated within one hour. These results are similar to those previously reported (Table 2). Steroid treatment improved postextubation stridor in 16 of 20 patients (80%), and in 7 patients (64%; 7/11) who were reintubated due to postextubation stridor. A significant increase in the leak volume was seen in the cuff leak test in the 8 patients who were reintubated after steroid administration.

An endotracheal tube exerts pressure or causes friction over the posterior larynx, resulting in ischemic mucosal damage. The histologic changes vary from vocal fold edema to ulceration, granulation formation, arytenoid cartilage dislocation, interarytenoid adhesion, posterior glottic stenosis, and vocal cord paralysis. Mucosal swelling and ulcer formation along the posterior aspects of the true vocal cords and the arytenoid process are responsible for 94% of laryngeal complications. There are several management strategies that are clinically reported to prevent or treat stridor after extubation. However, there is not enough evidence to decide on the most appropriate treatment. In an animal study,

![Figure 3 ROC curves for cut-off point of leak volume and percentage. The decision threshold of 88 ml and 18% were determined by best Youden index (sensitivity + specificity -1). The areas under the ROC curves for leak volume and percentage were 0.731 and 0.726 respectively.](image-url)

**Table 2. Comparison of Cuff Leak Tests in Different Studies**

<table>
<thead>
<tr>
<th>Study</th>
<th>Patient source and mean duration of mechanical ventilation</th>
<th>Stridor incidence</th>
<th>Reintubation rate due to stridor</th>
<th>Cut-off value (less than)</th>
<th>Leak volume (ml)</th>
<th>Leak percentage</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
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</thead>
<tbody>
<tr>
<td>Miller et al.</td>
<td>MICU</td>
<td>6%</td>
<td>50%</td>
<td>110</td>
<td>67%</td>
<td>99%</td>
<td>80%</td>
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<td></td>
<td>5.8 days</td>
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<tr>
<td>De Bast et al.</td>
<td>SICU and MICU</td>
<td>13%</td>
<td>80%</td>
<td>15.5%</td>
<td>75%</td>
<td>72%</td>
<td>25%</td>
<td>96%</td>
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<td></td>
<td>2 days (median)</td>
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<td>Jaber et al.</td>
<td>SICU and MICU</td>
<td>12%</td>
<td>69%</td>
<td>12%</td>
<td>85%</td>
<td>95%</td>
<td>69%</td>
<td>98%</td>
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<td></td>
<td>5.5~10.9 days</td>
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<td>Sandhu et al.</td>
<td>trauma ICU</td>
<td>11.8%</td>
<td>46%</td>
<td>10%</td>
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<td>96%</td>
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<td></td>
<td>2.6~6.5 days</td>
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<tr>
<td>Our study</td>
<td>MICU</td>
<td>18.2%</td>
<td>55%</td>
<td>18%</td>
<td>60%</td>
<td>88.9%</td>
<td>54.5%</td>
<td>90.9%</td>
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<td></td>
<td>13 days</td>
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**Abbreviations:** MICU: medical intensive care unit; SICU: surgical intensive care unit; PPV: positive predict value; NPV: negative predict value.
Dexamethasone was shown to be effective in the prophylaxis and treatment of laryngeal injuries caused by intubation. Corticosteroids have been used successfully to treat croup and reduce postextubation stridor in pediatric patients. A systematic review, conducted by Meade et al., concluded that there was a lower rate of stridor and reintubation in children given corticosteroids before extubation and that steroid administration decreased the risk of postextubation stridor by 40%. However, using steroid treatment to prevent stridor in adults is still debated. Ho et al. reported that hydrocortisone given 60 min before extubation did not reduce the incidence of stridor. A prospective, randomized, placebo-controlled, multicenter trial that enrolled 700 patients requiring tracheal intubation, conducted by Darmon et al., determined that, regardless of intubation duration, dexamethasone 8 mg given 1 hour before extubation could not prevent laryngeal edema after extubation. It is supposed that the low incidence of postextubation stridor makes it difficult to draw conclusions about the benefits of prophylactic steroid treatment. Also, a longer period of time might be needed for steroid treatment to produce its maximal anti-inflammatory effect. In our experiment (data not shown), an increased leak volume was observed 36 to 48 hours after steroid administration in those patients who were reintubated due to postextubation stridor. Although the sample size was small, our study provides preliminary evidence that steroid treatment improves postextubation stridor.

We could find no report about stridor developing in patients with a large leak volume. In our study, three patients suffering severe postextubation stridor who needed reintubation had a relatively large leak volume (more than 110 ml). They were found to have vocal cord paralysis on bronchoscopy and needed a tracheostomy to deal with permanent airway obstruction. The vocal process of the arytenoids and the posterior cricoid cartilage are the most vulnerable areas in tracheal intubation. Hsu et al. reported a patient who developed postextubation stridor due to arytenoid subluxation with anterior and medial displacement of an immobile vocal cord following exploratory laparotomy. The arytenoid cartilage was only moderately edematous. In our patients, we could not identify specific major events that could be associated with the trauma; it may have been caused by the fragile support provided by the laryngeal connective tissue and the repeated minor injuries that occur with daily nursing. We suggest that postextubation stridor with a large leak volume may be a sign of immobile vocal cords, rather than an anatomical narrowing caused by edema. Therefore, before reintubation, bronchoscopy is needed to confirm this irreversible complication.

It is difficult to evaluate the severity of laryngeal damage directly with a laryngoscope or fiberscope due to the presence of the endotracheal tube. On the other hand, the quantitative cuff leak test can be easily done to objectively assess laryngeal patency before extubation and identify those patients at risk of developing stridor. Several cut-off values have been used to predict which patients are at high risk for postextubation stridor in different populations (Table 2). Miller and Cole found a positive predictive value of 0.8 for postextubation stridor with a leak volume of less than 110 ml. De Bast et al. used a leak percentage of 15.5% as the watershed when considering the initial tidal volume setting related to the body mass. Jaber et al. set cut-off values of 130 ml and 12% in their study of 112 surgical patients. We chose a leak volume of 88 ml as the threshold value for predicting postextubation stridor in our study patients; the sensitivity was 60%, the specificity was 88.9%, the positive predictive value was 54.5%, and the negative predictive value was 90.9%. Based on the high negative predictive value with the modest positive predictive value, the cuff leak test is a better predictor to exclude postextubation stridor than to forecast the emergence of stridor. The presence of a large leak volume suggests that extubation is likely to be successful. However, a positive cuff leak test result cannot be used to exclude extubation, because this would lead to unnecessarily prolonged intubation or tracheostomy. Even though our sample sizes were small, our study objectively demonstrated a significant increase in the leak volume after steroid treatment in those patients who were reintubated because of postextubation stridor. Therefore, a cuff leak test is not only useful for identifying the risk of postextubation stridor, but it is also helpful for evaluating improvement in airway injury after steroid treatment.

Several mechanisms are thought to predispose to postextubation stridor, including prolonged duration of intubation, insufficient fixation of the tube, irritation from tracheal or oral aspiration during daily
nursing care, disease severity, self-extubation, and reintubation.\(^{(12,26)}\) In our study, a lower leak volume and female gender were the two risk factors associated with postextubation stridor. Several studies have also stressed that female gender is a risk factor for this complication.\(^{(5,24,27)}\) It is presumed that the smaller diameter of the female larynx relative to the endotracheal tube and a thinner vocal process mucosa make women more prone to injury.\(^{(27,28)}\) No other predisposing factors were evident.

The major limitation of our study was the small number of patients. Although a total 110 subjects were enrolled for study, only 20 patients eventually developed postextubation stridor which fulfilled the major criteria for our study goal. Therefore the statistical power may not have been adequate. In addition, because there was no placebo group. Therefore, although 9 patients recovered without reintubation after corticosteroid administration, we could not determine whether this occurred because of spontaneous regression of stridor or from the steroid effect. Further case-control study including a larger number of patients is necessary to verify our results.

In summary, our study demonstrates that corticosteroids are effective in the treatment of patients with postextubation stridor. The cuff leak test is a useful tool to predict the occurrence of stridor and to monitor the effects of steroid treatment in reintubated patients. In light of the high incidence of respiratory failure following postextubation stridor, we recommend prophylactic administration of corticosteroids to patients with a small or no leak volume before extubation.

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REFERENCES


氣囊漏氣測試在使用類固醇治療拔管後哮喘的角色

王智亮 1 蔡煒烱 1,4 黃崇祥 1,4 李耀光 1 葉明珠 2 周秀粼 2 徐士宸 2 林孟志 3,4,5

背景：氣管內插管會造成喉頭不同程度的損傷及腫脹，導致日後拔管發生哮喘。此為拔管失敗的一個重要原因。目前研究顯示，拔管前預防性使用類固醇並不能減少哮喘發生，而且也沒有有關拔管後發生哮喘的標準治療方法。氣囊漏氣試驗是一個簡單、非侵襲性測試，其能間接反映出咽喉部位腫脹的程度。我們假設類固醇可以減輕喉部局部發炎腫脹，對拔管後發生哮喘的病患施予類固醇治療，並使用氣囊漏氣試驗來檢證類固醇的療效。

方法：我們進行一項前瞻性研究，針對110位內科加護病房插管病患，統計拔管後發生哮喘機率及危險因子，並使用類固醇治療拔管後哮喘。利用氣囊漏氣試驗來追蹤拔管後發生哮喘的病人在接收類固醇治療前後，呼吸器漏氣量的變化來監測咽喉水腫改善的程度。

結果：有20個病人發生哮喘（18.2%），經類固醇治療後有9人哮喘逐漸改善。11個需再次插管的病患中，有7人經類固醇治療後成功拔管不再發生哮喘。整體而言，類固醇對拔管後發生哮喘的治療成功率為80%；對因哮喘而再次拔管的病人，其治療率為64%。氣囊漏氣試驗顯示在類固醇治療後，呼吸器漏氣量在統計學上有顯著增加（治療後152.4 ± 109.6 ml vs. 治療前29.9 ± 35.7 ml, p = 0.012）。女性和低漏氣量（本實驗的閾值為88 ml；陽性預測率為54.5%，陰性預測率為90.9%）為拔管後發生哮喘的高危險因子。插管時間長短、有無插管病史及血液白蛋白數值高低與拔管後哮喘發生無關。

結論：類固醇能治療因插管引起的喉頭水腫所造成的拔管後哮喘。氣囊漏氣試驗可以用來預測拔管後哮喘是否發生，並能監測類固醇治療喉頭腫脹的療效。
(長庚醫誌 2007;30:53-61)

關鍵詞：拔管後哮喘，咽喉水腫，氣管插管，皮質性類固醇，拔管失敗，氣囊漏氣試驗。