Diagnostic Study

Gargle test for successful extubation in critically ill patients underwent head and neck surgeries: A new test

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A R T I C L E   I N F O

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A B S T R A C T

Background: Improvement of predictive tools for recognition of airway edema is crucial for safe extubation and patient safety. This study aimed to evaluate the diagnostic accuracy of the Gargle test (GT) as a new test for assessing airway edema and predicting successful extubation in patients admitted to the intensive care unit (ICU).

Method: In this prospective observational study, patients underwent head and neck surgeries and admitted to ICU included. All the patients were weaned based on the same protocol. Quantitative Cuff Leak Test (CLT) and qualitative CLT were first applied followed by GT with normal saline 0.9%. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy were calculated.

Results: One hundred and eighteen (male 67, female 51) participated in this study. The agreement between GT and CLT was low (Kappa: quantitative CLT 0.07, qualitative CLT 0.21). The GT compared to CLT had higher sensitivity (33.3% vs 16.6%), specificity (96.3% vs qualitative CLT 92.8%, quantitative CLT 79.4%), PPV (33.3% vs qualitative CLT 11.11%, quantitative CLT 4.0%), NPV (96.3% vs qualitative CLT 95.4%, quantitative CLT 94.6%), and accuracy (92.92% vs qualitative CLT 88.98%, quantitative CLT 76.27%). The cut-off value for GT was estimated 16.5% (sensitivity 74.1% and specificity 60%).

Conclusion: The GT is a simple accurate test and can be used as a new test in the ICU for recognition of airway edema and prediction of safe extubation in patients with head and neck surgeries.

1. Introduction

The decision to extubate the patients in the intensive care unit (ICU) is critical and challenging. On the one hand, delay in removing endotracheal tubes is associated with increased stay in ICU and associated risks of invasive mechanical ventilation [1]. On the other hand, inappropriate decisions to extubate the patient with anatomical problems, trauma, head and neck surgeries, restricted mouth opening, and limited neck range of motion can result in difficult intubation, which eventually can be life-threatening [2]. According to studies, laryngeal edema affects 0.6–36.8% of patients, re-intubation affects up to 80% of patients [3], mortality affects 30–40% of patients, and difficult extubation causes increased pulmonary problems [4]. The high risk of stridor after extubation has been shown associated with vocal cord dysfunction or laryngeal edema, reduced tracheal cross-sectional area, different study populations, female gender, endotracheal tube size, and duration of intubation [3–7]. Thus, improving predictive tools and recognizing airway edema is crucial for safe extubation. It is necessary to predict if the patient can tolerate extubation and whether the reintubation is still possible [8–10].

Improving assessment methods is necessary for patient safety because it allows the intensivist to make a more accurate assessment and more appropriate decision for extubation in difficult scenarios [9,10]. Therefore, physicians attempts to employ more reliable techniques for airway assessment. Some techniques available include quantitative/ qualitative cuff leak test (CLT) [7], tracheal ultrasound [11], optic fibroscopy, direct laryngoscopy examination, video laryngoscopy [12, 13], and flow-volume curves for extra-thoracic stenosis [14].

The tongue and pharyngeal edema can be easily evaluated via direct laryngoscopy, however the assessment of laryngeal edema and its
severity in the presence of an endotracheal tube is challenging. Opti-
mally, the test should be used just before extubation for every patient [6, 14]. The assessment methods have limitations, as they require equipment, examiner skills, and are associated with limited accuracy or necessitate tube removal [8,13].

The cuff leak test (CLT) is a simple test for predicting the presence of laryngeal edema. However, factors such as tube-to-trachea size ratio, pulmonary mechanics, and rate of airflow can all affect the outcome [5, 15]. The CLT has high specificity but low sensitivity for post-extubation airway obstruction. As a result, significant false-negative suggests that the CLT may miss certain patients with post-extubation airway obstruction [16].

Gargle is washing the mouth and throat by filling the mouth with a liquid, tipping the head back and using the throat to blow bubbles of the liquid with a gargling sound, and finally spitting it out [17]. Gargling in an intubated patient seems impossible. But, we found that during the performance of the leak test with the absence of laryngeal edema, the air moves from lung to mouth and around the tube after deflating the balloon cuff of the endotracheal tube; we accidentally noticed that some patients could gargle their secretions and have reasonable control and function of their laryngeal muscles. This inspired us to assess gargling as a new test. Thus, this study was conducted to evaluate the diagnostic accuracy of the Gargle test (GT) for the assessment of airway edema and prediction of successful extubation in the patients who underwent head and neck surgeries.

2. Method

2.1. Study population and setting

This study was reviewed and approved by the University Ethics Committee (IR.TUMS.IKHC.REC. 1396.2004), and written informed consent was obtained from all participants or their relatives. In a prospective observational study, 210 intubated patients were admitted to the ICU, and 118 were eligible. They had undergone head and neck surgeries and admitted to general and surgical ICU in the tertiary mega-hospital of Imam Khomeini at Tehran University of Medical Sciences, Tehran, Iran.

Inclusion criteria were: 1) intubated patients with confirmed airway edema by positive cuff leak test on admission time, 2) age > 18 years, and 3) mechanical ventilation support for at least 12 h.

Exclusion criteria was the impossibility of extubation due to reasons other than airway edema (e.g. pneumonia or other reasons that prohibited ventilator weaning).

2.2. Weaning and airway assessment

Airway management and monitoring of the mechanical ventilation in the ICU were accomplished under supervision of an intensivist. All the patients had endotracheal tubes with low pressure-high volume cuffs (Well Lead Medical Co., China), and cuff pressure was monitored and maintained at less than 25 cmH2o every 4 h (Covidien Co., Germany). Weaning the patients from the ventilator was based on a same protocol utilizing pressure support ventilation (PSV) mode. Once the patient met all the criteria of ventilator weaning (Pressure Support = 6–8 cmH2o, Positive End Expiratory Pressure = 4 cmH2o, FiO2 ≤ 0.4 for 1–2 h, without tachycardia and tachypnea, no diaphoresis and reduction of Spo2), the decision for extubation was made by employing CLT. Patients were given the essential explanations to mentally prepare them, improve their cooperation, and obtain their consent. Whenever necessary, an appropriate dose of an opioid was applied to enhance the patient’s comfort and tolerance to the endotracheal tube. Initially, quantitative and qualitative CLT were done. Subsequently, gargling with normal saline 0.9% was implemented. None of the patients were on corticosteroid drugs.

Quantitative CLT: The patient was placed in a sitting position after suctioning of oral and tracheal secretions. The assist control ventilation mode, with 6–8 ml/kg tidal volume was assigned for 2 min. The average exhaled tidal volume was recorded over the next five respiratory cycles before and after cuff deflation. A difference of more than 15% in the mean tidal volume was associated with the absence of airway edema and warranted the removal of the tube [14].

Qualitative CLT: First, the patient was weaned from the ventilator. Then, the oral and tracheal secretions were suctioned. Subsequently, the patient was placed in a sitting position and the endotracheal cuff was deflated. Next, the opening of the endotracheal tube was blocked, and the patient was asked to breathe through the mouth. It was deemed an appropriate test if the patient could perform five respiratory cycles without any sign of suffocation or evidence of airway obstruction.

Gargle Test (GT): Like the qualitative CLT method, the patient was weaned from the ventilator and was in a sitting position. After performing oral and tracheal suction, the patient did a relatively deep inspiration and held his/her breath. Then, concurrent with breath-hold, the endotracheal tube was occluded, and about 3–5 ml of normal saline 0.9% was put in the patient’s mouth. The patient was asked to gargle water at the back of his mouth with long and slow exhalation. This indicated an appropriate air leak (volume, flow, and power) around the tube. Also, it indicated the patient’s ability to maintain the airway patency and prevent aspiration. Finally, the patient was asked to lean forward and spit the water out in a dish.

The decision for extubation was based on the result of CLT. Another anesthesiologist who performed all the tests allowed the extubation. The investigator was blinded to the result of the GT and just recorded the data immediately after extubation, such as stridor, dyspnea, and the patient’s ability to talk. The need for early reintubation in the next 12 h due to respiratory distress caused by airway edema and stridor was defined as the extubation failure.

Age, gender, type of the surgery, duration of anesthesia and surgery, comorbidities, duration of mechanical ventilation (from initiation of anesthesia to extubation), type of intubation, success or failure of extubation, and results of quantitative as well as qualitative CLT, and GT were documented.

2.3. Statistical analysis

The kappa coefficient (with 95% confidence interval) were calculated to examine the agreement between GT and quantitative CLT/ qualitative CLT. Quantitative and categorical data were presented as mean ± standard deviation and frequency (%), respectively. An independent sample t-test was applied on continuous data to examine the differences between groups. Chi-square or Fisher exact test was used for differences on categorical variables and rate of extubation failure between groups with positive and negative tests results. P-value < 0.05 was set as significant. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy were calculated for the CLT and GT. The receiving operating characteristic (ROC) curve was used to identify the cut-off value of an acceptable leak for removing the endotracheal tube.

3. Results

Of 210 patients admitted to ICU, 118 patients who had undergone head and neck cancer surgeries (e.g. thyroidectomy, neck dissection, mandibullectomy, maxillectomy, and glossectomy) were enrolled in this study (Fig. 1). Sixty-seven patients (56.8%) were male and 51 patients (43.2%) were female, with a mean age of 54.7 ± 12.2. Due to surgical manipulations and anatomical problems in the hypopharynx and larynx, five patients could not perform the GT and therefore were excluded from data analysis. The demographic characteristics of the patients are depicted in Table 1.

Seventy-six patients (64.4%) were nasally intubated, while 42 (35.6%) were orally intubated. Six patients faced extubation failure due
to respiratory distress and stridor. Extubation failure was not statistically significant based on the quantitative CLT and qualitative CLT (P = 0.647, P = 0.385, respectively) (Table 2). However, extubation failure in patients with positive GT was significantly lower than in patients with negative GT (3.7% vs. 33.4% respectively, P = 0.032) (Table 2). The agreement between GT and qualitative CLT and quantitative CLT were low (K = 0.21, k = 0.07, respectively). The GT had higher sensitivity (33.3%), specificity (96.3%), PPV (33.3%), NPV(96.3%), and accuracy (92.92%) than the quantitative CLT and qualitative CLT (Table 3) for groups with extubation failure and without extubation failure.

According to receiving operating characteristic curve (ROC) analysis, cut-off value (Fig. 2) in GT was estimated 16.5% with sensitivity of 74.1%, and specificity of 60% [AUC (area under the curve) = 0.62, 95% CI: 0.38–0.87].

Fig. 1. Flowchart of study.
4. Discussion

The primary aim of this study was to introduce the GT as a new test for predicting extubation failure in people with head and neck surgery admitted to the ICU and examine the diagnostic accuracy of GT compared to the CLT. We found the GT has adequate sensitivity, specificity, PPV, NPV, and accuracy supporting it as a useful test for predicting extubation failure in patients with head and neck surgery. We believe the GT may represent a suitable test for detecting airway edema in the ICU setting as it is simple and easy to administer, thus easily detectable by physicians.

After extubation, laryngeal edema and reintubation incidents are associated with extended mechanical ventilation and increased morbidity in ICU patients [3]. Up to 20% of reintubation, 24–72 h after extubation, has been reported in the ICU setting [18]. Reintubation increases up to 47% in head and neck trauma after maxillofacial surgery and extensive neck injuries. On the one hand, difficult intubation, on the other hand, airway edema, critical conditions, and inappropriate measures can lead to irreversible damage and death [19,20]. Zhou et al. found that prolonged intubation could cause laryngeal edema after extubation [3].

The rate of post-extubation stridor, laryngeal edema, and efficacy of the leak test varies in different studies [5,21,22]. Unlike Miller’s [21] and Jaber’s [22] studies, our study showed low sensitivity and PPV for CLT, but in line with them, specificity and NPV were high. Low PPV in our study was consistent with De Bast’s [14] study. Although PPV was higher in the GT, it was generally low in all three tests; PPV of quantitative CLT, qualitative CLT, and GT were 4%, 11.11%, and 33.3%, respectively. In other words, when these tests indicate the presence of laryngeal edema, it does not necessarily mean that patient’s extubation will be unsuccessful.

Essentially, evaluation of laryngeal edema and its severity in the presence of an endotracheal tube is difficult. Current tests have significant false results, and it is thus impossible to have a definitive prediction before removing the tube. Furthermore, it has been demonstrated that several measurements done by different individuals may not be consistent in identifying the extent of the edema [6]. In our study, all sensitivity, specificity, PPV, NPV, and accuracy, were better in the GT compared to CLT. High accuracy, NPV, and specificity (92.92%, 96.3%, 96.3%, respectively) of the GT indicates that it is more effective in

### Table 1
Demographic characteristics of patients.

| Variable       | Mean ± SD |
|----------------|-----------|
| Age, year      | 54.7 ± 12.2 |
| Weight, kg     | 70.8 ± 12.4 |
| Height, cm     | 169.3 ± 8.3 |
| BMI            | 24.6 ± 3.1 |
| ICU stay, day  | 3.1 ± 1.1  |
| **MV duration, hour** | 28 ± 19.1 |
| Surgery duration, hour | 5.8 ± 1.9 |
| **Weaning time, hour** | 16.9 ± 19.2 |

SD, standard deviation; BMI: body mass index; **MV: mechanical ventilation.

Duration of mechanical ventilation from anesthesia until extubation time. **Weaning time: time of ventilator. Discontinuation from admission in intensive care unit.

### Table 2
Comparison of extubation failure based on Quantitative/qualitative Cuff Leak Test (CLT) and Gargle Test results.

| Test                | Extubation failure | P value |
|---------------------|--------------------|---------|
|                     | Yes    | No     |         |
| Quantitative CLT (%)|        |        | 0.647   |
| ≤ 15% (positive)    | 1 (4.3) | 22 (95.7) |
| > 15% (negative)    | 5 (5.6) | 85 (94.4) |
| Qualitative CLT     | 0.385              |
| positive            | 1 (11.1) | 8 (88.9) |
| negative            | 5 (4.8)  | 99 (95.2) |
| Gargle test         | 0.032              |
| positive            | 2 (33.3) | 4 (66.7)  |
| negative            | 4 (3.7)  | 103 (96.3) |

Fisher’s Exact Test, CLT: cuff leak test.
Positive: laryngeal edema, Negative: No laryngeal edema.

### Table 3
Comparison of sensitivity, specificity, PPV, NPV and accuracy between qualitative/quantitative CLT and Gargle Test.

| Test                | Extubation failure | Sensitivity | Specificity | PPV | NPV | Accuracy |
|---------------------|--------------------|-------------|-------------|-----|-----|----------|
|                     | Yes    | No     |            |     |     |          |
| Quantitative CLT, % |        |        |             |     |     |          |
| ≤ 15% (positive)    | 1 (4.3) | 22 (95.7) | 16.6%      | 79.4% | 4%  | 94.6%    | 76.27%    |
| > 15% (negative)    | 5 (5.6) | 85 (94.4) |             |     |     |          |
| Qualitative CLT, %  |        |        |             |     |     |          |
| positive            | 1 (11.1) | 8 (88.9) | 16.6%      | 92.8% | 11.11% | 95.4%    | 88.98%    |
| negative            | 5 (4.8)  | 99 (95.2) |             |     |     |          |
| Gargle, %           |        |        |             |     |     |          |
| positive            | 2 (33.3) | 4 (66.7)  | 33.3%      | 96.3% | 33.3% | 96.3%    | 92.92%    |
| negative            | 4 (3.7)  | 103 (96.3) |             |     |     |          |

CLT: cuff leak test, PPV: positive predictive value, NPV: negative predictive value.
Positive = laryngeal edema, negative = No laryngeal edema.

![ROC Curve](image-url) Fig. 2. The best cut off value of GT for extubation (16.5%, sensitivity 74.1%, specificity of 60% (point A).
detecting airway edema.

Creating air bubbles during gargling requires the proper function of the laryngeal muscles and the prevention of aspiration. Without these, the patient cannot perform this maneuver. In contrast to the CLT, during gargling, the function of the nerves and muscles of the larynx and hypopharynx are practically evaluated. Prinianakis et al. [5] demonstrated that CLT was associated with lower efficacy in critically ill patients who have undergone mechanical ventilation for at least 48 h after surgery.

The use of CLT in selective patients has been shown higher than in non-selective patients [7]. CLT, regardless of measuring absolute volume or expiratory volume percentage, is a weak predictor for diagnosing airway edema and extubation. The CLT is not a reliable indicator for postponing extubation or initiation of specific treatments [15]. All tests have specific particular limitations. Imaging techniques such as plain cervical radiography [10,21], computed tomography (CT) scan, and Magnetic resonance imaging (MRI) can capture upper airway edema. However, they are expensive, are associated with technical limitations, and cannot be used routinely in clinical practice [1-4]. Studies found that the CLT and the laryngeal ultrasound both have low sensitivity and PPV in the prediction of stridor [11,23]. Thus, new accurate measures to detect airway edema are imperative.

The Gargle test has some advantages. With the GT, the patients can actively and consciously perform the tests and use their muscles, which indicates healthy neuromuscular function. It also evaluates the possibility of airway edema.

There are, however, several limitations to the GT. First, the physicians should provide patients with explanations about the maneuver, and the patient should be able to cooperate with the physician. Therefore, if the patients are unable to communicate due to medical conditions such as dementia, they might be unable to perform the maneuver [24]. Also, due to surgical manipulations in larynx surgeries, the functions of patients’ muscles might be inappropriate, and the patients might not be able to perform the test [25]. Good function and movement of hypopharynx and larynx muscles are needed to avoid aspiration and gargling sounds.

5. Conclusion

The GT is a simple, easy to apply and interpret test. We hope that this new simple test along with the sound diagnostic accuracy will prove it to be a useful test in the evaluation of patients in the ICU setting for safe extubation. Further study on the usefulness of the GT in the ICU with patients of various pathologies are warranted.

Ethical approval

This study protocol was approved by the Tehran University of Medical Sciences Research Ethics Committee (Approval number: (IR. TUMS.IKHC.REC.1396.2004).

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Author contribution

All authors were involved in designing study, data collection, data analysis, and preparing the manuscript. All authors have read and approved the final version of the manuscript.

Registration of research studies

1. Name of the registry:
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3. Hyperlink to your specific registration (must be publicly accessible and will be checked):

Guarantor

Mohammad Taghi Beigmohammadi.

Consent

Written informed consent was obtained from all the participants.

Declaration of competing interest

None authors are to be declared.

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Abbreviations

CLT cuff leak test
GT gargle test
ICU intensive care unit
PPV positive predictive value
NPV negative predictive value
PSV pressure support ventilation
AUC area under the curve
ROC receiving operating characteristic curve
CT computed tomography
MRI magnetic resonance imaging

References

[1] C.S. Tu, C.H. Chang, S.C. Chang, C.S. Lee, C.T. Chang, A decision for predicting successful extubation of patients in intensive care unit, BioMed Res. Int. 11 (2018) 1–18.
[2] A.B. Patel, C. Ani, C. Feeney, Cuff leak test and laryngeal survey for predicting post-extubation stridor, Indian J. Anaesth. 59 (2015) 96–102.
[3] T. Zhou, H.P. Zhang, W.W. Chen, et al., Cuff-leak test for predicting postextubation airway complications: a systematic review, J. Evid. Base Med. 4 (2011) 242–254.
[4] R.S. Sandhu, M.D. Pasquale, K. Miller, T.E. Wasser, Measurement of endotracheal tube cuff leak to predict postextubation stridor and need for reintubation, J. Am. Coll. Surg. 190 (2000) 682–687.
[5] G. Prinianakis, C. Alexopoulou, E. Mamidakis, E. Kondili, D. Georgopoulos, Determinants of the cuff-leak test: a physiological study, Crit. Care 9 (2005) R24–R31.
[6] L.F. Cavallone, A. Vannucci, Exubation of the difficult airway and extubation failure, Anesth. Analg. 116 (2) (2013) 368–383.
[7] D. De Backer, The cuff-leak test: what are we measuring? Crit. Care 1 (2004) 1–3.
[8] S. Epstein, Decision to extubate, Intensive Care Med. 28 (5) (2002) 535–546.
[9] C.H. Lee, M.J. Peng, C.L. Wu, Dexamethasone to prevent postextubation airway obstruction in adults: a prospective, randomized, double-blind, placebo-controlled study, Crit. Care 11 (2007) R72–R79.
[10] Y.H. Chung, T.Y. Chao, C.T. Chiu, et al., The cuff-leak test is a simple tool to verify severe laryngeal edema in patients undergoing long-term mechanical ventilation, Crit. Care Med. 34 (2006) 409–414.
[11] L.W. Ding, H.C. Wang, H.D. Wu, C.J. Chang, P.C. Yang, Laryngeal ultrasound: a useful method in predicting post-extubation stridor. A pilot study, Eur. Respir. J. 27 (2) (2006) 384–389.
[12] M. Popat, V. Mitchell, R. Dravid, A. Patel, C. Swamplilai, A. Higgs, Difficult airway society extubation guidelines group. Difficult airway society guidelines for the management of tracheal extubation, Anaesthesia 67 (3) (2012) 318–320.
[13] J.L. Newmark, Y.K. Ahn, M.C. Adams, E.A. Bitter, S.R. Wilcox, Use of video laryngoscopy and camera phones to communicate progression of laryngeal edema in assessing for extubation: a case series, J. Intensive Care Med. 1 (2013) 67–71.
[14] Y. De Basta, D. De Backer, J.I. Moraine, M. Lemaire, C. Vandenborgh, J.L. Vincent, The cuff leak test to predict failure of tracheal extubation for laryngeal edema, Intensive Care Med. 28 (2002) 1267–1272.
[15] E.J. Kriner, S. Shafazand, G.L. Colice, The endotracheal tube cuff-leak test as a predictor for postextubation stridor, Respir. Care 50 (2005) 1632–1638.
[16] A. Kurtiyama, J.L. Jackson, L. Kamei, Performance of the cuff leak test in adults in predicting post-extubation airway complications: a systematic review and meta-analysis, Crit. Care 24 (2020) 640.
[17] Gargle definition and meaning, collins English dictionary. (Available from:).

[18] S. Karmarkar, S. Vardhaney, Tracheal extubation, Cont. Educ. Anaesth. Crit. Care 8 (6) (2008) 214–220.

[19] A.P. Kulkarni, V. Agarwal, Extubation failure in intensive care unit: predictors and management, Indian J. Crit. Care Med. 12 (1) (2008) 1–9.

[20] A. Schmutz, R. Dieterich, J. Kalbhenn, F. Voss, T. Loop, S. Heinrich, Protocol based evaluation for feasibility of extubation compared to clinical scoring systems after major oral cancer surgery safely reduces the need for tracheostomy: a retrospective cohort study, BMC Anesthesiol. 18 (1) (2018) 43.

[21] R.L. Miller, R.P. Cole, Association between reduced cuff leak volume and postextubation stridor, Chest 110 (1996) 1035–1040.

[22] S. Jaber, G. Chanques, S. Matecki, M. Ramonatxo, C. Vergne, B. Souche, P. F. Perrigault, J.J. Eledjam, Post-extubation stridor in intensive care unit patients, Intensive Care Med. 29 (1) (2003) 69–74.

[23] H. Mikaeili, M. Yazdehi, M.K. Tarzamni, K. Ansarin, M. Ghasemzadeh, Laryngeal ultrasonography versus cuff leak test in predicting postextubation stridor, J. Cardiovasc. Thorac. Res. 6 (1) (2014) 25.

[24] P.L. Manfredi, B. Breuer, D.E. Meier, L. Libow, Pain assessment in elderly patients with severe dementia, J. Pain Symptom Manag. 25 (1) (2003) 48–52.

[25] E.N. Myers, K.H. Hong, Y.K. Kim, Phonatory characteristics of patients undergoing thyroidectomy without laryngeal nerve injury, Otolaryngology-Head Neck Surg. (Tokyo) 117 (4) (1997) 399–404.