Comparison of "cough peak expiratory flow measurement" and "cough strength measurement using the white card test" in extubation success: A randomized controlled trial

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Background: Failed extubation and subsequent re-intubation in ventilated patients can lead to many adverse consequences, including organizational and personal expenditures. Extubation decisions based on subjective methods are a major contributor to extubation failure. This study compared the effect of cough peak expiratory flow (PEF) measurement and cough strength measurement using the white card test (WCT) on extubation success. **Materials and Methods:** This randomized clinical trial was conducted in two groups in 2018 on 88 ventilated patients in intensive care units of Imam Reza Hospital in Mashhad, Iran. Ninety patients were divided into two groups of 45, but two were excluded from the white card group. The criteria established for extubation included PEF ≥60 L/min during coughing in the cough PEF group and noticing card humidity in the WCT group. In both groups, extubation success was determined as the sole outcome and was compared with the standard PEF and cough strength. The researcher who assessed the outcome and statistician were blinded about group allocation. **Results:** Extubation success was measured as 97.8% in the cough PEF group and 76.7% in the WCT group ($P = 0.003$) during the first 24 h. In the second 24 h, however, successful extubation was reported as 90.9% in the cough PEF group and 60.6% in the WCT group ($P = 0.002$). **Conclusion:** Using the cough PEF rate increases the likelihood of extubation success and reduces adverse effects, and is recommended to be used for extubation decision-making.

Key words: Cough peak expiratory flow, effective cough, extubation, ventilator weaning, white card test

INTRODUCTION

Intubation in patients with inadequate oxygenation/ventilation is among the most common medical emergencies.[1,2] Although lifesaving at first, prolonged mechanical ventilation (MV) has some adverse outcomes; therefore, patients should be extubated as soon as possible and be able to breathe independently.[1,3] It is worth noting that both early and delayed extubation can increase the complications.[4]

Unsuccessful extubation or need for re-intubation has been reported as 2%–25% in intensive care unit (ICU) patients[5] and can lead to 2.5–10 times higher mortality than in patients with successful extubation.[6-8] Researchers' attention has, therefore, turned to identifying the best predictors of a successful extubation.[9] One of the most important factors in extubation decision-making is effective coughing.[10] An effective cough demonstrates the patient's airway protection ability.[11]

Cough ability and strength are commonly measured by nurses' direct observation or using the white card

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test (WCT). If secretions were propelled onto the card, it was termed a positive WCT. Some studies have suggested that the WCT is reliable.[12,13] Nonetheless, such methods are error prone and less quantitative.[14] Accordingly, other approaches are recommended to prevent the inherent challenges of the previously mentioned methods, for example, cough peak expiratory flow (CPEF) measurement. Measuring CPEF during MV weaning has been reported as a metric for predicting successful extubation in some studies.[15] However, in our comprehensive search of literature, no studies have been found that had compared the rate of success after extubation decisions based on the WCT with objective methods, such as CPEF measurement. Due to the variety of methods available to improve the rate of successful extubation, the present study was conducted to compare the effect of these methods on the rate of successful extubation.

METHODS

Design and population

This two-group clinical trial was performed on ninety patients admitted to the ICU setting of Imam Reza Hospital in Mashhad, Iran. The patients who met the inclusion criteria were selected based on nonprobability convenience sampling and were then randomly assigned to the intervention (CPEF) and WCT groups using a randomized sequence generated by www.randomization.com. To conceal the allocation sequence, closed envelopes were used; the said sequence was written down on small pieces of paper and kept in envelopes. Then, when a new participant entered the study, the envelope would be opened, and the participant would be assigned to the relevant group based on the code written on the first piece of paper. A research assistant was in charge of allocating the participants to the two groups and carrying out the statistical analysis, but the implementation of the intervention and the measurement of the outcomes were carried out by one of the researchers, as blinding the researchers to the intervention was not possible.

Inclusion and exclusion criteria

The inclusion criteria were as follows: consciousness (score-1-1 based on the Richmond Agitation-Sedation Scale/RASS), age 18–60 years, success in the Spontaneous Breathing Trial, being on MV for at least 24 h, and judged to be ready for extubation by their attending physician.

The study exclusion criteria consisted of the patient's inability to breathe spontaneously, need for frequent suctioning, and inability to cough.

Sample size

The sample size was estimated as 42 per group based on the results of a pilot study on ten participants from each

of the study groups using the formula for comparing two population proportions ($n = [Z_{1-a/2} + Z_{1-b}] \, p_1 \, [1 - p_1] \times p_2 \, [1 - p_2]/[p_1 - p_2]^2$), with a confidence coefficient of 95% and test power of 80% for the outcome being "successful extubation" (0.59 in CPEF vs. 0.30 in WCT). However, 45 eligible patients were enrolled in each group to take participant attrition into account.

Instruments

The tools used in this study included the RASS for assessing the level of consciousness, the Nursing Delirium Screening Scale (Nu-DESC) to assess delirium, the APACHE II checklist to assess the severity of the disease, and finally a researcher-made demographic questionnaire.

The RASS is a standard tool with confirmed validity and reliability as per previous studies.[16] This tool contains only ten items, each of which represents one of the levels of consciousness (from "combative" to "deep sedation" and "unarousable sedation"). To determine the RASS score, the patient is first merely observed without any interactions, and if he is alert, a score from 0 to 4 is given to him; if the patient is not alert, his name will be called out loud and he will be asked to look at the researcher; this step can be repeated if necessary. If the patient reacts to this voice, he will receive a score from −3 to −1. If he lacks reactions completely, he will receive a score from −5 to −4.

The Nu-DESC assesses five areas, including disorientation, inappropriate behavior, inappropriate communication, illusions or hallucinations, and psychomotor retardation. Symptoms are rated from 0 to 2 based on their presence and intensity, and the individual ratings are added to obtain the total score of each area. The validity and reliability of this tool have been confirmed in previous studies.[17]

The APACHE II consists of three sections. The first section assesses 13 physiological parameters, including temperature, mean arterial pressure, heart rate, respiratory rate, $AaDO_2$ or PaO_2, pH arterial, serum sodium, serum potassium, creatinine, hematocrit, white blood cell count, sodium bicarbonate, and Glasgow Coma Scale (GCS). The first 12 physiological parameters are scored from 0 to 4. The standard scoring for the GCS is performed this way: for a normal state, the patient receives a score of 15, and each point below the normal level adds a point to the severity of the disease. The second (adjustment of age) and third (adjustment of the underlying chronic diseases) sections of the APACHE II were scored based on the relevant classifications in the standard checklist. The total score of these three sections forms the APACHE score of the patient in the first 24 h after hospital admission, with 0 indicating "no severe disease" and 71 indicating "maximum disease

severity." The validity and reliability of this tool have also been confirmed in previous studies.[18]

Data collection
After the attending physician declared the patients ready for extubation, the patients of CPEF group were connected to Bellavista 1000 e (IMT Medical, Switzerland) in the pressure support ventilation (PSV) mode (positive end-expiratory pressure = 5, PSV = 5), and were asked to cough three times, consecutively; then the CPEF was measured for these three coughs, and if the flow was >60, the patient would be extubated. This threshold was chosen according to a previously published study.[19] In the WCT group, with the white card placed 1–2 cm away from the tracheal tube, the patients would cough three consecutive times, and if moisture was observed on the card, it would be considered an effective cough and the patients would be extubated.

To begin extubation, the suction of the oral cavity and the tracheal secretions was performed after the cough strength was confirmed. The cuff of the endotracheal tube was then depleted, and the patient was asked to take a deep breath during the removal of the endotracheal tube. The endotracheal tube was then removed. The oral cavity was then suctioned again, and oxygen therapy was administered after the extubation.

The patients were evaluated in both groups in terms of extubation success as the only outcome of this study after 24 h and 48 h. The extubation was considered unsuccessful, and the patient was re-intubated based on the following criteria: sign of respiratory distress; decreased levels of consciousness; SaO_2 <90% (on FiO_2 >50%), PaO_2 <60 mmHg (FiO_2 >50%), or PaO_2/FiO_2 ratio <150; or any other signs of unstable hemodynamics and airway protection inability.

The hemodynamic status of the patients was carefully monitored at this interval to determine any variation in the patient's condition that requires re-intubation. Patients who had extubation failure within the first 24 h were excluded from both groups to prevent from selection bias.

Data were collected from April 21, 2018, to February 19, 2019, and included the implementation of the intervention, follow-up of the study patients, and performing the measurements.

Statistical analysis
Data were analyzed in SPSS (IBM SPSS Inc, Chicago, IL, USA) software, V.21. The Chi-squared test and the independent *t*-test (for the quantitative variables with normal distribution) and Mann–Whitney's test (for the quantitative variables without normal distribution) were used to compare the two groups in terms of background and confounding variables, so that the homogeneity of the two groups and the lack of effect of this factor on the research outcomes could be determined as the only confounding variable. A 95% confidence interval was taken as the level of statistical significance. As the study was cross-sectional and did not include a long-term follow-up, there were no missing data.

Ethics approval and consent to participate
This study was approved by the Ethics Committee of Mashhad University of Medical Sciences (code: IR.MUMS. REC.1397.013). The patients/their families were informed about the voluntary nature of their participation, the purpose of the study, and the confidentiality of their personal information. Written informed consents were obtained from all the participants or their families prior to entering the study.

RESULTS

Out of the ninety patients examined, two were excluded from the WCT group due to their lack of cooperation in coughing. Then, the final analysis was performed on 43 participants in the WCT group and 45 participants in the intervention group.

Characteristic data
The mean age of the patients was 34.9 ± 13 years in the CPEF group and 43.5 ± 10.2 years in the WCT group. In addition, 66.7% of the patients in the CPEF group and 55.8% of those in the WCT group were male. The mean duration of tracheal intubation before beginning of the study was 6.6 ± 4.0 days in the CPEF group and 8.0 ± 4.2 days in the WCT group. In terms of the level of consciousness based on RASS, the patients in both groups had a mean score of 0.2 ± 0.4. Table 1 presents the details of the patients' demographics.

Extubation success rate
The frequency of extubation success in the first 24 h ($P = 0.003$) and second 24 h ($P = 0.002$) was statistically significant in both groups based on the Chi-squared test. In addition, the results of McNemar's test suggested that the success of extubation in the second 24 h was not significantly different from the first 24 h ($P = 0.125$) in the intervention group; however, this difference was significant in the WCT group ($P < 0.001$). In other words, failed extubation in the second 24 h among patients with a successful extubation in the first 24 h was higher in the WCT group compared to the intervention group [Table 2 and Figure 1]. In addition, there were no threatening side effects related to the interventions in either of the groups.

Table 1: Demographic and baseline variables of the participants

Variable	Group		P
	CPEF (45)	WCT (43)	
Age (year), mean±SD	34.9±13	43.5±10.2	0.112*
Gender (%)			
Female	15 (33.3)	19 (44.2)	0.296
Male	30 (66.7)	24 (55.8)	
Body mass index (kg/m²), mean±SD	26.5±3.9	28.0±4.3	0.093**
Length of intubation (day), mean±SD	6.6±4.0	8.0±4.2	0.067*
Duration of ventilation before extubation (days), mean±SD	4.4±3.4	5.3±3.7	0.067*
Duration from weaning to extubation (h), mean±SD	2.2±0.8	2.5±0.9	0.073*
Tracheal tube diameter, mean±SD	7.7±0.3	7.8±0.3	0.483*
FiO_2 percent before extubation, mean±SD	34.3±4.5	35.8±4.9	0.094*
Duration of hospital stay (day), mean±SD	9.6±5.9	9.0±4.8	0.926*
Richmond Agitation-Sedation Scale score, mean±SD	0.2±0.4	0.2±0.4	0.908*
APACHE score, mean±SD	25.5±5.0	26.9±5.1	0.188**
Delirium score, mean±SD	0.1±0.1	0.0±0.0	0.087**
History of diabetes (percent), mean±SD	10 (22.2)	9 (20.9)	0.883***
History of hypertension (percent)	15 (33.3)	19 (44.2)	0.296***
Previous reintubation (percent)			
Once	15 (33.3)	19 (44.2)	0.295***
More than once	30 (66.7)	24 (55.8)	

*Mann–Whitney, **Independent *t*-test, ***χ^2. CPEF=Cough peak expiratory flow; WCT=White card test; SD=Standard deviation

Table 2: Frequency of the extubation success rate in the first and second 24 h in cough peak expiratory flow and white card test groups

Extubation success	Group, *n* (%) CI (95%)		P*
	CPEF	WCT	
The first 24 h			0.003
Successful	44 (97.8) 83.3-100.0	33 (76.7) 62.7-100.0	
Unsuccessful	1 (2.2) 0.0-5.11	10 (23.3) 14.3-32.3	
Total	45 (100.0)	43 (100.0)	
The second 24 h			0.002
Successful	40 (90.9) 83.3-100.0	20 (60.6) 47.0-74.3	
Unsuccessful	4 (9.1) 3.3-14.9	13 (39.4) 27.9-50.9	
Total	44 (100.0)	33 (100.0)	
McNemar test (P)	0.125	<0.001	

*Chi-square test. CPEF=Cough peak expiratory flow; WCT=White card test; CI=Confidence interval

DISCUSSION

The results of the study showed that extubation in the first 24 h and second 24 h was more successful in the CPEF
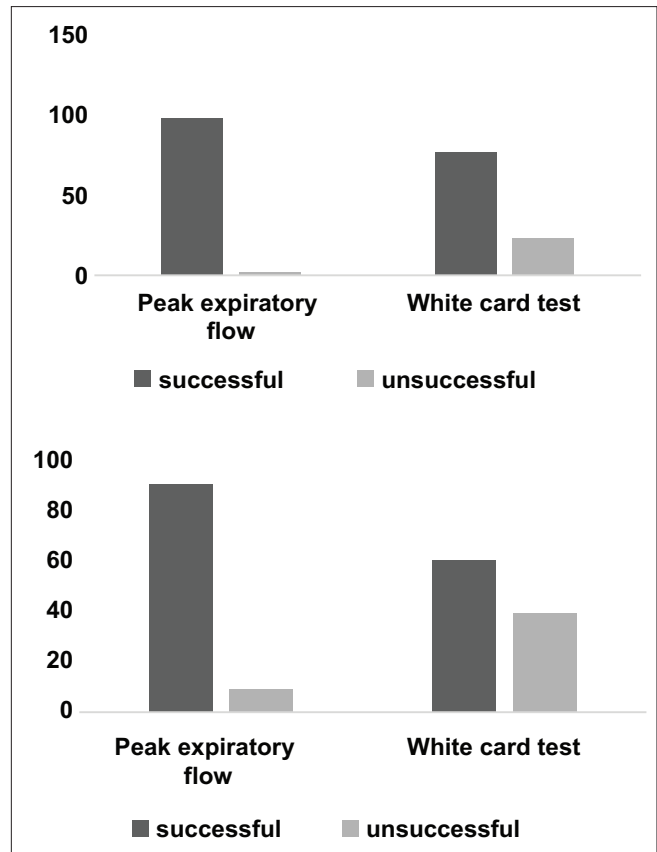

Figure 1: Percent of the extubation success rate in the first and second 24 h in cough peak expiratory flow and white card test groups

group compared to the WCT group. The exclusive outcome of this study lies in the design of the study, as the criteria for re-intubation were monitored at successive intervals and there was a 48-h follow-up, and this design was not observed in any similar studies.

In line with the present study, the results reported by Kutchak *et al.* demonstrated the efficacy of CPEF in extubation success.[1] Meanwhile, the rest of the results of the cited study indicated the effect of the GCS score on the rate of extubation success in patients. The odds of extubation success increased by 36% with a GCS score increment of one more than 8, which indicates the importance of controlling the confounding variables when measuring CPEF. The results of the present study and those of a previous ones propose CPEF as an efficient tool for the prediction of extubation; however, it should be noted that the patients' stable state of consciousness is a prerequisite for extubation decisions and patients with the recommended standard level of consciousness can be safely extubated. Otherwise, the level of consciousness should be regarded as a confounding variable, and one cannot solely rely on the cough severity measurement if the patient's level of consciousness is unstable. In the present study, the patients with a stable consciousness as

per the RASS (−1, +1) were extubated. It is imperative to train the medical staff on the importance of this issue and on how to use effective tools for assessing their patients' consciousness level.

The results of some studies suggest that the CPEF is reliable for the prediction of extubation success,[13,20-23] as in accordance with the present findings. Meanwhile, there were different CPEF thresholds in some of the studies. For example, in the study by Beuret *et al*. on 130 intubated patients, this threshold was measured as ≥35 CPEF thresholds for the prediction of extubation success.[14] This difference could be attributed to the study's lack of homogenization of disease severity in their study population, as their analysis included patients with disorders of consciousness, mental disorders, and chronic obstructive pulmonary disease. The present study, however, only included medical patients with similar APACHE scores in both groups.

The results of another study signified that successful extubation was mostly observed among patients with effective high-strength cough and, to a lesser extent, in patients with effective moderate-strength cough,[24] which is in line with the present findings. In the present study, the majority of the patients with successful extubation were those with effective high-strength cough, and a small number of the patients with successful extubation were below this level and had moderate-strength cough.

In a study with similar findings, the CPEF was calculated along with the tidal volume, and the same instrument (CPEF/Tidal Volume) was used for the patients' extubation. In the present study, however, the CPEF was measured over three consecutive coughs in both groups, and the patients were extubated based on their mean CPEF.[25]

Duan *et al*. also used the Semi-quantitative Cough Strength Score (SCSS) to predict extubation and found similar results. Their threshold for CPEF success was reported as 62.4 L/min.[21] The mean CPEF was estimated as 70.54 L/min in the present study. Furthermore, the patients in the present study received training on how to cough as forcefully as possible three times, and they were extubated if their mean cough was above 60 L/min. Whereas in the study by Duan *et al*., CPEF values during cough were calculated based on a relative rating of cough severity from 0 to 5.[21] It seems essential to train the patients to cough as forcefully as possible when calculating the maximum expiratory flow and making extubation decisions, because the aim is to investigate the highest severity of cough and assess the patients' airway protection ability and pulmonary excretion after extubation. Otherwise, the patients may not perform an effective cough when using a relative cough severity score (SCSS) tool, due to a lack

of understanding of the quality of the cough on a scale of 0 to 5 and be extubated.

Su *et al*. conducted a study on the effect of involuntary cough (stimulated by dripping 2 mL of normal saline into the endotracheal tube) on the output of patients in ICUs. Their findings on the reliability of the CPEF are consistent with the present findings.[23] Nonetheless, although judgment based on involuntary cough determines the severity of the cough, the patient's voluntary cough should be ensured prior to extubation, because one should consider not only the severity and quantity of the cough, but also its quality. If the patient does not cough voluntarily after extubation, the accumulation of secretions, air retention, atelectasis, and the need for re-intubation are definite possibilities.

Another finding of this study was the greater success of extubation in the maximal expiratory flow group in the second 24 h compared to the first 24 h. Therefore, there is an apparent need to monitor the criteria for re-intubation in these patients. Further studies are recommended to shed more light on this issue. The researchers recommend using the CPEF, as the application of this method can increase the odds of extubation success, resulting in the reduction of hospital stays, adverse effects of re-intubation, and organizational and personal expenditures.

Limitations
The lack of peak expiratory flow meter device for bedside measurement of expiratory flow in intubated patients was one of our limitations in this study, therefore we had to connect the patients to a special ventilator.

Suggestion for further studies
Assessing the extubation failure at shorter intervals (e.g., first 6, 12, and 18 h) or intervals longer than 48 h can be suggested for future studies.

CONCLUSION

Using the CPEF instead of the WCT can increase the probability of extubation success, resulting in the reduction of adverse effects, and is therefore recommended to be used for extubation decision-making. As the conditions of the ICU patients in this study are similar to those of patients hospitalized in the other general ICUs in many ways, the present findings can be generalized to other patient groups as well.

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Conflicts of interest

There are no conflicts of interest.

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