Association of Diaphragm Movement During Cough, as Assessed by Ultrasonography, With Extubation Outcome

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BACKGROUND: A cough peak flow (CPF) of < 60 L/min was associated with increased risk of extubation failure after a successful spontaneous breathing trial (SBT). Passive cephalic excursion of the diaphragm (PCED), measured by ultrasonography during cough expiration, was reported to predict CPF in healthy adults. We hypothesized that PCED, diaphragm peak velocity, or both during cough, as measured by ultrasonography, might predict CPF and extubation outcomes in mechanically ventilated patients. This study attempted to identify associations of diaphragm movement during cough, as assessed by ultrasonography with simultaneously measured CPF, and to determine predictive values of ultrasonographic indices for extubation outcomes after a successful SBT. METHODS: In the study, 252 mechanically ventilated subjects with a successful SBT were enrolled in a prospective cohort study. Right hemidiaphragm passive cephalic excursion and peak velocity were measured by ultrasonography during voluntary cough expiration with maximum effort. CPF was measured simultaneously by ultrasonography. RESULTS: A multiple regression model adjusted for age and sex showed a significant association between PCED and CPF ($P < .001$, adjusted β coefficient 11.4, 95% CI 8.88–14.0, adjusted $R^2 = 0.287$) and between diaphragm peak velocity and CPF ($P < .001$, adjusted β coefficient 1.71, 95% CI 1.91–2.24, adjusted $R^2 = 0.235$). The areas under the curves of PCED, diaphragm peak velocity, and CPF for extubation failure were 0.791 (95% Cl 0.668–0.914), 0.587 (95% Cl 0.426–0.748), and 0.765 (95% Cl 0.609–0.922), respectively. CONCLUSIONS: PCED on ultrasonography was significantly associated with CPF and extubation failure after a successful SBT. Future studies should investigate if this method is applicable for determination of tracheostomy decannulation in stable patients in general wards. *Key words: cough strength; diaphragm; ultrasonography extubation outcome.* [Respir Care 2021;66(11):1713–1719. © 2021 Daedalus Enterprises]

Introduction

Cough strength is important in clearing secretions and protecting the airway and thus in successful extubation.[1,2] Several parameters have been proposed for evaluating cough strength, including maximum expiratory pressure, cough gastric pressure, cough bladder pressure, and cough peak flow (CPF).[3-8] A CPF of < 60 L/min was associated with increased risk of extubation failure in patients with a successful spontaneous breathing trial (SBT).[8-10]

Cough strength is mainly determined by contraction of abdominal expiratory muscles, which can be evaluated by

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measuring intra-abdominal pressure (gastric pressure or bladder pressure) during cough.[4,7] The pressure gradient between the thoracoabdominal cavity and airway during cough generates air flow to the mouth as well as passive cephalic excursion of the diaphragm (PCED). For some patients, concern regarding cough strength is the only factor that prevents clinicians from extubating an endotracheal tube or decannulating tracheostomy, such as those who have a T-piece connected to the endotracheal tube or those with a tracheostomy tube without mechanical ventilation. Therefore, it is important to identify a method that allows clinicians to easily evaluate cough strength at the bedside, without the need for special devices such as a peak flow meter, which must be connected to the endotracheal tube or tracheostomy tube, or mechanical ventilators. We previously reported that PCED during the cough expiratory phase was significantly associated with CPF in healthy adults.[11] We hypothesized that PCED, peak velocity of the diaphragm, or both during the cough expiratory phase might predict CPF in patients with endotracheal tubes and that low PCED or peak velocity of the diaphragm might thus predict extubation failure. The aims of this study were to identify association of diaphragm movement during cough, as assessed by ultrasonography with simultaneously measured CPF, and to evaluate the predictive value of ultrasonographic indices for extubation outcomes after a successful SBT.

QUICK LOOK

Current knowledge

Evaluation of cough strength in patients who have passed an SBT is clinically important. Several parameters have been proposed for evaluating cough strength, including maximum expiratory pressure, cough gastric pressure, cough bladder pressure, and cough peak flow (CPF). Association of diaphragm movement during cough in mechanically ventilated patients with extubation outcome has not been investigated previously.

What this paper contributes to our knowledge

The present study shows that diaphragm excursion during the cough expiratory phase, as measured by ultrasonography, significantly predicted cough strength and extubation outcome.

Methods

Study Design

This single-center, prospective cohort study was approved by the institutional review board of Tokyo Bay Urayasu Ichikawa Medical Center. A waiver of informed consent was obtained because the study exposed patients to less than minimal risk.

Subjects

The study was performed in the medical-surgical ICU during the period from May 2017 through October 2018. All mechanically ventilated subjects 18 y or older who had been endotracheally intubated and had passed an SBT of longer than 30 min with a Richmond Agitation Sedation Scale score of −2 to 2 were eligible for inclusion. Sedation was interrupted in all subjects at 30–120 min before the SBT. The SBT was conducted on pressure-support ventilation with a pressure support 5 cm H_2O, a PEEP ≤ 8 cm H_2O, and a fraction of inspiratory oxygen F_{IO_2} ≤ 0.50. All subjects with a positive result on the Confusion Assessment Methods for the ICU (CAM-ICU) instrument were actively reoriented to the situation, and only those able to follow instructions to produce a voluntary cough were included. Patients with comfort care only or do not reintubate status were excluded. Patients at high risk for upper-airway obstruction, such as those with airway burn and inhalation injury and those with a positive cuff-leak test result, were also excluded. Each eligible subject was included in the analysis only once. The success of an SBT was determined by using the standard Tokyo Bay Urayasu Ichikawa Medical Center Respiratory Care Weaning Protocols (namely, no evidence of severe anxiety, dyspnea, or excessive accessory muscle use; a rapid shallow breathing index ≤ 105 breaths/min/L; and adequate gas exchange, ie., S_{aO_2} ≥ 90% with an F_{IO_2} ≤ 0.50 and PEEP ≤ 8 cm H_2O). If a subject had excessive secretion, extubation was postponed until secretion decreased to a degree that was acceptable for extubation, as determined by the clinicians in charge.

Observations and Measurements

Subjects in a supine position were instructed to produce 2 coughs with maximum effort within 10 min before extubation. A CX50 ultrasound device (Philips, Amsterdam, the Netherlands) was used to assess ultrasonographic indices of the diaphragm with a sector transducer (3.5 MHz). The transducer was positioned on the abdominal wall just below the lowest right rib, between the midaxillary line and mammillary line in the longitudinal scanning plane to the cephalic direction, with the liver as an acoustic window.[12-14] The angle of the transducer was adjusted so that the ultrasound beam was perpendicular to the posterior third of the right hemidiaphragm.[15] Because PCED and diaphragm peak velocity cannot be measured simultaneously, PCED was measured during the first cough, and diaphragm peak velocity was measured during the second cough. To measure PCED, the M-mode interrogation line was adjusted to ensure that it was perpendicular to the movement of the posterior one-third of the right hemidiaphragm.[11,14] PCED

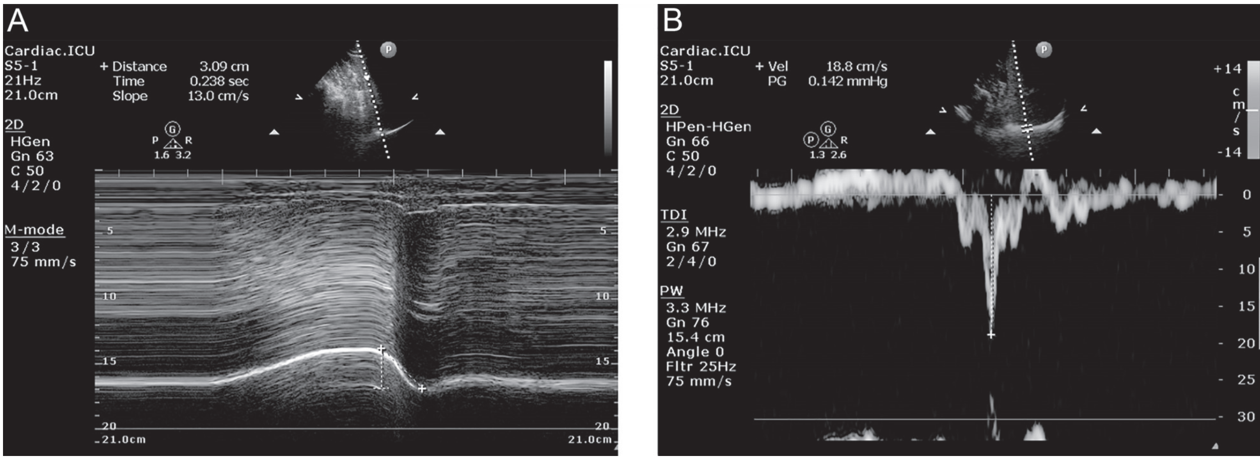

Fig. 1. M-mode ultrasonographic measurement of A: passive cephalic excursion of the diaphragm; and B: diaphragm peak velocity by tissue Doppler ultrasonography during the cough expiratory phase.

was measured on the vertical axis of the M-mode and was traced from the end of inspiration to the end of cough expiration. Peak velocity of the diaphragm was measured by placing the tissue Doppler imaging cursor at the posterior one-third of the right hemidiaphragm (Fig. 1).[11] Simultaneous measurement of CPF was performed for both coughs by using the internal flow meter of the ventilator (Puritan Bennett 840, Covidien, Mansfield, Massachusetts).[16] Four critical care fellows with at least 2 y experience in diaphragm ultrasonography performed the evaluations. Attending physicians who were responsible for clinical decisions, including extubation and re-intubation, were blinded to the results of all cough measurements.

Definitions of Extubation Success and Failure

Extubation failure was defined as re-intubation within 72 h after extubation. Use of prophylactic or therapeutic noninvasive positive-pressure ventilation without consequent re-intubation was not regarded as extubation failure.

Sample Size

The predicted extubation failure rates were 8% in all subjects and 5–6% in subjects who were able to follow instructions, as indicated by the past extubation failure rates in our ICU.[7] Thus, we estimated that the sample size needed to determine the cutoff value with an area under the curve (AUC) of 70% and a power of 0.8 would be 12 for the extubation failure group and 233 for the extubation success group.[17] We, therefore, planned to recruit 250 subjects for this study.

Statistical Analysis

A data analysis and statistical plan was written and posted on the publicly accessible Japanese server (UMIN Clinical Trials Registry) before data were accessed. The primary study outcome was extubation failure. Secondary outcomes included in-hospital mortality and hospital length of stay. Pearson coefficients were calculated to show correlations between variables. To determine whether ultrasonographic indices predicted CPF, we constructed regression models with CPF as the dependent variable and PCED and diaphragm peak velocity as independent variables. If a model showed a significant association between an independent variable and CPF, an adjusted regression model was constructed with age, sex, and height. A Bland-Altman plot was constructed to analyze agreement between measured and predicted CPF, as determined by ultrasonographic indices. Cutoff values of ultrasonographic indices and CPF for extubation failure were estimated with receiver operating characteristic (ROC) analysis. A multivariable-adjusted logistic regression model was used to calculate odds ratios for extubation failure based on PCED, diaphragm peak velocity, and CPF adjusted for Acute Physiology and Chronic Health Evaluation (APACHE) II score. The *t* test was used to compare the means of variables. The Fisher exact test was used to compare grouped data such as sex, CAM-ICU results, and in-hospital mortality. A 2-tailed $P < .05$ was considered to indicate statistical significance. R3.3.3 (R Foundation for Statistical Computing, Vienna, Austria) was used for all statistical analyses except the adjusted regression model, which was constructed with Stata version 14 (StataCorp, College Station, Texas).

Results

Subjects

A total of 252 subjects were included in the analyses. A flowchart of the subject enrollment process is shown in Supplementary Figure 1. Twelve subjects (4.8%) were re-intubated within 72 h after extubation. APACHE II score,

Table 1. Patient Baseline Characteristics and Cough Variables in Each Group

Characteristics	Extubation Success ($n = 240$)	Extubation Failure ($n = 12$)	P
Male, n (%)	156 (65)	9 (75)	.55
Age, y	66.7 ± 14	69.3 ± 15	.54
BMI, kg/m^2	23.6 ± 4.9	23.3 ± 5.1	.83
CAM-ICU, n positive (%)	58 (24)	4 (33)	.50
RASS	−0.53 ± 0.84	−0.50 ± 0.8	.91
APACHE II score	16.5 ± 5.9	21.0 ± 7.9	.01
SAPS II score	38.2 ± 13.1	52.6 ± 11.3	< .001
Duration of ventilation, d	2.58 ± 2.42	5.33 ± 3.06	< .001
P_{aO_2}/F_{IO_2}, mm Hg	341 ± 235	323 ± 106	.79
V_T, mL	473 ± 150	415 ± 90	.18
Minute ventilation, L/min	7.09 ± 2.21	7.57 ± 2.02	.47
RSBI, breaths/min/L	38.4 ± 18.6	48.7 ± 19.9	.063
ICU length of stay, d	4.01 ± 4.80	10.7 ± 3.26	<.001
ICU mortality, n (%)	9 (3.8)	1 (8.3)	.39
CPF L/min,	71.1 ± 26.9	47.1 ± 21.3	.003
PCED, cm	2.32 ± 1.13	1.22 ± 0.67	.001
Velocity, cm/s	10.7 ± 5.91	8.79 ± 3.95	.27

Data are shown as mean ± SD unless otherwise stated.
BMI = body mass index
CAM-ICU = Confusion Assessment Method for the Intensive Care Unit
RASS = Richmond Agitation Sedation Scale
APACHE II = Acute Physiology and Chronic Health Evaluation II
SAPS II = Simplified Acute Physiology Score II
P/F = P_{aO_2}/F_{IO_2}
V_T = tidal volume
RSBI = Rapid Shallow Breathing Index
ICU = intensive care unit
CPF = cough peak flow
PCED = passive cephalic excursion of diaphragm

Table 2. Indications for Intubation

Characteristics	Extubation Success	Extubation Failure
Emergent surgery	43	5
Elective cardiothoracic surgery	51	0
Elective upper abdominal surgery	10	0
Elective lower abdominal surgery	14	0
Altered mental status	7	0
Acute coronary syndrome	17	1
Congestive heart failure	21	0
Pneumonia	12	1
Sepsis	18	1
COPD	6	0
Drug intoxication	2	0
Hemorrhagic strole	11	2
Ischemic stroke	2	0
Gastrointestinal bleeding	5	0
Others	21	2

Simplified Acute Physiology Score (SAPS) II, duration of mechanical ventilation, ICU length of stay, and in-hospital mortality were significantly higher in the extubation failure group than in the extubation success group (Table 1). Table 2 shows the indications for intubation.

Associations Between PCED and CPF and Between Diaphragm Peak Velocity and CPF

The Pearson coefficient was 0.496 ($P < .001$) for the correlation between PCED and CPF and 0.347 ($P < .001$) for the correlation between diaphragm peak velocity and CPF. A simple regression model with CPF as the dependent variable in relation to PCED showed significant associations between PCED and CPF ($P < .001$, β coefficient 11.9, 95% CI 9.28–14.5, adjusted $R^2 = 0.243$; Supplementary Fig. 2) and between diaphragm velocity and CPF ($P < .001$, β coefficient 1.97, 95% CI 1.44–2.49, adjusted $R^2 = 0.175$; Supplementary Fig. 3). A multiple regression model adjusted for age and sex showed modestly stronger associations between PCED and CPF ($P < .001$, adjusted β coefficient 11.4, 95% CI 8.88–14.0, adjusted $R^2 = 0.287$) and between diaphragm velocity and CPF ($P < .001$, adjusted β coefficient 1.71, 95% CI 1.91–2.24, adjusted $R^2 = 0.235$). Height was not used in the regression models because it was not significantly associated with CPF in relation to PCED or diaphragm peak velocity.

The equation for predicting CPF with PCED, age, and sex in mechanically ventilated subjects was

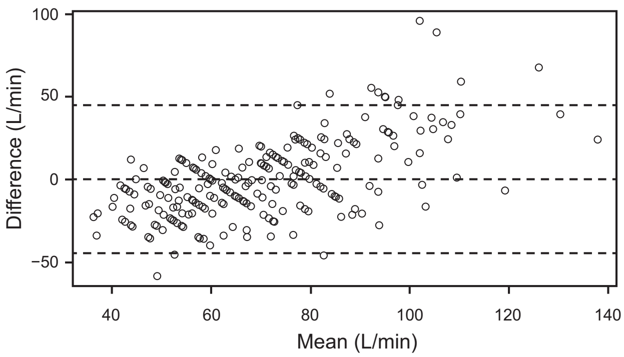

Fig. 2. Bland-Altman plot showing the difference between cough peak flow (CPF) and predicted CPF using passive cephalic excursion of the diaphragm, sex, and age. Center line denotes bias, whereas outer lines show ± 2 SD.

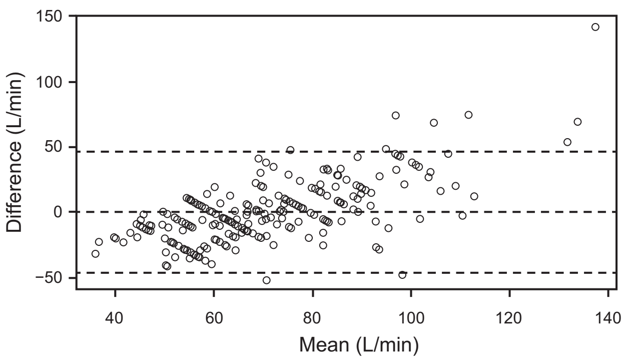

Fig. 3. Bland-Altman plot showing the difference between cough peak flow (CPF) and predicted CPF using diaphragm peak velocity, sex, and age. Center line denotes bias, whereas outer lines show ± 2 SD.

$$\text{Predicted CPF} = \text{PCED(cm)} \times 11.4 - \text{age(years)} \times 0.197 + \text{male sex} \times 10.2 + 50.5.$$

The equation for predicting CPF with diaphragm velocity, age, and sex in mechanically ventilated subjects was

$$\text{Predicted CPF} = \text{diaphragm peak velocity(cm/s)} \times 1.71 - \text{age (years)} \times 0.009 + \text{male sex} \times 14.9 + 43.2,$$

where male sex = 1 and female sex = 0.

Bland-Altman plots were used to assess agreement between measured CPF and CPF predicted by PCED, age, and sex and between measured CPF and CPF predicted by diaphragm peak velocity, age, and sex (Figs. 2 and 3). The differences between predicted CPF and measured CPF were larger at higher values for both PCED and diaphragm peak velocity.

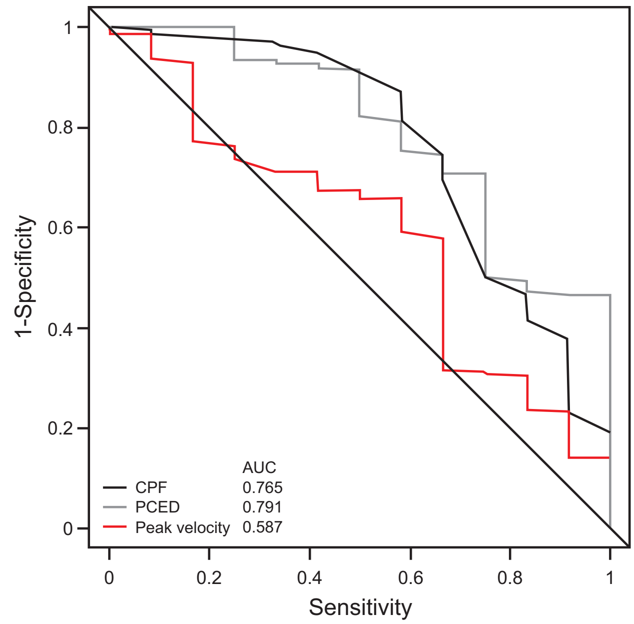

Fig. 4. Receiver operating characteristic curves for passive cephalic excursion of the diaphragm (PCED), diaphragm peak velocity, and cough peak flow (CPF) to predict extubation failure.

Ultrasonographic Indices, CPF, and Extubation Outcome

PCED and CPF were significantly lower in the extubation failure group than in the extubation success group (mean PCED: 1.22 ± 0.67 cm vs 2.32 ± 1.13 cm, P = .001; mean CPF: 47.1 ± 21.3 L/min vs 71.1 ± 26.9 L/min, P = .003), whereas diaphragm peak velocity did not significantly vary between the 2 groups (Table 1). A PCED < 1.6 cm and CPF < 50 L/min were significantly associated with extubation failure, after adjusting for APACHE II score (adjusted OR for PCED: 7.28, 95% CI 1.88–28.3, P < .001; adjusted OR for CPF: 6.1, 95% CI 1.81–20.6, P < .001). Figure 4 shows the ROC curves of PCED, diaphragm peak velocity, and CPF to predict extubation failure. The AUCs of PCED, diaphragm peak velocity, and CPF for extubation failure were 0.791 (95% Cl 0.668– to 0.914), 0.587 (95% Cl 0.426– to 0.748), and 0.765 (95% Cl 0.609–0.922), respectively. The specificity and sensitivity for extubation failure with a PCED ≤ 1.6 cm H_2O were 0.708 and 0.750, respectively. The specificity and sensitivity for extubation failure with a CPF ≤ 50 L/min were 0.741 and 0.666, respectively. There was no significant difference in predictive accuracy between PCED and CPF (P = .61).

Discussion

The present results show that PCED during voluntary cough significantly predicted CPF and that low PCED was significantly associated with extubation failure. PCED appears to be as accurate as CPF in predicting extubation failure after a successful SBT. These results are consistent with those of previous studies, which reported that low CPF was significantly associated with extubation failure and that PCED was significantly correlated with CPF in healthy adults.[8,9,16-20] This is the first study to investigate associations of ultrasonographic indices of diaphragm movement during cough with simultaneously measured CPF and extubation outcomes in mechanically ventilated subjects.

Diaphragm excursion was positively correlated with inspiratory volume in previous studies.[21,22] Our results suggest that cough inspiratory volume is important in generating adequate CPF and that PCED is, therefore, closely associated with CPF. The coefficients in the equation used to predict CPF with PCED in the present subjects with endotracheal tubes were significantly different from those for healthy adults,[11] mostly because of the absence of glottic closure secondary to endotracheal tubes and the consequent absence of a compressive phase before cough expiration.

The association between diaphragm peak velocity and CPF was weaker than that between PCED and CPF. In addition, diaphragm peak velocity did not vary significantly between the extubation failure and success groups. These results are consistent with those reported by a study of the associations of PCED and diaphragm peak velocity with CPF in healthy adults, which showed a weak association of diaphragm velocity with CPF in women only.[11] A possible explanation for our result is that diaphragm peak velocity is merely the highest velocity at one point and does not reflect the entire cough process. It might be high even for a small cough with a tidal volume that is too low to generate adequate air flow and CPF.

Bland-Altman plots showed that the predictive accuracy of PCED was not sufficiently high for high CPF values. Because the main use of PCED is to identify subjects with weak cough, the substantial variability in high values would not be clinically relevant. The incidence of extubation failure in the present study was lower (4.8%) than previously reported incidences, which ranged from 10–20%.[23-26] This was expected because our ICU is a mixed medical and surgical ICU that cares for a substantial number of patients after elective surgery. In addition, we excluded patients who could not or would not produce a voluntary cough as instructed.

The main advantage of the present method of estimating cough strength is that it is simple and noninvasive—it does not require mechanical ventilators or devices such as a peak flow meter to be connected to the endotracheal tube when measuring cough strength. Future studies should determine whether our method is applicable to tracheostomized patient because for stable patients in general wards and not on mechanical ventilation clinicians sometimes need to decide whether to decannulate the tracheostomy tube without an objective evaluation of cough strength.

This study has limitations that warrant mention. In theory, PCED is affected by respiratory system mechanics such as compliance of the lung and chest wall and airway resistance. Second, maximum expiratory pressure—another index of expiratory muscle strength—was not measured for comparison with PCED. Third, the high percentage of subjects undergoing elective surgery with limited duration of mechanical ventilation and the exclusion of uncooperative or cognitively impaired patients limit the generatability of this method. Fourth, 2 cough efforts may not be sufficient to ensure patients' maximal cough effort. Fifth, we did not examine the interexaminer validity of ultrasonographic measurement in the present study. Lastly, the sample size of the present study was not sufficiently large for comparison of diagnostic accuracies between CPF and PCED.

Conclusions

In conclusion, PCED measured by ultrasonography was a significant predictor of CPF and extubation failure after a successful SBT. Further studies are warranted to determine whether this method is applicable to determination of tracheostomy decannulation in stable patients in general wards.

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