Prediction of Extubation Success in Myasthenic Crisis Using Bedside Functional Residual Capacity Measurement: A Prospective Feasibility Study

Yatak Başı Fonksiyonel Rezidual Kapasite Ölçümünün Myastenik Krizde Ekstübasyon Başarısının Tahminindeki Rolü: Prospektif Pilot Çalışma

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Abstract

Aim: Extubation failure often complicates the recovery phase of a myasthenic crisis (MC). Bedside functional residual capacity (FRC) is a relatively new technique shown to be promising in the improvement of ventilation management in the intensive care unit (ICU), and may have a role in the estimation of extubation success. Since the prediction of extubation success is difficult due to the absence of formally evaluated disease-specific criteria, the appropriateness of any strategy described for non-neuromuscular conditions should be validated for specific neuromuscular diseases such as MC. In accordance, we designed a pilot study to determine the feasibility of bedside FRC measurement in the prediction of extubation success in MC and to determine its yield when added to the conventional parameters.

Material and Methods: We prospectively studied the additive value of bedside FRC measurements to predict extubation outcome in 11 MC episodes. The area under the receiver operating characteristic curve (ROC AUC), sensitivity and specificity of all weaning and extubation indices that passed exploratory analysis were determined.

Results: The frequency of extubation failure, defined as the need for reinstitution of ventilatory support within 72 hours of planned endotracheal tube removal, was 55% in this study population, in which all patients met the standard weaning indices indicating safety of extubation. The risk of extubation failure was connected to higher airway pressures (peak inspiratory and plato pressures; PIP and Pplato; ROC AUCs: 0.933 and 0.917), increased gradient of end-tidal CO_2 to arterial CO_2 (CO_2 gradient; ROC AUC:0.900) and total airway care score (ACS; ROC AUC:0.983), but not to FRC, the simplified acute physiology score (SAPS-II) and the traditional weaning criteria such as the rapid shallow breathing index (RSBI) and mouth occlusion pressure (P0.1). Although perhaps useful when measurable, the utility of maximal inspiratory/expiratory mouth pressures (MIP and MEP) was also low due to the inability of MC patients to perform the maneuvers required to obtain these parameters. In contrast, FRC measurement was easily attainable at the bedside, with zero risk to the patient and correlated well to the aerated lung volume measured by chest CT (r=0.717).

Conclusion: This preliminary study suggests that bedside FRC measurement is safe and feasible for long-term monitoring of intubated myasthenic patients. Its utility in determining weaning and extubation outcomes requires further studies with larger samples. Standard weaning parameters may not be accurate enough in the prediction of extubation outcome in MC, probably reflecting differences in the pathophysiology of failure of extubation and weaning. As a new semi-objective measurement of pulmonary secretion status, ACS can be helpful in the identification of the risk of extubation failure. (Yoğun Bakım Derg 2012; 3: 36-42)

Key words: Myasthenic crisis, maximum expiratory pressure, maximum inspiratory pressure, atelectasis, recruitment

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Özet

Amaç: Ekstübasyon başarısızlığı myastenik kriz (MK) sürecinin sıklıkla olumsuz etkileyen bir durumdur. Yatak başında yapılabilen fonksiyonel rezidüel kapasite (FRC) ölçümünün yoğun bakımda ventilator yönetimini olumlu yönde geliştirebileceğine dair ön veriler bulunmakla birlikte bu metodoloji ekstubasyonun kaderini ön görme açısından da yararlı olabilir. Formel olarak hastalığa özgün kriterlerinin belirlenmemiş olması ektübasyonun kaderinin saptanmasını güçleştirdiği için non-nöromusküler hastalıklar için önerilmiş olan herhangi bir stratejinin MK gibi nöromuskuler hastalıklar için uygunluğunun validasyonu gereklidir. Bu görüşle dizayn edilen bu pilot çalışmada yatak başı FRC ölçümünün fizibilitesi belirlenmiş ve konvansiyonel kriterlere ilave edilmesi durumundaki verimi incelenmiştir.

Gereç ve Yöntemler: Bu çalışmada 11 MK episodunda ektübasyon sonucunun tahminde yatak başında elde olunan fonksiyonel rezidüel kapasite (İngilizcesini akronimi FRC) ölçümünün katkısı araştırılmıştır. ROC eğrisi altında kalan alan [ROC AUC], sensitivite ve spesifisite değerlerinin %95 güven aralığının alt limiti tek yönlü analizi geçen parametreler için hesaplanmıştır.

Bulgular: Ekstübasyon sonrası 72 saat içinde tekrar invazif mekanik ventilasyona bağlanma ihtiyacı 11 episodun 6'sında (%55) ortaya çıkmıştır. Bu hastaların hepsinde klasik ayırma kriterleri sağlanmış durumdadır. Ekstübasyon başarısızlığı artmış hava yolu başınçları (Pik İnspiratuar ve Plato basıncı- PIP ve Pplato; ROC AUC: 0,933 ve 0,917); artmış alveolo-arteriyel CO_2 gradienti ($etCO_2$-PCO_2; ROC AUC: 9,900) ve total hava yolu bakım skoru (ACS; ROC AUC: 0,983) ile ilişkili iken FRC ve bunun yanında SAPS-II, RSBI ve P100 gibi sık kullanılan parametrelerle ilişkili değildir. Olasılıkla ölçüldüğünde yararlı olan maksimum inspiratuar ve ekspiratuar ağız içi basınçlarının (MIP, MEP) hastaların gereken manevraları yapamaması nedeniyle kullanımının kısıtlı olduğu görülmüştür. Oysa, FRC hasta başında hasta için herhangi bir risk oluşturmaksızın başarılı bir şekilde ölçülebilmekte olup havalanan akciğer volümü için tomografi ile yüksek korelasyon göstermektedir (r=0,717).

Sonuç: Bu alanında bir ilk olan çalışmada hasta başında FRC ölçümünün ve uzun süreli monitörize edilmesinin myastenik kriz olgularında güvenli ve uygulanabilir olduğu ortaya konulmuş olmaktadır. Ayırma ve ekstübasyon kararında FRC ölçümünün öngörü değerini belirlemek için ise fazla sayıda hasta içeren etkinlik çalışmalarına ihtiyaç vardır. Bu çalışmada tespit edilen diğer önemli bir unsur aralarındaki patofizyolojik farkın aslında bir yansıması olan ayırma kriterlerinin ekstübasyonun öngörülmesinde belirgin pozisyonu olmadığıdır. Pulmoner sekresyon durumunun semi-objektif bir göstergesi olarak "Hava-yolu Bakım Skoru (Airway Care Score) veya benzerlerinin ekstübasyon başarısızlığının öngörülmesindeki yeri araştırmaya değerdir. (Yoğun Bakım Derg 2012; 3: 36-42)

Anahtar sözcükler: Myastenik kriz, maksimum ekspiratuar basınç, maksimum inspiratuar basınç, atelektazi, rekrütman

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Introduction

Extubation of patients following weaning from mechanical ventilation initiated due to a myasthenic crisis (MC) is one of the most challenging tasks in neurological intensive care units (NICU). After subsidence of the MC, the extubation failure rate is in the range of 27%-44% (1-3). Extubation failure and re-intubation are associated with significant morbidity and mortality along with a prolongation in intensive care unit (ICU) and hospital length of stay (4). The factors that influence extubation outcome are not well-established in this specific population. In a few retrospective studies, atelectasis has been shown to be the strongest predictor for extubation failure (1, 3). Other suggested indicators of poor prognosis are old age, male sex, history and perhaps number of previous MC, duration of intubation >10 days, low pH on arterial blood gas analysis, low forced vital capacity (FVC) and poor cough strength assessed by maximal expiratory pressure before extubation, as well as the presence of pneumonia (1-3, 5).

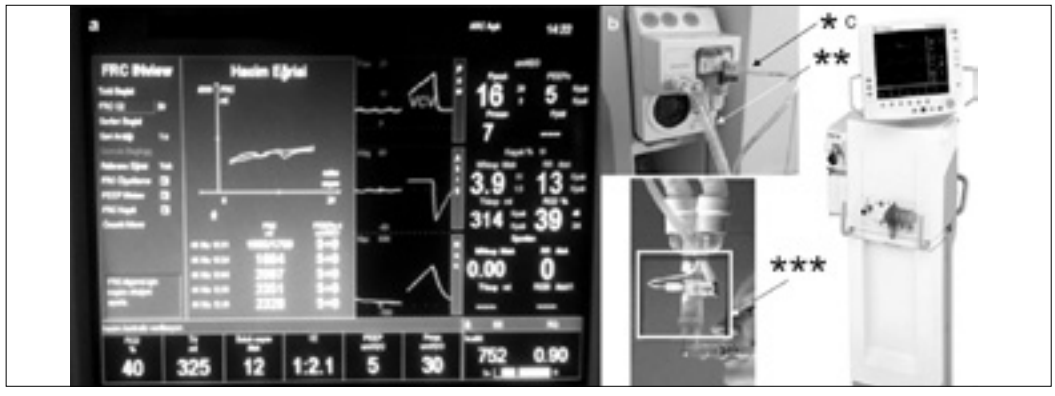
Atelectasis affects MC negatively by resulting not only in reduced or absent alveolo-capillary gas exchange and increased shunting, but also in the creation of a focus for pulmonary infection. In MC, the causes of atelectasis are various, and include muscle weakness, inability to clear the airway along with insufficient care of oropharyngeal, nasotracheal and tracheal secretions (obstruction atelectasis) and the use of an unnecessarily high fraction of inspired oxygen (FiO_2) (absorption atelectasis) (6). Chest radiography is usually used for the diagnosis and daily monitoring of atelectasis, but its sensitivity is low. Computed tomography (CT) is the most sensitive method, but radiation exposure limits its value as a monitoring tool in addition to difficulties related to the transfer of critically ill patients to the CT suite. Therefore, non-invasive and radiation-free methods that can detect changes in lung volume and ventilation distribution at the bedside are of critical importance. New techniques such as electrical impedance tomography and direct measurement of functional residual capacity (FRC) can be useful in this respect (7, 8). Because atelectasis decreases FRC, its bedside measurement and monitoring during mechanical ventilation can guide the clinician in predicting extubation failure. In this study, we first assessed the feasibility of bedside FRC measurements in assessing extubation outcome in a consecutive series of MC patients necessitating invasive mechanical ventilatory (IMV) support. We also assessed the yield of conventional parameters useful in forecasting extubation fate in MC.

Material and Methods

After approval of the study protocol by the Ethical Committee of Hacettepe University, we prospectively studied patients admitted to our NICU with a diagnosis of MC necessitating IMV between October 2008 and September 2011. Post-thymectomy crises and patients with asthma, chronic obstructive pulmonary disease or significant congestive heart failure were not included in the study.

From the initiation of IMV to the weaning period, FRC was measured daily (at least six times per day) with a nitrogen wash-out method as described and standardized by Stenqvist (FRC INview®, GE Engström Care Station®) (9). The details of the theory and measurement technique can be found elsewhere (10, 11) and are briefly summarized in Box 1. The average and variability (represented as its standard deviation) of FRC and average of FRC values measured on the extubation day were calculated for each patient. In 9 out of the 11 MC episodes, chest CT (Somatom® Emotion Duo or Sensation 16, Siemens, Germany) was obtained at the discretion of the clinical team during the intubation period. Aerated lung, atelectasis and effusion volumes were measured on these CT images. The aerated lung volume calculation was based on fixed density thresholds (lower threshold -1024 HU, upper threshold -200 HU) and semiautomatic segmentation was done using a Syngo® workstation (12). The contours of atelectasis and effusion were outlined and the volume was calculated on the workstation. Total lung volume

Box 1. FRC Measurement technique



The FRC measurement system is pictured as a calculation and recording screen on the right (a); modular connections, including the Defend® side-stream capnogram (*) and spirometry (**), a piece of the Y-arm (***) in the middle (b) and the hardwire (ventilator) on the left (c). The system operates based on the principle of nitrogen wash-out. No interruption of ventilation is required for measurement. However, it is important to note that all ventilation parameters should be maintained unchanged during measurement. Furthermore, no tracheal suctioning or nebulization is permitted. First, inspired [FiN_2=1-FiO_2] and end-tidal nitrogen [etN_2= 1-etO_2-etN_2] are measured via the internal side-stream capnograph. Then, expired and inspired alveolar tidal volumes (Vt) are calculated with energy expenditure formulas [VO_2=VCO_2/RQ; $Vt_{alv}(E)$= VCO_2/ $etCO_2$ x RR (respiratory rate); $Vt_{alv}(I)$ = $Vt_{alv}(E)$ + (VO_2-VCO_2) / RR]. Subsequently, the nitrogen volumes in a single inspired and expired breath (VE and VI) are calculated [VEN_2=etN_2x$Vt_{alv}(E)$ and ViN_2= FiN_2x$Vt_{alv}(I)$]. Afterwards, difference in a single breath is calculated [ΔVN_2=VEN_2-ViN_2]. Then, a trail of stepwise FiO_2 increases (up to 10% FiO_2) is applied. Before the trial, VO_2, VCO_2 and $etN_2^{baseline}$ are measured and considered a priori as constant during the trial. After completion of the trial, the FRC is calculated [FRC=$\Delta VN_2/\Delta etN_2$]. After a total 20 cycles, the total FRC is determined by averaging [FRC= $\sum \Delta VN_2$ / ($etN_2^{baseline}$ -etN_2)]. To estimate the baseline nitrogen concentration, FiO_2 should be maintained between 40% and 65% and should be stable for at least 5 minutes before measurement. The results are more dependable for volume-controlled modes, and these modes should be preferred but are not mandatory. Curves (picture) are observed for artifacts. The measurement is repeated twice and averaged. When a difference greater than 25% occurs between repeats, the FRCs are considered artifactual and omitted from analysis.

was calculated as aerated lung compartments + (atelectasis volume + effusion volume).

We followed a standardized protocol for intubation, weaning, extubation and re-intubation in these patients. All these procedures were predominantly driven by treating neurointensivists. Four sets of criteria were used to assess readiness for weaning (13): a) pulmonary criteria: partial pressure of arterial oxygen (PaO_2) >60 mmHg and partial pressure of arterial carbon dioxide ($PaCO_2$) within normal limits or close to baseline level when FiO_2 ≤40% and positive end-expiratory pressure (PEEP) ≤5 cmH_2O together with a PaO_2/FiO_2 ratio (PF ratio) >150 and the ability of the patient to trigger inspiration (by flow mode), which is quantified further by measuring the airway occlusion pressure (P0.1 or P100); b) hemodynamic criteria: absence of acute myocardial ischemia (or normal serum troponin level), heart rate (HR) <140 beats per minute (bpm) and systolic blood pressure (BP) >90 mmHg with no or minimal vasopressor support; c) adequate level of consciousness as quantified by the Glasgow coma scale (GCS); d) absence of fever and significant electrolyte abnormalities, particularly sodium, calcium and phosphate along with hemoglobin level >10 gr/dL. Beyond all these, successful control of MC and improvement in weakness was a must before attempting weaning. An improvement in the strength of neck flexors (to greater than grade 4 according to the Medical Research Council Scale or able to hold head off the bed for at least 5 seconds) was considered critical in this respect.

In patients satisfying these weaning criteria, a spontaneous breathing trial (SBT) with continuous positive airway pressure (CPAP) was performed. Before this trial, patients were removed from mechanical ventilation for approximately 2 minutes, and tidal volume (V_t), respiratory rate (RR), minute volume (V_E, calculated as $RRxV_t$) and rapid-shallow breathing index (RSBI, calculated as RR/V_t) were measured. Patients with V_t>5 cc/kg, RR <40 bpm, V_E >10 L/minute and RSBI<105 were considered ready for SBT. For CPAP, minimal support was used (PEEP: 3-5 cmH_2O, pressure support: no more than 5 cmH_2O; FiO_2 <40%; automatic tube compensation, at least 35%). During SBT, pulse oxygen saturation (SaO_2), main-stream end-tidal carbon dioxide ($etCO_2$), HR, BP and RR were monitored. The patient's appearance and presence of signs of tiredness, dyspnea, tachypnea, cyanosis and anxiety were noted. The SBT was stopped when there were significant changes in RR (decrease to <8 bpm or increase to >40 bpm), BP (30 mmHg change in systolic BP or 10 mmHg in diastolic BP), HR (increase of >20 bpm or HR>110 bpm) and appearance of cardiac arrhythmia (more frequent than 6 per minute). Other criteria for discontinuation were sustained decrease of SaO_2 below 90%, decrease in GCS, occurrence of significant agitation, diaphoresis, progressive recruitment of accessory respiratory muscles and appearance of the thoracoabdominal paradox.

For subjects who passed the SBT, maximal inspiration mouth pressure (MIP, also called PImax) and maximal expiratory mouth pressure (MEP, also called PEmax) were measured (MicroRPM®, Micro Medical/Care Fusion Ltd-UK), SpiroMed Ltd-Turkey). These measurements were repeated three to four times in the presence of variable results. For cough effectiveness, the white paper test was used. For this test, the size of the wet spot after a forceful cough onto a white paper towel held 1-2 cm from the tracheal tube was qualitatively classified as none, weak or strong. To assess the ability to control respiratory secretions, the modified Airway Care Score (ACS) was calculated (14, 15). Briefly, this system consists of five parameters (see Box 2), providing a total score of 0 to 15. The score was determined by consensus between one of the attending neurointensivists and the nurses examining the patient separately. Only subjects whose total ACS equal to or less than 7 underwent the extubation procedure. Afterwards, we proceed to a standardized cuff-leak test (13). Of note, ventilation mode was switched to volume-cycled ventilation for this test. Inspiratory and expiratory V_t were measured for at least six breaths before and after cuff deflation and the difference between the medium three values was calculated and then averaged. The criterion for the absence of significant laryngeal edema was considered if the difference was less than 2 cc per body weight or less than 25%.

Patients who fulfilled these criteria were extubated using a standardized protocol. Briefly, two physicians (at least one as the attending neurointensivist) were present during the procedure. Prednisolone (usually 1 mg/kg IV) was administered before the leak test. Extubation was performed in high semi-Fowler position with the head in a neutral position. After explaining the process to the patient, an appropriate size Guedel (oropharyngeal) airway was placed to prevent tube biting. Before and after tube removal, 100% oxygen was applied (at least 5 minutes for each epoch). After suctioning the tube, subglottic catheters and the mouth for the last time, the tube was removed using an exchanger. Patients were monitored closely after removal, received nebulized salbutamol (200 µg) and ipratropium bromide (500 µg) along with furosemid (0.5 mg/kg IV, if there was excess fluid on the last day). The exchanger was removed according to secretion status, at the latest 48 hours following extubation).

Extubation failure was defined as the reappearance of the need for ventilatory support within 72 hours of planned endotracheal tube removal. The criteria for reintubation after extubation were the presence peri-arrest status, serious air grasping, gagging or stridor, progressive decrease in cooperation and level of consciousness, significant hemodynamic instability (systolic BP <90 mmHg despite vasopressor support), intolerably high amount of secretions and jeopardized airway patency. In addition, in the presence of persistent hypoxemia (SaO_2 <90% at least for 5 minutes), tachypnea (>40 bpm), accessory or superficial ventilation, throraco-abdominal paradox, hypoxemia (PaO_2<50 mmHg), acidosis (arterial pH<7.3) or hypercapnia ($PaCO_2$>60 mmHg), re-intubation was performed. An attempt for non-invasive MV (CPAP; with titration of PEEP and pressure support; via an oronasal mask) was performed in one of the patients with post-extubation ventilatory failure,

Box 2. The airway care score*

Grading	Cough to suction	Sputum quantity	Sputum character	Sputum viscosity	Suctioning frequency
0	Vigorous	None	Clear	Watery	>3 hours
1	Moderate	1 pass	Tan	Frothy	Every 2 to 3 hours
2	Weak	2 passes	Yellow	Thick	Every 1 to 2 hours
3	None	≥3 passes	Green	Tenacious	<Every 1 hour

* Passes refers to number of passes of a suctioning catheter that is required to clear the endotracheal tube of secretions. The total score is the summation of all grades (14, 15)

but re-intubation was performed 3 hours later, as this attempt was unsuccessful.

Statistical analysis

All values are displayed as mean ± standard deviation and percentage, as appropriate. Mann-Whitney U and Chi-square tests were used for exploratory analysis. For indices with p values less than 0.05, the area under the curve (AUC) of the receiver operator characteristic (ROC) curves and the 95% confidence intervals (95% CI) were calculated. The correlation between FRC and CT volumes was evaluated using the Spearman test. The SPSS® 15.0 and MedCalc® statistical package programs were used for the analyses. Due to the small sample size and primarily hypothesis-generating nature of the study, no adaptation of statistical significance level was considered, and $p<0.05$ was set as significant.

Results

We studied a total of 11 MC episodes in 10 patients (female/male: 8/2; mean age: 57±17 years; body mass index: 24.2±3.4). All patients underwent IMV for longer than 72 hours (mean: 11.8±5.2 days; range: 5-23 days). Extubation failure occurred in 55% of our MC patients who complied thoroughly with the standard weaning and extubation parameters indicating a sufficient extubation outcome. Individual patient data regarding myasthenia gravis and MC characteristics are presented in Tables 1 and 2, respectively.

The bedside FRC volumes (average and SD measured during the entire intubation period; latest 3 hours before SBT as absolute and normalized volumes ("cc" and "cc/kg")) were not significantly associated with extubation failure (Table 3). However, average FRC, last FRC and

Table 1. Patient characteristics

Patient	Extubation fate	Age	Gender	Height (cm)	Weight (kg)	BMI (kg/m²)	MG diagnosis age	MC number	Thymus Pathology	Acetylcholine receptor antibody	Pyridostigmine dose (mg)	Prednisolone dose (mg)
1	Successful	64	Male	180	90	27	48	1	Hyperplasia	+	240	0
2	Successful	75	Female	158	67	26	70	2	Hyperplasia	+	540	16
3	Successful	34	Female	172	70	23.7	33	2	Hyperplasia	+	360	64
4	Successful	16	Female	157	55	22.3	15	2	Hyperplasia	+	420	48
5	Successful	59	Male	172	75	25.4	49	2	Thymoma	+	360	35
6	Failed	73	Female	153	43	18.4	73	1	Normal	+	360	0
7	Failed	56	Female	151	60	26.3	53	2	Thymoma	-	300	48
8a	Failed	60	Female	157	50	20.3	59	2	Thymic carcinoma	+	360	36
9	Failed	69	Female	155	70	29.1	67	3	Thymoma	+	480	0
8b	Failed	60	Female	157	50	20.3	59	2	Thymic carcinoma	+	360	36
10	Failed	56	Female	155	65	27.1	48	1	Metastatic thymoma	+	480	80

Table 2. Myasthenic crisis characteristics

Patient	Extubation fate	Provocation	Plasmapheresis	Intravenous immunoglobulin	Intubation duration (day)	Chest CT	Chest CT findings	Facial muscle strength	Neck flexion strength	Neck extension strength
1	Successful	Post-cholecystectomy	+	-	7	+	Normal	4	4	4
2	Successful	Pneumonia	+	+	17	+	Lobar pneumonia. Bilateral pleural effusion	4	4	4
3	Successful	Pneumonia, GIS bleeding	+	+	11	-	Not done	3+	3+	4
4	Successful	-	+	-	5	+	Linear atelectasis	5	5	5
5	Successful	-	+	+	8	+	Normal	5	5	4
6	Failed	Pneumonia	+	+	11	+	Bilateral pleural effusion	4	4	4
7	Failed	-	+	-	16	+	Subsegmental atelectasis. Pneumothorax	4	4	4
8a	Failed	-	+	+	10	-	Not done	4+	4+	4+
9	Failed	-	+	+	9	+	Normal	4	4	4
8b	Failed	Pneumonia	+	+	13	+	Subsegmental atelectasis. Lobar pneumonia	4+	4+	4+
10	Failed	-	+	+	23	+	Normal	4+	4+	4+

normalized FRC were non-significantly lower in subjects who were successfully extubated compared to those who required reintubation. No significant time trend was observed over the intubation period (Figure 1).

There was no difference in total lung, effusion and atelectasis volumes measured on lung CT obtained during intubation period among patients with (n=5) and without (n=4) failed extubation (Table 3). Of note, FRC and total as well as operant (defined as total volume-atelectasis volume) lung volume was well correlated (r=0.717; p=0.03 and r=0.733; p=0.025, respectively).

Most of the clinical, laboratory and pulmonary characteristics didn't differ significantly between patients with and without extubation failure, except for PIP, Pplato, CO_2 gradient and airway care scores (Table 3). The AUC of ROC curves was 0.933 for PIP and 0.917 for Pplato (Figure 2). Of note, all the values of PIP and Pplato remained within normal limits regardless of the success or failure of extubation. The gradient of end-tidal CO_2 to arterial CO_2 was high in five out of the six patients who could not been liberated from intubation. The mean (Pa-et) CO_2 was significantly higher in these patients (13.9±7 vs. 4.8±2.9 mmHg). The AUC of the ROC was 0.900 (Figure 2). The optimum threshold to predict success of extubation was 9.9 mmHg with a sensitivity of 22.7% and specificity of 48.0% specificity (lower limit of 95% CIs). Patients who tolerated extubation had significantly lower ACS compared to those who did not (2.8±0.8 vs. 5.3±1.0; p=0.004) (Table 4). The AUC of the ROC was 0.983 (Figure 2). The lower limit of the 95% CI of the sensitivity and specificity of the calculated cut-off value (4) was 36.1% and 48.0%, respectively.

Discussion

This study aimed to evaluate the value of bedside FRC measurement to predict success or failure of extubation in the MC recovery phase. Our results did not support our hypothesis that a low FRC volume relates to extubation failure in patients with MC. Considering the low enrollment rate and the need for more patients to achieve enough power to test this hypothesis, we stopped the study prematurely upon our first interim analysis. Therefore, the value of the residual lung vol-

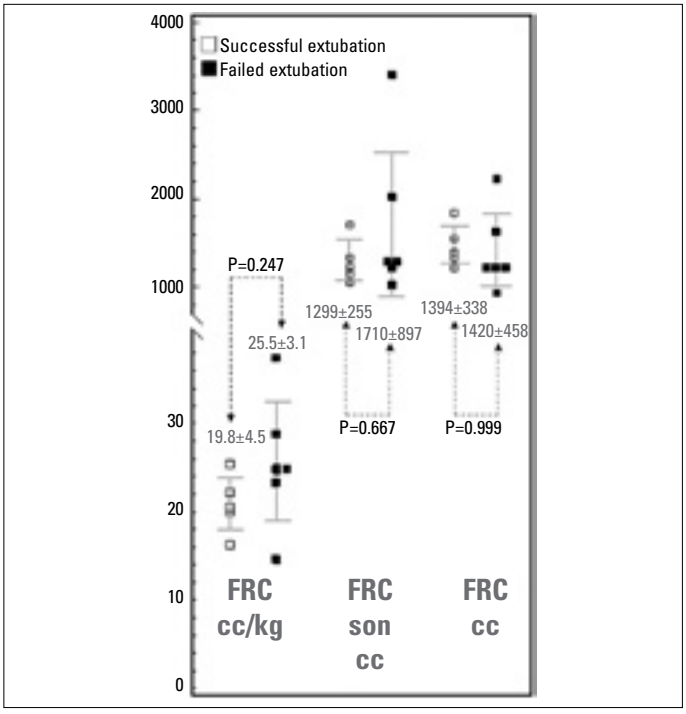


Figure 1. Results of the FRC indices

Table 3. Results*

	Successful extubation	Failed extubation
N	5	6
Age (year)	49.8±23	62.3±7
Gender (female/male)	3/2	6/0
BMI	24.9±1.9	23.6±4.4
Disease duration (year)	6.8±6.2	2.5±2.9
Intubation duration (day)	9.6±4.7	13.7±5.2
Expiration Vt (cc/kg)	6.1±0.8	6.8±1.4
Respiratory rate	18±4.8	16±3.6
Minute volume (VE) (cc/kg)	7.8±2.3	5.8±1.4
RSBI	61±20.3	49.2±28
MEP**	52±28	21.7±4.2
MIP**	53±2.8	22.3±10.5
P0.1 (or P100)	2.3±1.3	3.0±1.3
PaO_2	89.3±16.6	92.7±13.4
$PaCO_2$	40.9±4.7	41.6±3.4
HCO_3	27.2±2.2	30.7±4.1
PH	7.44±0.02	7.48±0.03
FiO_2 (%)	37±3	38±3
PaO_2/FiO_2 ratio	241±40	243±33
SaO_2	96.5±2	97.6±0.7
$etCO_2$	37.1±4.1	30.9±9.2
PaO_2-$etCO_2$	**4.8±2.9**	**13.9±7.0**
PEEP (cmH_2O)	3.2±2	3.8±2
Pressure support (cmH_2O)	6±2.6	10±5.4
PIP (peak inspiratory pressure)	**13.4±3.6**	**21.3±3.2**
Pmean	7.2±2.2	10.3±3.7
Pplato	**7.0±2.2**	**11.8±3.8**
Heart rate	92±10	87±8
Systolic blood pressure	109±7	108±22
Diastolic blood pressure	64±7	69±16
Temperature	37±0.18	36.7±0.4
Sodium	138.4±3.4	137±4.5
Potassium	3.2±0.2	3.4±0.6
Albumin	3.7±0.6	2.9±0.5
Hemoglobin	10.9±1.1	10.1±1.0
Leukocytes	10.8±1.6	9.3±3.7
Troponin	0.004±0.003	0.012±0.004
SAPS II	21.8±8.2	26.8±2.4
SAPS II expanded	5.1±1.03	5.43±0.67
SPAS mortality %	13.9±12.1	16.9±7.6
FRC (cc)	1394±338	1420±458
FRC last (cc)	1299±255	1710±897
FRC SD (cc)	252±124	208±104
FRC (cc/kg)	19.8±4.5	25.5±3.1
Total lung volume***	2040±739	2182±271
Atelectasis+effusion volume***	169±113	151±147
% Atelectasis volume***	10.2±7.2	7.5±7.8
Aerated lung volume***	1871±840	2032±402
Airway care score sum	**2.8±0.4**	**5.2±1.2**
Cuff leak (cc/kg)	1.78±1.22	1.63±0.87

*: Bold text indicated statistically significant (p<0.05) results; **MIP and MEP could be measured in two patients in whom extubation failed and in three patients with successful extubation. ***: Lung CT

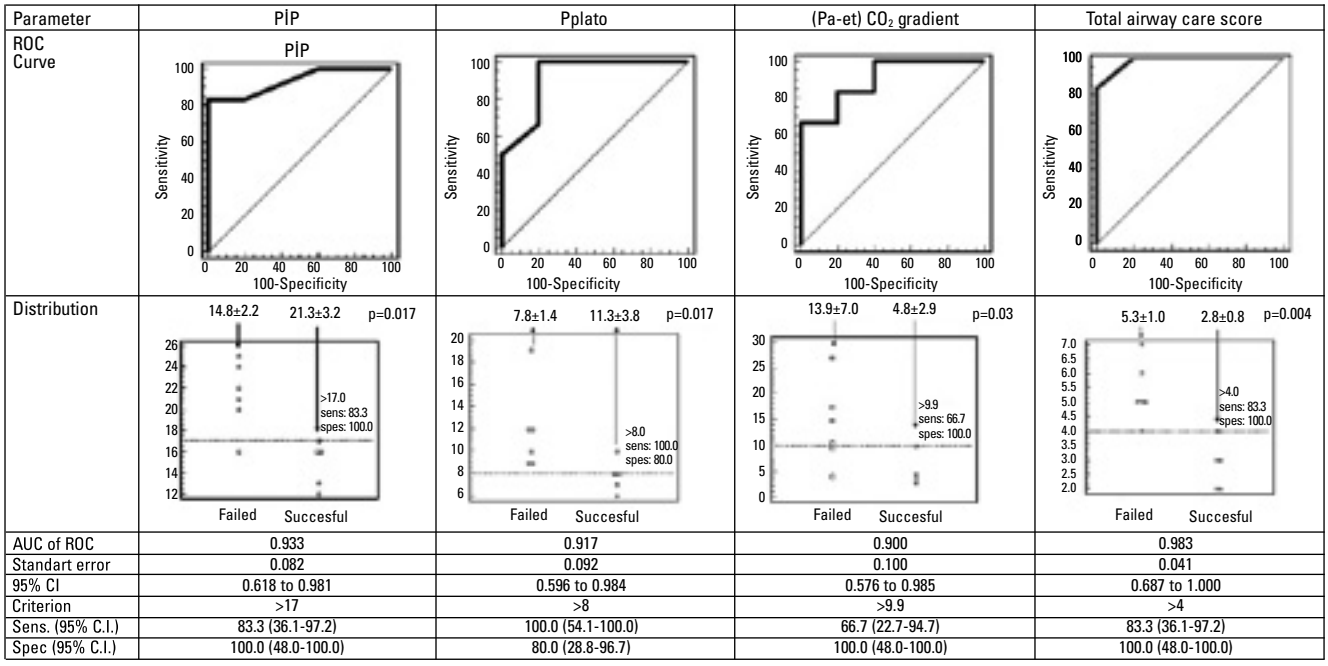


Figure 2. ROC analysis results for the conventional parameters that passed univariate analysis

Table 4. Airway secretion characteristics

	Extubation fate	Cough to suction	Sputum quantity	Sputum character	Sputum viscosity	Suctioning frequency	Total ACS	Paper test
1	Successful	Vigorous	1 pass	Clear	Frothy	>Every 3 hours	3	Strong
2	Successful	Vigorous	1 pass	Tan	Frothy	>Every 3 hours	4	Strong
3	Successful	Vigorous	1 pass	Clear	Watery	>Every 3 hours	2	Strong
4	Successful	Vigorous	1 pass	Clear	Watery	>Every 3 hours	2	Strong
5	Successful	Vigorous	1 pass	Clear	Frothy	>Every 3 hours	3	Strong
6	Failed	Moderate	1 pass	Tan	Frothy	>Every 3 hours	5	Strong
7	Failed	Moderate	2 pass	Tan	Frothy	>Every 3 hours	6	Weak
8a	Failed	Vigorous	1 pass	Yellow	Frothy	>Every 3 hours	5	Weak
9	Failed	Vigorous	1 pass	Tan	Frothy	Every 2-3 hours	5	None
8b	Failed	Vigorous	1 pass	Tan	Frothy	>Every 3 hours	4	Strong
10	Failed	Moderate	2 pass	tan	Frothy	Every 2-3 hours	7	Weak

umes determined either by lung CT or bedside FRC measurement in predicting success or failure of extubation remains to be confirmed in future studies. However, this study underscores the fact that serial bedside FRC measurement is safe, feasible and easily attainable in this population. Its correlation to lung CT was satisfactory despite the low number of subjects studied.

This prospective pilot study supports the concept that usual weaning criteria may not be accurate in predicting reintubation after planned extubation (4). Indeed, extubation failure could not be predicted based on most of the individual weaning parameters such as RSBI, Vt, V_E, PF ratio, P100, and respiratory rate in our patients. Certainly, the pathophysiology underlying success in weaning and extubation are significantly different (4). In patients recovering from MC and passing the SBT successfully, it is crucial to pay special attention to usual extubation predictors such as the ability to protect upper airways, adequacy of cough strength, extent of respiratory secretions and the degree of consciousness. However, all of our patients who required reintubation had passed most of these criteria as well. Therefore, extubation still remains problematic for a significant proportion of MC patients who totally comply with the widely-used criteria. Our univariate analyses suggest the role of higher PIP, Pplato and (Pa-et) CO_2 gradient and a lower airway care score in predicting failed extubation.

While Pplato reflects elastic recoil force (elastance) of the lungs and chest wall, PIP reflects both elastance and airway resistance. Therefore, when both PIP and Pplato are increased, the problem is decreased compliance, frequently due to pneumothorax, atelectasis, edema, pneumonia, abdominal distention, auto-PEEP or fighting against the ventilator. When PIP is increased but Pplato stays within the normal limits, the problem is usually airway obstruction due to secretions, aspiration, tube problems or bronchospasm. In our series, patients unable to

be liberated from the endotracheal tube showed higher PIP and Pplato values compared to those who remained extubated. Although all the values were below the permitted levels (30 and 40 cmH_2O for Pplato and PIP, respectively), this finding can still indicate a potential role of abnormalities at the pulmonary level in the extubation process.

An arterial to end-tidal CO_2 gradient exceeding 3 (or 5) mmHg indicates increased anatomic and/or physiological dead space, as well as low cardiac output due to heart failure, pulmonary embolism or overdistention. In complicated weaning, an increase of $etCO_2$ indicates an increase in the work of breathing, which may be a signature of weaning failure. In contrast, a decrease in $etCO_2$ and a corresponding increase in the gradient can signify respiratory muscle weakness, which is also a marker of weaning failure. Our study indicated that extubation failure was also associated with an increase in the CO_2 gradient due to a decrease in $etCO_2$. This was probably due to residual neuromuscular weakness. Because of simplicity of this parameter, we think that future weaning and extubation studies should consider this parameter, which actually has not previously been studied in neuromuscular respiratory failure.

The total points on the airway care score was the best predictor of extubation in this small group of patients recovering from MC. This score consists of cough strength to stimulation by a suction catheter, sputum quantity, character and viscosity along with suctioning frequency correlated with the amount of secretions (15). In myasthenic patients, the most important cause of increased bronchial secretions is pneumonia. However, the most prevalent cause is perhaps over dosage of parasympathomimetic reversible cholinesterase inhibitors such as pyridostigmine used in these patients. A meticulous titration against atropine oral drop and an ipratropium inhaler may be important in this respect, in addition to infection protection and management. Aggressive airway suction and chest physiotherapy are also valuable strategies.

In addition to an excess of secretions, cough capacity and airway protection ability are critical factors for extubation success. Bedside tests such as an evaluation of the gag reflex, evaluation of cough strength by MEP and MIP and the paper test have been reported to be useful. MEP is a measure of cough power, which is based on the flow generated by expiratory muscles to allow airway clearance. Some studies have indicated the superiority of MEP over other parameters such as vital capacity. However, we found that the measurement of MEP and MIP is quite complicated in patients with an endotracheal tube in place.

Conclusion

The predictive value of widely-used criteria may be not more than moderate for assessing extubation in MC. Secretions and perhaps cough status are the most important parameters. Capacity to control airway patency and aspiration are the second most important. Our study did not support but still recognizes the value of lung volumes and reserves in this process.

Conflict of Interest

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