### Predictors of prolonged weaning among mechanically ventilated patients in respiratory intensive care unit

Hamdy A. Mohammadien\*(<u>h mohammadien@yahoo.com</u>, tel 01006870068), Doaa G. Hassanin\*(<u>drdoaagad@yahoo.com</u>, tel 0102177683), Mona T Hossien\*(<u>monataha441@yahoo.com</u>, tel: 01221090439), andMostafa I. Ali\*\* (<u>Elshazly66@hotmail.com</u>, tel: 01001272020), Departments of Chest, Faculty of Medicine, Sohag University\* and Cairo University\*\*.

#### Abstract

**Background**: Weaning is an essential part of critically ill patients who are on mechanical ventilation. Weaning was classified into simple, difficult and prolonged. Some patients are easily weaned off and others require a more prolonged duration.

**Methods**: 52 patients admitted to the respiratory intensive care unit (RICU) and requiring mechanical ventilation were successfully weaned and classified into simple (20, 37.7%), difficult (20, 37.7%) and prolonged weaning (13, 24.5%). Factors associated with prolonged weaning and outcomes were determined.

**Results:** A total of 53 intubated patients admitted to the RICU (30 (56.6%) males), aged (59.8±14.3) years were included. The following factors are associated with prolonged weaning:  $\downarrow$ ed serum mg++(P<0.0001) & CA++(P<0.0001),  $\uparrow$ ed BUN level (P=0.001),  $\uparrow$ ed PaCO2 (P0.04),  $\downarrow$ ed SaO2% (P0.0001), presence of  $\geq$ 2 co-morbidities (P0.02), prolonged duration of MV (P<0.0001) and long ICU stay (P<0.0001). There was no significant relation between prolonged weaning and Modes of MV (p0.2), also A-a gradient 1ed in patients with prolonged weaning but not significant (P=0.5). In multivariate analysis, prolonged weaning was independently associated with serum Mg+ (OR 0.03, 95% CI 0.003-0.24, P < 0.001), and SaO2% change (the beginning- the end of weaning trial) OR 0.91, 95% CI 0.83–0.99, P <0.04). Regarding baseline serum Mg++ & tidal volume, the cutoff point for predicting prolonged weaning was (<1.5 .mmol/l & <450 ml) with, sensitivity, specificity, PPV NPV and accuracy (61.5%, 92.5%, 72.7%, 88.1%, 77%, P <0.0001 and 77%, 55%, 36% 88%, 66%, P < 0.02, respectively). The cutoff points of PaCO2  $\geq$ 49 mmHg & SaO2%  $\leq$ 91 at first weaning trial & SaO2% change  $\geq 5$  (between the beginning and the end of a weaning trial) were strongly associated with prolonged weaning (P < 0.02, < 0.0001 & < 0.003, respectively). Prolonged weaning was significantly associated with high mortality rate (P<0.0001).

**Conclusions**: Several factors were associated with prolonged weaning, however, when subjected to multivariate analysis, only serum Mg++& SaO2% change significantly predict prolonged weaning. Prolonged weaning is associated with increased ICU stay and higher rate of tracheostomy.

**Clinical Implications**: Prolonged mechanical ventilation is associated with higher rate of reintubation, tracheostomy rate, longer ICU stay and higher mortality. Identification and correction of factors associated with prolonged weaning may change the outcome and prognosis of these patients. In addition, early intervention such as tracheostomy is likely to benefit these patients

Key words: Mechanical ventilation, Intensive care unit, Respiratory intensive care unit, prolonged weaning

#### **Introduction**:

The process of weaning implies two separate, the withdrawal of ventilator assistance and extubation, its complete success is achieved when the patient is able to maintain spontaneous unassisted breathing after extubation. Weaning failure may occur when the patient fails to breathe soon after withdrawal of the ventilator support, as defined by the incapacity to successfully pass the SBT.<sup>1</sup>

An International Consensus Conference (ICC) on weaning from MV <sup>1</sup>proposed a new classification based on the difficulty and duration of the weaning period: simple, difficult, and prolonged weaning. Although it is considered that prolonged weaning is associated with the lowest survival.<sup>2,</sup> <sup>3</sup>The identification of these factors could be important in influencing the survival of ventilated patients in whom weaning has been initiated.

Prolonged weaning is mainly caused by an imbalance of ventilator demand and ventilatory capacity, which leads to hypercaphicventilatory insufficiency due to overloaded or weak respiratory muscles, i. e. the respiratory pump. Prolonged weaning is associated with a broad spectrum of complications (e.g. early and late damage of the airways, nosocomial infections) depending on the duration of MV. Therefore strategies are needed to shorten duration of invasive mechanical ventilation and the weaning process.<sup>4</sup>

The prolonged weaning is associated with increased mortality and morbidity.<sup>5</sup>A large proportion of patients admitted to RICUs have chronic respiratory disorders, which are associated with a longer duration of weaning .<sup>6</sup> In fact, chronic respiratory failure is more frequent in patients with prolonged weaning .<sup>7</sup>

**The aim of the work:** is to assess predictors of prolonged weaning& survival in RICU.

#### Patients and methods:

It was a prospective observational study included fifty three (53) patients who were admitted to the RICU and required invasive MV for more than 24 hours and they were ready to be weaned. The study was conducted in RICU of Chest Department, ELkasrALainy Hospital, in the period from July 2016 to June 2017 after the approval of the ethical committee and written consents where taken from the patients or relatives.

The patients with accidental extubation and patients with previous decision to limit life-sustaining treatments were excluded from the study.

All patients were subjected to full clinical evaluation including thorough history taking from patients or their relatives and clinical examination, chest radiograph, electrocardiogram, abdominal ultrasonography, (if indicated), echocardiography computed tomography (if indicated), complete blood count and arterial blood gases analysis: including (PH, PaO2, PaCO2, SaO2%, HCO3),the samples were analyzed using automated blood gases analyzer (GEM Premier 3000: Instrumentation Laboratory Inc. Lexington MA 02421, USA). , blood chemistrywas done, including: renal function tests, liver function tests and serum electrolytes K+. (Na+. Ca++. Mg++)(Roche/Hitachi cobas с 311systen, Germany).

# Weaning from mechanical ventilation:

Weaning from MV was initiated when the patients presented with following:

clinical criteria: resolution or improvement of cause of the respiratory failure, suppressed sedation or neuromuscular blockade, satisfactory level of consciousness (Glasgow scale  $\geq$  8), absence of fever (T  $\leq$  37.5 °C), hemodynamic stability at minimal doses or in the absence of vasoactive drugs, absence of decompensated coronary insufficiency or arrhythmia with hemodynamic reperfusion.

**Gasometric criteria:** PaO2  $\geq$  60 mm Hg with FIO2  $\leq$  0.4, PaCO2 within normal (35-45mmhg) or increase  $\leq$  10 mmHg, PH within normal (7.33-7.44) or decrease  $\leq$  0.1.<sup>8</sup>

*Ventilator parameters:* Peak airway pressure of < 45cmH2O,plateau pressure of < 30 cmH2O,static lung compliance of > 33 mL/cm H2O, dynamic lung compliance of > 22 mL/cm H2O, the rapid shallow breathing index (RSBI) was less than 105 on continuous positive airway pressure (CPAP) of 5 cmH2O for 3 minutes, inspiratory oxygen fraction (FiO2) <0.4, PEEP  $\leq$  5 - 8 cm H2O.<sup>9</sup>

#### Weaning method:

A SBT was performed with a T-piece. Prior to the SBT, assisted-control or pressure-support ventilation was used depending on the patient's preference or tolerance. SBT failure was defined as the presence and persistence of one following criteria of the (1)respiratory frequency >35 cycle/min; (2) arterial  $O_2$  saturation by pulse oximetry <90% at FIO<sub>2</sub> $\geq$ 0.4; (3) heart rate >140 or <50 b/min, or increases or decreases of more than 20% compared to MV; (4) systolic blood pressure >180 or <70 mmHg, or increases or decreases of more than 20% compared to MV; (5) decreased consciousness, agitation or (6) diaphoresis and thoracicabdominal paradoxical movement.<sup>10</sup> Patients were classified as simple, difficult and prolonged weaning.simple *weaning* is defined as patients who proceed from initiation of weaning to successful extubation on the first attempt without difficulty, *difficult weaning* is defined as patients who fail initial weaning and require up to three SBTs or as long as7 days from the first SBT to achieve successful weaning and *prolonged weaning* is defined as patients who require more than three SBTs or >7 days of weaning process after the first SBT. <sup>12</sup>

#### Statistical analysis

Data was analyzed using STATA intercooled version 12.1. Quantitative data was represented as mean, standard deviation, median and range. Data was analyzed using student t-test to compare means of two groups and ANOVA with post-hoc for comparison of the means of three groups or more. Qualitative data was presented as number and percentage and compared using either Chi square test or fisher exact test. P value was considered significant if it was less than 0.05.

#### **Results**:

*Table (1): Relationship between prolonged weaning and demographic data of the studied population* 

X7	Prolonged weaning	P value	
Variable	No	Yes	
Age (year)	60.08±12.65	59±12.65	0.82
Gender	17 (42 59()	C (4C 150()	0.02
Females Males	17 (42.5%) 23 (57.5%)	6 (46.15%) 7 (53.85%)	0.82
Smoking status Non-smoker	19 (47.5%)	7 (53.85%)	0.92
Smoker Ex-smoker	10 (25%) 11 (27.5%)	3 (23.85%) 3 (23.1%)	
Smoking index Mild	1 (9.09%)	0	0.15
Moderate Heavy	4 (36.36%) 16 (100%)	0 6 (54.55%)	0110
History of previous ICU admission	10 (100 %)	0 (37.3370)	
No Yes	33 (82.5%) 7 (17.5%)	9 (69.23%) 4 (30.77%)	0.43

Data are presented as mean  $\pm$  SD (unless otherwise indicated)ICU: Intensive care unit Table (1) shows that there was no statistically significant relationship between prolonged weaning and demographic data as regard age (P= 0.82), gender (P= 0.82), smoking (status & index) (P= 0.92& 0.15 respectively) and history of previous ICU admission (P= 0.43).

 Table (2): Relationship between prolonged weaning and co-morbidities

a	Prolonged weaning		P value
Co-morbidities	No	Yes	
Cardiac disease	15 (37.5%)	7 (53.85%)	0.3
DM	13 (32.5%)	7 (53.85%)	0.2

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Hypertension	13 (32.5%)	7 (53.85%)	0.2
Neurological disease	7 (17.5%)	5 (38.48%)	0.67
Thyroid disease	3 (7.5%)	0	0.57
Hepatic disease	2 (5%)	0	1.00
Rheumatological disease	2 (5%)	0	1.00
Renal disease	1 (2.5%)	0	1.00

DM: Diabetes mellitus

Table (2) shows that there was no statistically significant relationship between prolonged weaning and co-morbidities.

*Table (3): Relationship between prolonged weaning and the causes of respiratory failure* 

Cause of respiratory failure	Prolonged weaning		P value
Cause of respiratory failure	No	Yes	
COPD	17 (61.54%)	5 (38.46%)	0.3
Pneumonia	13 (32.5%)	3 (23.08%)	0.52
IPF	4 (10%)	2 (15.38%)	0.63
Overlap syndrome	3 (7.5%)	2 (15.38%)	0.59
Bronchiectasis	2 (5%)	3 (23.08%)	0.09
OH syndrome	2 (5%)	0	0.59
Malignancy	4 (10%)	1 (7.69%)	1.00
Kyphoscoliosis	1 (2.5%)	0	1.00

COPD:Chronic obstructive pulmonary disease IPF:Interstitial pulmonary fibrosis OH syndrome: Obesity hypoventilation syndrome

Table (3) shows that there was no statistically significant relationship between prolonged weaning and the cause of respiratory failure as regard COPD (P=0.3), pneumonia (P=0.52), IPF (P=0.63), overlap syndrome (P=0.59), bronchiectasis (P=0.09), OH syndrome (P=0.59), malignancy (P=1.00) and kyphoscoliosis (P=1.00).

Table (4): Relationship between prolonged weaning and laboratory investigation

	Prolonge	d weaning	P value
Variable	No	Yes	
WBCs (/L)	13.7±5.52	16.51±4.37	0.08
Haemoglobin (gm/dL)	11.85±2.76	11.02±1.53	0.31
PLTs(/L)	231.45±94.61	210.31±72.62	0.48
ALT (IU/L)	49.05±65.56	20.77±10.03	0.0001
AST (IU/L)	67.43±131.33	22.23±8.77	0.0005
Creatinine (mg/dL)	1.28±1.35	1.06±0.36	0.54
Albumin (gm/L)	2.76±0.64	2.37±0.75	0.12
Urea (mg/dL)	26.98±21.81	46.55±21.69	0.001
Serum Na + (mmol/L)	138.58±5.48	140.46±6.70	0.38
Serum Mg++(mg/dL)	2.06±0.38	1.43±0.47	<0.0001
Serum K+(mmol/L)	4.18±0.76	3.93±0.78	0.33
Serum Ca ++(mg /dL)	8.48±0.81	6.93±1.49	<0.0001

Data are presented as mean  $\pm$  SD (unless otherwise indicated)

*Table* (5): *Relationship between prolonged weaning and arterial blood gases parameters at the beginning of the first weaning trial* 

	Prolonged weaning		P value
Arterial blood gases	No	Yes	
РН	7.43±0.06	7.42±0.11	0.73

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PaCO2 (mmHg)	45.23±11.33	53.93±13.16	0.04
PaO2 (mmHg)	76.28±20.16	70.38±14.13	0.41
SaO2%	92.18±5.65	81.31±8.75	<0.0001
HCO3(mEq/l)	34.51±7.35	33.82±6.75	0.76
P/F	191.21±52.25	172.15±37.1	0.23
Shunt (%)	11.67±3.05	11.78±1.67	0.91
(A-a) O2gradient (mmHg)	158.34±46.22	150.66±22.7	0.57

Data are presented as mean  $\pm$  SD (unless otherwise indicated)

PaCO2: Partial arterial tension of carbon dioxide PaO2: Partial arterial tension of oxygen SaO2%: Oxygen saturation

Table (5) shows the relationship between prolonged weaning and arterial blood gases parameters at the beginning of the first weaning trial: the mean level of PaCO2 was significantly higher in patients with prolonged weaning in comparison to other weaning outcomes (P=0.04). The mean level of SaO2% was significantly low in patients with prolonged weaning in comparison to other weaning outcomes (P=0.04). The mean level of SaO2% was significantly low in patients with prolonged weaning in comparison to other weaning outcomes (P=0.04).

*Table (6):* Relationship between prolonged weaning and change of arterial blood gases between the beginning and the end of weaning trial

Black and an and a strengthered	Prolonged weaning		P value
Blood gases parameters	No	Yes	
PH change	0.14±0.12	0.17±0.13	0.44
PaCO2 change	[-15.33] ± 22.73	[-18.69] ± 27.3	1.00
PaO2 change	19.5±28.70	17.85±21.49	0.99
SaO2% change	9.58±13.34	[-1.23] ± 9.64	0.006
нсоз-	3.79±6.07	6.53±5.97	0.18

Data are presented as mean ± SD (unless otherwise indicated)

Table (6)shows the relationship between prolonged weaning and change of arterial blood gases between the beginning and the end of weaning trial; there was a significant relationship between prolonged weaning and deterioration of SaO2% in the form of decrease of mean level of SaO2% (P=0.006).

*Table (7): Relationship between prolonged weaning and duration of MV&ICU stay, complications and outcomes* 

Variable	Prolonge	ed weaning	P value
variable	No	Yes	
Duration of MV(day)	8.28±5.22	18.38±4.38	0.0001
Duration in ICU(day)	13.58±6.81	22.69±3.17	0.0001
Complications			
No	33 (82.5%)	11 (84.62%)	
VAP	2 (5%)	2 (15.38%)	
CVS	1 (2.5%)	0	0.81
HAP	1 (2.5%)	0	
Hematemesis	1 (2.5%)	0	
Shock	1 (2.5%)	0	
Tracheoesophageal fistula	1 (2.5%)	0	
Death			
Yes	12 (30%)	7 (53.85%)	
No	28 (70%)	6 (46.15%0	0.18

Data are presented as mean  $\pm$  SD (unless otherwise indicated)

MV: Mechanical ventilation ICU: Intensive care unit VAP: Ventilator associated pneumonia HAP: Hospital associated pneumonia CVS: Cerebrovascular stroke

Table (7) shows that the duration of MV and ICU stay were significantly longer in patients with

prolonged weaning than other weaning outcomes (P=0.0001 for both).

Table (8): Multivariate analysis of factors predicting prolonged weaning

Variable	Odds ratio (95% confidence interval)	P value
Two or more co-morbidity compared to none or	5.21 (0.29-93.69)	0.26

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one		
WBCs (×10 <sup>3</sup> cells/mcL)	1.05 (0.77-1.45)	0.73
ALT (IU/L)	0.91 (0.81-1.03)	0.13
AST (IU/L)	0.86 (0.72-1.02)	0.1
Mg++ (mg/dL)	0.04 (0.004-0.47)	0.01
Ca++ (mg/dL)	0.32 (0.08-1.19)	0.09
Tidal volume (baseline)	1.02 (0.98-1.06)	0.35
PaCO2 (first weaning trial)	1.01 (0.90-1.14)	0.8
SaO2% (first weaning trial)	1.03 (0.67-1.57)	0.89
SaO2% change	0.68 (0.54-1.04)	0.03
Urea (mg/dL)	0.99 (0.96-1.04)	0.91
Albumin (gm/L)	0.37 (0.04-3.44)	0.38
ICU stay (day)	1.09 (0.71-1.69)	0.68
MV duration (day)	1.32 (0.79-2.21)	0.28
RSBI	1.10 (0.85-1.42)	0.46
Minute ventilation (L/min)	0.67 (0.20-2.21)	0.73

Table (8) shows; the multivariate analysis demonstrates that serum Mg++ level (P=0.03) and SaO2% changebetween the beginning and the end of weaning trial (P=0.02) were a significant predictors of prolonged weaning.

Table (9): Optimum diagnostic cut off value, AUC (parentheses 95% CI), sensitivity,
specificity, and positive (PPV) and negative predictive values (percentages) of
ventilator and blood gases parameters at baseline for predicting prolonged weaning

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Variable	Cutoff	AUC (95% CI)	Sensitivity	Specificity	PPV	NPV	Accuracy	P value
Serum Mg++(mg/dL)	≤1.5	0.83 (0.70-0.92)	61.5	92.5	72.7	88.1	77.00	<0.0001
Tidal volume(mL)	≤450	0.69 (0.55-0.81)	76.9	55.0	35.7	88	65.95	0.02
РН	≤7.1	0.57 (0.42-0.70)	30.8	95.0	66.7	80.9	62.90	0.54
PaCO2(mmHg)	≥52	0.57 (0.43-0.71)	61.5	75.0	44.4	85.7	68.25	0.55
PaO2(mmHg)	≤40	0.59 (0.44-0.72)	38.5	87.5	50.0	81.4	63.00	0.41
SaO2%	≤78	0.51 (0.37-0.65)	38.5	75.0	33.3	78.9	56.75	0.93
HCO3(mEq/L)	≤31	0.64 (0.49-0.76)	84.6	45.0	33.3	90.0	64.80	0.09

Table (9) showsthatoptimum diagnostic cut off value of baseline serum Mg++ level ( $\leq 1.5$ mg/dL) was statically significant for predicting prolonged weaning (P < 0.0001). Optimum diagnostic cut off value of baseline tidal volume ( $\leq 450$  mL) was statically significant for predicting prolonged weaning (P < 0.02).

Fig. (1): ROC curve analysis of baseline serum Mg++ level in predicting prolonged weaning

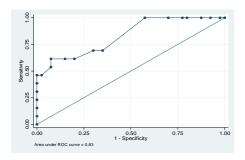
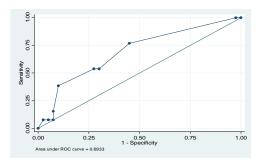


Fig. (2): ROC curve analysis of baseline tidal volume in predicting prolonged weaning



**Table (10):** Optimum diagnostic cut off value, AUC (parentheses 95% CI), sensitivity, specificity, and positive (PPV) and negative predictive values (percentages) of ventilator and blood gases parameters at the beginning of the first weaning trial for predicting prolonged weaning

0 5		01	0	0	0			
Variable	Cutoff	AUC (95% CI)	Sensitivity	Specificity	PPV	NPV	Accuracy	P value
Tidal volume(mL)	≤480	0.61 (0.47- 0.75)	69.2	52.5	32.1	0.84	60.85	0.18
Respiratory rate(cycle/min)	>19	0.64 (0.49- 0.77)	69.2	67.5	40.9	87.1	68.35	0.1
РН	>7.44	0.53 (0.39- 0.67)	46.5	72.5	35.3	80.6	59.50	0.79
PaCO2(mmHg)	≥49	0.69 (0.55- 0.81)	69.2	62.5	37.5	86.2	65.85	0.02
PaO2(mmHg)	≤94	0.58 (0.43- 0.71)	100	17.5	28.3	100	58.75	0.39
SaO2%	≤91	0.88 (0.77- 0.96)	100	60	44.8	100	80.00	<0.0001
HCO3(mEq/L)	≤31	0.52 (0.38- 0.66)	46.2	70.0	33.3	80.0	58.10	0.86
P/F	≤151	0.62 (0.47- 0.75)	38.5	85.0	45.5	81.0	61.75	0.19
Shunt	>10.3	0.59 (0.45- 0.72)	92.3	37.5	32.4	93.7	64.90	0.27
(A-a) gradient	>136	0.51 (0.37- 0.65)	92.3	40	33.3	94.1	66.15	0.87

Table (10) shows that optimum diagnostic cut off value of PaCO2 at first weaning trial ( $\geq$ 49mmHg) was statically significant for predicting prolonged weaning (P <0.02). Optimum diagnostic cut off value of SaO2% at first weaning trial ( $\leq$ 91%) was statically significant for predicting prolonged weaning (P <0.0001).

Fig. (3): ROC curve analysis of PaCO2 (first weaning trial) in predicting prolonged weaning

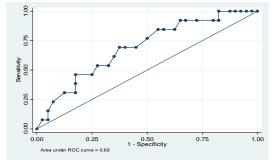
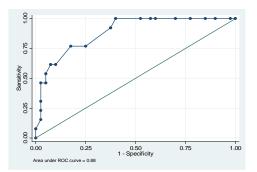


Fig. (4): ROC curve analysis of SaO2% (first weaning trial) in predicting prolonged weaning



**Table (11):** Optimum diagnostic cut off value, AUC (parentheses 95% CI), sensitivity, specificity, and positive (PPV) and negative predictive values (percentages) of changes in ventilator and blood gases parameters between the beginning and the end of weaning trial for predicting prolonged weaning

Variable	Cutoff	AUC (95% CI)	Sensitivi ty	Specificity	PPV	NPV	Accurac y	P value
PH change	>0.23	0.57 (0.43-0.71)	38.5	85	45.5	81.0	61.75	0.48
PaCO2 change	>[-46]	0.50 (0.36-0.64)	69.2	10.0	20	50	39.60	1.00
PaO2 change	≤42	0.50 (0.36-0.64)	100	20	28.9	100	60.00	0.99
SaO2% change	≥5	0.76 (0.62-0.86)	84.6	65.0	44.0	92.9	74.80	0.003
HCO3 change	>6	0.62 (0.48-0.75)	61.5	67.5	38.1	84.4	64.50	0.19

Table (11) shows that optimum diagnostic cut off value of SaO2% change in the form of decrease between baseline and first weaning trial ( $\leq$ 5) was statically significant for predicting prolonged weaning (P < 0.003).

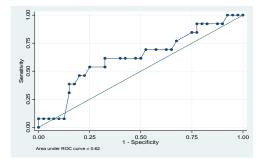


Fig. (5): ROC curve analysis of SaO2% change between the beginning and the end of weaning trial in predicting prolonged weaning

#### **Discussion:**

We tried in this study to determine the predictors of prolonged weaning weaning during of mechanically ventilated patients in respiratory intensive care unit; we included 13 patients (24.5%)with prolonged weaning, 40 cases other weaning outcomes (simple and difficult weaning).

We found in our study that there was no significant relationship between prolonged weaning and age, gender this result was in agreement with the study of Jacobo et al  $^{12}$ , who found that there was no significant difference among weaning outcomes as regarding age and gender (P= 0.99).

This study found that there was no significant relationship between prolonged weaning and the cause of respiratory failure as regard COPD (P= 0.3), pneumonia (P= 0.52), IPF (P= 0.63), overlap syndrome (P= 0.59), bronchiectasis (P=0.09), OH syndrome (P= 0.59), malignancy (P= 1.00) and kyphoscoliosis (P=1.00) this result disagreed with the study of Jacoboet al,<sup>12</sup> who found that there was significant relation between patient with COPD and prolonged weaning (p=0.018) and in other study Awaloei and Luke;<sup>13</sup> who found that patients with pneumonia are associated with prolonged weaning (P=0.002).

There was no significant relationship between prolonged weaning and co-

morbidities this result disagreed with the study of Awaloei and Luke;<sup>13</sup>who found that patients with cardiovascular failure (P= 0.047) are associated with prolonged weaning.

We found that patients with prolonged weaning associated with low serum Mg++ level, this result agreed with the study of Adel et al, <sup>14</sup>who found that, there was an association between low serum magnesium levels and weaning failure. This can be explained by its effect on neuromuscular abilities and direct impairment of the contractile properties of the diaphragm.

We found in our study that optimum diagnostic cut off value of serum Mg++ level (≤1.5) was asignificant predictor for prolonged weaning (P <0.0001), this result was in agreement with the study of Thongprayoon et al,<sup>15</sup>who found that hypomagnesaemia atadmission (< 1.5 mg/dl) was associated with an increased requiring MV in patients with acute respiratory failure (OR: 1.69; 1.19-2.36) and as a cause of failure of weaning from mechanical ventilation and proposed patients to difficult and prolonged weaning.

Our study showed that the mean level of baseline tidal volume was significantly lower in patients with prolonged weaning in comparison to patients with other weaning outcomes and was a significant predictor of prolonged weaning, this result disagreed with the result of Conti et al,<sup>16</sup> who found that, vital capacity, tidal volume, VE, respiratory frequency (RR), maximum inspiratory pressure (PImax) and RSBI are poor predictors of weaning outcome in an ICU population. This was being explained by low tidal volume can lead to inadequate ventilation with causing atelectotrauma.<sup>17</sup>

We found that optimum diagnostic cut off value of tidal volume ( $\leq 450$ ) was a significant predictor for prolonged weaning (P < 0.02).

As regard measurement of PaCO2 at the beginning of the first weaning trial we found that PaCO2 was significantly higher in patients with prolonged weaning in comparison to other weaning outcomes (P= 0.04) this result agreed with the study of Jacoboet al, <sup>12</sup> who found that on the day of the first SBT patients with prolonged weaning had a higher PaCO2 (P= 0.006), so higher PaCO2 was independently related to the prolongation of weaning as these patients develop increased cardiopulmonary stress during an unsuccessful SBT.

PaCO2 is directly associated with the imbalance between ventilatory demands and capacity in patients who are not yet ready to be disconnected from the ventilator, increased CO2 retention during spontaneous breathing strongly predicts prolonged weaning and worse survival. If high level of PaCO2 was detected in the patient at the onset of weaning, the clinician should implement measures aimed to improving the outcome of weaning from MV.<sup>18</sup>

Our study found that optimum diagnostic cut off value of PaCO2 at first weaning trial ( $\geq$  49) was a significant predictor for prolonged weaning (P <0.02), this result agreed with the studyof Jacobo et al, <sup>12</sup>who found that PaCO2  $\geq$  54 mmHg during

the spontaneous breathing trial independently predicted prolonged weaning (P=0.001).

Our study showed that at the beginning of the first weaning trial, the mean level of SaO2% was lower in patients with prolonged in comparison to patients with other weaning outcomes (P= 0.0001), this result disagreed with the study of Georgakas et al,<sup>19</sup> who found that, there was no difference between weaning groups, regarding measurement of SaO2% at the start of SBT. This can be explained by hypoxemia increases the work of breathing per minute by increasing total minute ventilation and in the presence of hypoxemia oxygen delivery to the respiratory muscles may be inadequate and predisposing to muscle fatigue or failure.<sup>20</sup>

Our study found that optimum diagnostic cut off value of SaO2% at beginning of first weaning trial  $\leq$  91 was a significant predictor for prolonged weaning (P < 0.0001).

Multivariate analysis of our study showed that SaO2% change in the form of decrease of mean level of SaO2% ( $\geq$ 5) between the beginning and the endof a weaning trial (P=0.02)was significant predictor for prolonged weaning this result agreed with study of Georgakas et al, <sup>20</sup>who found that, a decrease of less than 4% in ScvO2 values between the beginning and the end of an SBT was also independently associated with а successful outcome.

Our study showed that duration of MV was significantly long in patients with prolonged weaning, this result agreed with the study of Awaloei and Luke; <sup>14</sup> who found that duration more than 5 days on MV prior to start of weaning are associated with prolonged weanin

#### **Conclusions**:

Several factors were associated with prolonged weaning, however, when subjected to multivariate analysis, only serum Mg++& SaO2% change significantly predict prolonged weaning. Prolonged weaning is associated with increased ICU stay and higher rate of tracheostomy.

#### **References**:

- BolesJ M, Bion J, Connors A ,et al., Weaning from mechanical ventilation .European Respiratory Journal. 2007; 29(5):1033-56.
- 2. Esteban A, Alia I, Ibañez J, et al., Modes of mechanical ventilation and weaning. A national survey of Spanish hospitals.The Spanish Lung Failure Collaborative Group.Chest.1994; 106:1188–1193.
- 3.Vallverdú I, Calaf N, Subirana M, Net A, Benito S, Mancebo J. Clinical characteristics, respiratory functional parameters, and outcome of a twohours T-piece trial in patients weaning from mechanical ventilation. Am J RespirCrit Care Med:1998; 158:1855– 1862.
- 4. Schönhofer B, Geiseler J, Dellweg D et al., Prolongedweaning: S2kguidelinepublished by the German Respiratory Society. Pneumologie. 2014; 68: 19-75
- Funk GC, Anders S, Breyer MK, Burghuber OC, Edelmann G, Heindl W, Hinterholzer G, Kohansal R, Schuster R, Schwarzmaier-D'Assie A, Valentin A, Hartl S.Incidence and outcome of weaning from mechanical ventilation according to new categories.EurRespir. 2010; J 35:88–94
- Brochard L, Rauss A, Benito S, et al., Comparison of three methods of gradual withdrawal from ventilatory support during weaning from mechanical ventilation. Am J RespirCrit Care Med. 1994; 150:896– 903.
- 7. Funk GC, Anders S, Breyer MK, et al., Incidence and outcome of weaning from mechanical ventilation according to new categories. EurRespir J. 2010;35: 88–94.
- Goldwasser R, Farias A, Freitas EE, Saddy F, Amado V, Okamoto V. Mechanical ventilation of weaning interruption.J Bras Pneumol. 2007; 33(Suppl 2S):S128–136.

- 9. Patel KN, Ganatra KD, Bates JH, et al., Variation in the rapid shallow breathing index associated with common measurement techniques and conditions. Respir Care.2009; 54:1462– 1466.
- 10. Ferrer M, Sellares J, Valencia M, Carrillo A, Gonzalez G, Badia JR, Nicolas JM. Torres A. Non-invasive ventilation after extubation in hypercaphic patients with chronic respiratory disorders: randomised controlled trial. Lancet. 2009: 374:1082-1088.
- 11. Brochard L. Pressure support is the preferred weaning method. As presented at the 5th International Consensus Conference in Intensive Care Medicine: Weaning from Mechanical Ventilation. Hosted by ERS, ATS, ESICM, SCCM and SRLF; Budapest, April 28–29, 2005.
- Jacobo S, Miquel F. Predictors of prolonged weaning and survival during ventilator weaning in a respiratory ICU Intensive Care Med. 2011 May; 37(5):775-84.
- Awaloei A, Luke's St. Medical Center

   Quezon City, Quezon, Philippines Predictors and Outcomes of Prolonged Weaning Among Intubated Patients on Mechanical Ventilation.China Critical Care chest.2016.02.168.
- 14. Adel Hassan A G, El-Komy M H, Gad D M et al., Assessment of weaning failure in chronic obstructive pulmonary disease patients under mechanical ventilation in Zagazig University Hospitals, Egyptian Journal of Chest Diseases and Tuberculosis. January 2017; 66 (1): 65-74
- 15. Thongprayoon C., Cheungpasitporn W., Srivali N., Erickson S. B. Admission serum magnesium levels and the risk of acute respiratory failure Int J ClinPract, November 2015, 69, 11, 1303–1308.
- 16. Conti G, Montini L, Pennisi MA, et al., A prospective, blinded evaluation of indexes proposed to predict weaning from mechanical ventilation. Intensive Care Med 2004; 30:830–836.
- 17.Gajic, Ognjen; SaqibDara; Jose Mendez; AbedolaAdensanya; Emir

Festic; Sean Caples; RimkiRana; Jennifer StSauver; James Lymp; BekeleAfessa "Ventilator-associated lung injury in patients without acute lung injury at the onset of mechanical ventilation". Critical Care Medicine-Baltimore. 2004; 32 (9): 1817–1824.

- MacIntyre NR. Respiratory mechanics in the patient who is weaning from the ventilator.Respir Care. 2005 Feb; 50(2):275-86.
- Georgakas I, Afroditi K. Boutou, Georgia Pitsiou1, Ioannis Kioumis4, Milly Bitzani3, Kristina Matei5, Paraskevi Argyropoulou1,

IoannisStanopoulos Central Venous Oxygen Saturation as a Predictor of a Successful Spontaneous Breathing Trial from Mechanical Ventilation: A Prospective, Nested Case-Control Study the Open Respiratory Medicine Journal ISSN: 2018, 12; 1874-3064.

 Jubran, A, Mathru, M, Dries, D. Continuous recordings of mixed venous oxygen saturation during weaning from mechanical ventilation and the ramifications thereof .Am J RespirCrit Care Med. 1998; 158; 1763-9.