DISCUSSION

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Weaning from mechanical ventilation can be defined as the process of abruptly or gradually withdrawing ventilatory support. Two large multicenter studies [1, 2] have demonstrated that mechanical ventilation can be discontinued abruptly in approximately 75% of mechanically ventilated patients whose underlying cause of respiratory failure has either improved or been resolved. The remaining patients will need progressive withdrawal from mechanical ventilation.

Weaning from mechanical ventilation usually implies two separate but closely related aspects of care, discontinuation of mechanical ventilation and removal of any artificial airway. The first problem the clinician faces is how to determine when a patient is ready to resume ventilation on his or her own. Several studies[1-5]have shown that a direct method of assessing readiness to maintain spontaneous breathing is simply to initiate a trial of unassisted breathing. Once a patient is able to sustain spontaneous breathing, a second judgement must be made regarding whether the artificial airway can be removed. This decision is made on the basis of the patient's mental status, airway protective mechanisms, ability to cough and character of secretions. If the patient has an adequate sensorium with intact airway protection mechanisms, and is without excessive secretions, it is reasonable to extubate the trachea.

Chronic Obstructive Pulmonary Disease (COPD) is a major cause of chronic morbidity and mortality throughout the world. Many people suffer from this disease and die prematurely from it or its complications. [44, 45] and the Global Burden of Disease Study projected that COPD will become the third leading cause of death worldwide by 2020. [44, 45]

Our study was carried on 100 COPD patients admitted to alexandria main university hospital and successful weaning was observed in67 patients while failed weaning was observed in 33 patients.

In our study while assessing GCS as predidtor of weaning Glascow Coma Score of less than 11T was recorded in4 patients(12.1% of the total number of patients in group1)and Glascow Coma Score of 11T was recorded in29 patients(87.9% of the total number of patients in group1),while in group2 there was no patients with Glascow Coma Score of less than 11T and Glascow Coma Score of 11T was recorded in 67 patients(100% of the total number of patients in group2) with statistical significance between the 2 groups(p=0.01)as Glascow Coma Score of 11 was recorded in significantly higher number of patients in group2.

GCS showed the highest specificity 100% ,positive predictive value(PPV) 100% and accuracy 71%, while it showed the lowest sensitivity 12.1% and it showed a negative predictive value of 69.8% as a predictor of failure of weaning from MV..In relation to our study a study was carried by Zheng et al(2011) [202]on 20 COPD patients with respiratory failure who had undergone endotracheal intubation and MV from March2007 to November 2009(treatment group).

These patients were put on SIMV plus PSV mode of mechanical ventilator. When the period of improved GCS of 15 time window had appeared and kept for2 hours endotracheal tube was removed and nasal mask with PSV plus PEEP was used with gradual decrease of pressure support till weaning of MV. Nineteen patients who were treated with MV with ordinary way of weaning from March 2005 to March 2007 served as the control group. Prior to the MV, the ventilation and oxygenation index , the length of invasive MV, total MV time, total hospital stay, re intubation and ventilator associated pneumonia (VAP) occurred in the number of cases were observed and compared between two groups. [202]

There was no significant difference in the ventilation and oxygenation index prior to the MV. Compared with control group, in treatment group, the length of invasive ventilation (days: 3.2±1.1 vs. 10.5±3.2), the total duration of MV (days: 4.8±2.5 vs. 10.5±3.2), the length of hospital stay (days: 17±3 vs. 22±7) were significantly shorter (all $P<0.01$), and the incidence of VAP was significantly lower (cases: 0 vs. 5, $P<0.01$), while the number of re intubation was slightly higher but without statistical significance (cases: 3 vs. 1, $P>0.05$). [202]

In our study on assessing presence of structural brain damage as a predictor of weaning, structural brain damage was present in 2patients(6.1% of the total number of patients in group1),while in group2 structural brain damage was present in4 patients(6% of the total number of patients in group2) with no statistical significance between the 2groups. (p=1). The 2 patients in group1 presented with altered mental status, while the 4 patients in group2 presented with one side lag or facial palsy. As observed structural brain damage was present in 6 patients in our study,4 patients of them(67%) presented with successful weaning and extubation while 2 patients(33%) presented with failed weaning and extubation. In relation to our study, a study carried by Karanjia N et al(2011) [203].They conducted a retrospective review of patients admitted to the neurocritical care unit of a tertiary care hospital from January 2002 to March 2007.

Of 1,265 patients who were intubated because of primary neurological injury of brain, spinal cord, or peripheral nerve, 25 (2%) died before extubation and 767 (61%)(compared to 4patients(67%) successfully extubated in our study) were successfully extubated. Tracheostomies were placed in 181 (14%) patients, of which, 77 (6.1%) were completed before a trial of extubation and 104 (8.2%) after extubation failure. A total of 129 (10%) patients were reintubated(compared with 2 patients(33%)failed extubation in our study); 77 (6.1%) were reintubated within 72 h, meeting the definition of extubation failure. The other 52 (4.1%) were intubated after 72 h usually in the setting of pneumonia or decreased mental status. Ninety-nine of the patients reintubated had primary brain injury and resulting encephalopathy. All were successfully reintubated. Most patients intubated as a result of a primary brain injury (981) were successfully extubated. The most common clinical scenario leading to reintubation in these encephalopathic patients was respiratory distress associated with altered mental status [59 patients (59%)]. These patients usually had atelectasis and decreased minute ventilation, independent of fever, pneumonia, aspiration, and increased work of breathing [39 patients (39%)].This study concluded that in patients with encephalopathy and primary brain injury who were reintubated, respiratory distress caused by altered mental status was the most common cause of reintubation. These patients demonstrated signs disrupted ventilation usually with periods of prolonged hypoventilation.

Increased work of breathing from lung injury due to pneumonia or aspiration was not the most common cause of reintubation in this population.[203] In our study the 2 patients with failed weaning and extubation were suffering from altered mental status. The absence of statistical significance in our study is explained by the limited number of patients having structural brain damage (only 6 patients).

In our study, on assessing the presence of electrolyte disturbance as a predictor of weaning, electrolyte disturbance was present in 4 patients (12.1% of the total number of patients in group1), while in group2 electrolyte disturbance was present in12 patients (17.9% of the total number of patients in group 2) with no statistical significance between the 2 groups. 95 patients in our study presented with normal phosphorus level and 29 patients of them suffered failed weaning. While 4 patients presented with very low phosphorus and all of them suffered failed weaning. Only one patient presented with both low levels of phosphorus and potassium and was successfully weaned. ($p=0.458$). In relation to our study, a study was carried out by Farah R et al on 2013[204].They studied two hundred and fifty-five patients who were admitted because of worsening in COPD, from October 2010-April 2011. A comparison was made between the group with normal blood phosphorus (2.5-4.5 mg%), group of patients with low phosphorus (2-2.5 mg%) and group with very low phosphorous values (<2.0 mg%). Ninety-five per cent of all admissions had normal blood phosphorus levels (compared to 95 patients (95%)in our study), 3.3% had low phosphorus levels, and only 1.7% of all admissions had very low phosphorus levels(compared to 4 patients(4%) in our study). 2.4% of patients had both low levels of phosphorus and potassium(compared to 1 patient(1%)in our study). All patients (100%) with very low phosphorus needed mechanical ventilation(compared to 4patients in our study had very low phosphorus levels and all of them suffered from failed weaning(100%)), compared to 62.5% of patients with low phosphorus and 16.9% of patients with normal phosphorus levels(compared to 95 patients with normal phosphorus levels of which 29 patients suffered failed weaning(30%)in our study).This difference in percentage can be explained by the difference in number of patients between the 2 studies(100 patients in our study compared with255 patients in the other study). In addition, 16 ventilated patients (33% of all ventilated patients) had low potassium values. So, the conclusion was that low blood phosphorus levels contribute to an increase in: COPD flare-up, need for ventilation, duration of hospitalisation, days in intensive care units and finally increased rate of mortality. Accordingly, close monitoring and careful adjustment of disorders correlated to electrolyte such as phosphorus, are crucial and may improve prognosis and also increase the survival rate of patients with COPD.[204] The absence of statistical significance in our study can be explained by the small number of patients having abnormal blood phosphorus level (only 5 patients).

In our study, on assessing the presence of taking sedatives or hypnotics as a predictor of weaning , taking sedatives or hypnotics before the trial of weaning was absent in group1,while in group2 it was present in4 patients(6% of the total number of patients in group2) with no statistical significance between the 2 groups.($p=0.299$).In relation to our study, a study was carried by Barrientos VR et al on 1997 [205].This study was done on all ICU admissions (medical, surgical and trauma) requiring mechanical ventilation for > 24 hrs in a community hospital. A total of 108 patients were included in the study. Patients were randomized to receive midazolam or propofol. The dose range allowed for each drug was 0.1 to 0.5 mg/kg/hr for midazolam and 1 to 6 mg/kg/hr for propofol. The lowest dose that achieved an adequate patient-ventilator synchrony was infused. All patients received

0.5 mg/kg/24 hrs of morphine chloride. If sedation could not be achieved by infusing the highest dose of midazolam or propofol, the case was recorded as a therapeutic failure. In the propofol group, serum triglycerides were determined every 72 hrs. Concentrations of > 500 mg/dL were also recorded as a therapeutic failure. When the patient was ready for weaning, sedation was interrupted abruptly and the time from interruption of sedation to the first T-bridge trial and to extubation was measured. Cost analysis was performed based on the cost of intensive care in our unit ($54/hr). In the midazolam group (n = 54), 15 (27.8%) patients died; 11 (20.4%) patients had therapeutic failure; and 28 (51.8%) patients were subjected to a T-bridge trial. In the propofol group (n = 54), these proportions were 11 (20.4%), 18 (33.4%) [including seven due to inadequate sedation, and 11 due to hypertriglyceridemia]), and 25 (46.2%), respectively. None of these values was significantly different between the two groups. Duration of sedation was 141.7 +/- 89.4 (SD) hrs and 139.7 +/- 84.7 hrs (p = NS), and cost (US dollars) attributed to sedation was $378 +/- 342 and $1,047 +/- 794 (p =.0001) for the midazolam and propofol groups, respectively. In the midazolam group, time from discontinuation of the drug infusion to extubation was 97.9 +/- 54.6 hrs (48.9 +/- 47.2 hrs to the first disconnection, and 49.0 +/- 23.7 hrs to extubation). In the propofol group, time from discontinuation of the drug infusion to extubation was 34.8 +/- 29.4 hrs (4.0 +/- 3.9 hrs to the first disconnection, and 30.8 +/- 29.2 hrs to extubation). The difference between the two groups in the weaning time was 63.1 +/- 12.5 (SEM) hrs (p <.0001). Cost per patient in the midazolam group (including ICU therapy and sedation with midazolam) was $10,828 +/- 5,734. Cost per patient in the propofol group was $9,466 +/- 5,820, $1,362 less than in the midazolam group. [205]

In this study of critically ill patients sedated with midazolam or propofol over prolonged periods, the conclusion was that midazolam and propofol were equally effective as sedative agents. However, despite remarkable differences in the cost of sedation with these two agents, the economic profile is more favorable for propofol than for midazolam due to a shorter weaning time associated with propofol administration. [205] In our study only 4 patients (4%) who received sedation before the trial of weaning and all of them(100%) were successfully weaned and this is quietly adequate with the study done by Barrientos VR et al on1997[205] as they observed that in the midazolam group (n = 54), 28 (51.8%) patients were subjected to a T-bridge trial and time from discontinuation of the drug infusion to extubation was 97.9 +/- 54.6 hrs (48.9 +/- 47.2 hrs to the first disconnection, and 49.0 +/- 23.7 hrs to extubation),while in the propofol group 25 patients (46.2%) were subjected to a T-bridge trial, and time from discontinuation of the drug infusion to extubation was34.8 +/- 29.4 hrs (4.0 +/- 3.9 hrs to the first disconnection, and 30.8 +/- 29.2 hrs to extubation).while in our study 4 patients were receiving sedation and 100% of them were subjected to t-piece trial and extubation.this difference in percentage can be explained by the difference in the number of patients between the 2 studies(4 in our study vs. 108 in the other study). According to these 2 studies we can also conclude that the use of sedation prior to weaning can provide better weaning outcome. The absence of statistical significance in our study can be explained by the small number of patients who received sedation prior to the trial of weaning (only 4 patients).

In our study we tested the ability of the presence of abnormal (high) value of static compliance as a predictor of weaning and we found that abnormal value of static compliance was present in 18 patients(54.5% of the total number of patients in group1),while in group2 abnormal value of static compliance was present in 46 patients

(68.7% of the total number of patients in group2) with no statistical significance between the 2 groups.($p=0.167$).In relation to our study, a study was done by Gamal M[11] et al on 2010.This study was conducted on 70 adult patients admitted to Critical Care Department at Alexandria University Main Hospital after being approved by the ethical committee. Then patient was discontinued from MV by the physician of charge and success of weaning was determined by the ability to breath normally away from MV for 48 hours. The decision to return to MV was made by the physician in charge (who was completely blind to the study).

According to the success of the weaning trial patients were classified into 2 groups: group 1 : failure of weaning group and group 2 : success of weaning group.

55 patients succeeded in the weaning trial (78.5%) while 15 patient failed (21.5%). Static compliance (Cst) in group 1 ranged from 22 to 33 with a mean of (27.60 ± 3.18) while it ranged from 27 to 40 with a mean of (32.60 ± 2.94) in group 2. Static compliance was significantly higher in group 2 ($p<0.001$). Static compliance had sensitivity (71.45), specificity (81.82), PPV (50.68), NPV (91.48), accuracy (79) and AUC (0.875).This study used a threshold value of ≥30 ml/cmH2O to best predict successful weaning.[11] In contrast to this study, our study showed that static compliance ranged from 30.0-114.2 ml/cmH20 with a mean of(61.7 ± 20.5) in group1, while in group2 it ranged from40.0-121.4ml/cmH2O with a mean of(65.1 ± 15.3) with no statistical significance between the 2 groups.($p=0.351$). This difference in statistical significance between the 2 studies can be explained by the fact that that study was done on mechanically ventilated patients in general while our study was done on COPD patients in particular and COPD patients tend to have higher values of static compliance than other categories of patients due to pathological changes present in their alveoli that may affect plateau pressures and tidal volumes in these patients. In addition, assessing the degree of severity of COPD according to GOLD staging classification in our study was not applicable due to lack of facility to measure FEV1 and this may have altered the significance of static compliance. Another study was done by Zanotti E et al on 1995.[206] The study included 23 COPD patients ventilated for acute respiratory failure and studied within 24 hours from intubation. A significant difference ($p < 0.001$) has been found in Cst, rs (62.7 +/- 17.% versus 111.6 +/- 18.0 ml/cm H2O) in the weaned group (A) and the not weaned group (B) respectively. The threshold value of 88.5 ml/cmH2O was identified by discriminant analysis and provided the best separation between the two groups, with a sensitivity of 0.85 and a specificity of 0.87. [206] Again this difference in statistical significance between our study and the other study can be explained by 2 factors. First, the cut off value used in this study(88.5ml/cmH2O) was different from that of our study(40-60cmH2O).Second, this study was done in the first 24 hours after intubation, while in our study static compliance was measured just before weaning.

In our study we examined the effect of the presence of abnormal(high) value of resistance as a predictor of weaning and we found abnormal value of resistance was present in 33 patients (100% of the total number of patients in group1),while in group 2 abnormal value of resistance was present in 32 patients(47.8% of the total number of patients in group2) with statistical significance between the 2groups as abnormal value of resistance was present in significantly lower percentage of patients in group2.($p<0.0001$). Presence of abnormal value of resistance showed the highest sensitivity 100% and NPV 100% and it showed a specificity of 52.2% , PPV 50.8% and accuracy 68% as a predictor of failure of weaning from MV.In relation to our study, a study was done by Nozawa E et al on 2003.[207] This study was conducted on 45 patients in their postoperative period of cardiac surgery, who required long-term mechanical ventilation for more than 10 days and had to undergo tracheostomy due to unsuccessful weaning from mechanical ventilation. Successful weaning from mechanical ventilation was achieved in 22 patients, while the procedure was unsuccessful in 23 patients. No statistically significant difference was observed between the groups in regard to resistance (p=0.21). Success in mechanical ventilation weaning was defined as the patient's complete independence of the ventilator for a period > 48 hours, maintaining oxygen saturation above 93% with oxygen support and no fatigue in the respiratory pattern (tachypnea, use of the accessory muscles, paradoxical movements, or asynchrony between the chest and the abdomen). Failure in mechanical ventilation weaning was defined as the patient's dependence on the ventilator for a period longer than 8 weeks (56 days) or when death occurred. Resistance ranged from 8.7+/-6.3cmH2O/L/sec in successful weaning group while it ranged from 7+/-6 cmH2O/L/sec.[207]This difference in statistical significance between the 2 studies can be explained by the fact that that study was done in the postoperative cardiac surgery patients while our study was done in COPD patients and post operative patients do not have abnormalities in small airways that may be found in COPD patients.

We tried in our study to assess the effect of acid base disturbances on weaning of COPD patients and we found acid base disturbance was assessed just before weaning and it was present in 4 patients (12.1% of the total number of patients in group1), while in group2 acid base disturbance was present in 10 patients (14.9% of the total number of patients in group2) with no statistical significance between the 2groups (p=1). A total of 14 patients was documented to have acid base disturbances, 11 patients suffered mild respiratory acidosis with PH ranged between 7.32-7.34 and 4 of them (36%) suffered failed weaning and needed NIV after extubation. PaCO2 ranged between 45-50mmHg. Serum HCO_3 between 22-25meq/L with administration of IV $NaHCO_3$ (renal impairment was present) The remaining 3 patients suffered metabolic and respiratory alkalosis and none of them required NIV (successful weaning).

In relation to our study, a study was done by Terzano C et al on 2012.[208] In that study sixty-seven consecutive patients who were hospitalized for hypercapnic COPD exacerbation had their arterial blood gases and blood lactate assessed. Nine patients were transferred to the intensive care unit. NIV was performed in 11/17 (64.7%) mixed respiratory acidosis-metabolic alkalosis, 10/36 (27.8%) respiratory acidosis and 3/5 (60%) mixed respiratory-metabolic acidosis patients ($p = 0.026$), with durations of 45.1 ± 9.8, 36.2 ± 8.9 and 53.3 ± 4.1 hours, respectively ($p = 0.016$). The duration of ventilation was associated with higher blood lactate ($p<0.001$). That study concluded that mixed acid-base and lactate disorders during hypercapnic COPD exacerbations predict the need for and longer duration of NIV. [208]

As a comparison, in our study a total of 14 patients was documented to have acid base disturbances, 11 patients suffered respiratory acidosis and 4 of them (36%)suffered failed weaning and needed NIV after extubation. This is different from the percentage found in the other study (27.8%) and this can be explained by the smaller number of patients having acid base disturbance in our study. And the remaining 3 patients suffered metabolic and respiratory alkalosis and none of them required NIV(successful weaning). There was no cases in our study reported to have mixed respiratory and metabolic acidosis as these cases is considered to be not fit for weaning so, they were not included in the study. The absence of statistical significance in our study can be explained by the small number of patients having acid base disturbances (14 patients).

We tried to identify the effect of BMI on weaning of COPD patients. We found that body mass index (BMI) ranged from16.0-33.8kg/m2 with a mean of 22.7±3.4 in group1, while in group2 it ranged from18.8-36.8kg/m2 with a mean of 22.7±3.5 with no statistical significance between the 2groups.(p=0.817). In relation to our study, a study was carried out by Li-dong S et al on 2013.[209] 94 patients with severity COPD were divided into the control group (BMI<21)(56 patients) and the study group (BMI>21)(38 patients). These two groups were treated by similar symptomatic therapies such as mechanical ventilation, antibacterial, antispasmodic, relieving asthma, antitussive, expectorant, correction of electrolyte imbalance and acid-base balance disorders, strengthen nutritional support. Compared with the control group, the study group had shorter duration of invasive mechanical ventilation (8.56 ±047 vs 12.45±1.18days), non-invasive mechanical ventilation time (5.50 ±0.61 vs. 12.5 ±1.18days), total mechanical ventilation time (12.23 ±0.40 vs. 18.50±0.61days), total hospital stay (P<0.01). There are significant differences between these two groups in re-intubation rate(3(7.9%) vs. 11 (19.60%)), VAP occurred in the number of case(5 vs. 23patients), hospital mortality rate in 28 days(7 (21.78%)vs. 25 (45.45%))(P<0.05).That study concluded that it is difficult to wean successfully from sequential mechanical ventilation for severity COPD patients (BMI<21), so BMI as one of important reference index can be used to estimate the optimal time for weaning from sequential mechanical ventilation for severity COPD patients. [209] In agreement to that study, our study showed that normal BMI(18.5-25kg/m2) was found in 92 patients.63 patients(63%) showed normal BMI and successful weaning, while 29 patients(29%) showed normal BMI and failed weaning. There was only 1 patient with BMI less than 18.5 and this case suffered failed weaning. The difference in the percentage of failed weaning between the 2 studies (3% reintubation rate in their study vs. 29% failed weaning rate in our study) can be explained by the difference in the number of patients having normal BMI in the 2 studies(38 in their study vs. 92 in our study). The absence of statistical significance in our study can be explained by the small number of patients having BMI outside the normal range (only 8 cases).

In our study we tried to examine whether the presence of ischaemic heart disease has an effect on weaning of COPD patients or not and we found that ischaemic heart disease was present in 10 patients (30.3% of the total number of patients in group1),while in group2 ischaemic heart disease present in 18 patients(26.9% of the total number of patients in group2) with no statistical significance between the 2 groups.(p=0.719).

In relation to our study, a study was done by Frazier SK et al on 2006.[210] This study was a prospective, repeated-measure, descriptive investigation that studied 43 ventilated MICU patients. Slightly more than half of participants were male (53%), and participants had a mean age of 51.1 +/- 14.6 years. Myocardial ischemia was evaluated by examination of plasma cardiac troponin I, creatine phosphokinase-myocardial band (CK-MB), and ST-segment changes on electrocardiogram. Continuous electrocardiographic data were obtained by a calibrated, frequency-modulated, continuous 3-channel electrocardiographic recorder using leads I, II, and V2. The patients were examined to detect whether they exhibited ST-segment deviation at some point during data collection (baseline mechanical ventilation, during weaning, after extubation). Twenty-four participants exhibited ST-segment deviation at baseline, 7 during weaning, and 8 after extubation. Nine participants exhibited ST-segment deviation at >1 data collection time point. None had ST-segment deviation at all 3 time points. Cardiac enzyme concentrations were highly variable; five participants demonstrated clinically important increases in either CK-MB and/or troponin I. Thirty-five percent of participants required >1 weaning trial. There were no significant differences in CK-MB or troponin I levels between those participants who were successfully weaned with 1 trial and those who failed to wean during that first trial. [(210)] As a comparison, in our study we could not detect the exact time of ST segment deviation due to lack of facility of continuous ECG monitoring, but we found that 28 patients had ishaemic heart disease and 10 of them (35%) suffered failed weaning and this was similar to the other study which discovered that thirty-five percent of participants required >1 weaning trial.

Heart failure was also described as a predictor of weaning and we found that heart failure was present in 6 patients(18.2% of the total number of patients in group 1),while in group2 heart failure was present in 10 patients (14.9% of the total number of patients in group2) with no statistical significance between the 2groups.(p=0.676). In relation to our study, a study was conducted by Lara TM et al on 2013.[(211)] They conducted a prospective, observational cohort study of 101 patients who underwent on-pump coronary artery bypass grafting. B-type natriuretic peptide was measured postoperatively after intensive care unit admission and at the end of a 60-min spontaneous breathing test. Weaning failure was considered as either the inability to sustain spontaneous breathing after 60 min or the need for reintubation within 48 h. Of the 101 patients studied, 12 patients failed the weaning trial. There were no differences between the groups in the baseline or intraoperative characteristics, including left ventricular function, and lengths of the cardiac procedure and cardiopulmonary bypass. The B-type natriuretic peptide levels were significantly higher at intensive care unit admission and at the end of the breathing test in the patients with weaning failure compared with the patients who were successfully weaned. The BNP levels were significantly higher in the patients who failed to wean compared with those who weaned successfully, both at ICU admission (214 ng/mL [65-487] *vs*. 73 [28-127], $p =$ 0.02) and after the SBT (416 ng/mL [311-561] *vs*. 140 [80-226], $p<0.001$). A BNP concentration of 299 ng/L at the end of the SBT identified weaning failure with 92% sensitivity and 88% specificity. In a multivariate model, a high B-type natriuretic peptide level at the end of a spontaneous breathing trial was the only independent predictor of weaning failure from mechanical ventilation. That study concluded that a high B-type natriuretic peptide level is a predictive factor for the failure to wean from mechanical ventilation after cardiac surgery. These findings suggest that optimizing ventricular function should be a goal during the perioperative period.[(211)] Also, in relation to our study, a study was done by Mekontso DA et al on 2012.[(212)] They allocated 304 patients to either a BNP-driven or physician-driven strategy of fluid management during ventilator weaning. To standardize the weaning process, patients in both groups were ventilated with an automatic computer-driven weaning system. The primary end point was time to successful extubation. In the BNP-driven group, furosemide and acetazolamide were given more often and in higher doses than in the control group, resulting in a more negative median (interquartile range) fluid balance during weaning (-2,320 [-4,735, 738] vs. -180 [-2,556, 2,832] ml; P < 0.0001). Time to successful extubation was significantly shorter with the BNP-driven strategy (58.6 [23.3, 139.8] vs. 42.4 [20.8, 107.5] h; P = 0.034). The BNP-driven strategy increased the number of ventilator-free days but did not change length of stay or mortality. The effect on weaning time was strongest in patients with left ventricular systolic dysfunction. The two strategies did not differ significantly regarding electrolyte imbalance, renal failure, or shock. That study concluded that a BNP-driven fluid management strategy decreases the duration of weaning without increasing adverse events, especially in patients with left ventricular systolic dysfunction. (212)

We tried also in our study to detect the effect of haemoglobin level on weaning of COPD patients from MV and we found that haemoglobin level ranged from9.1-17.5g/dl with a mean of 11.4±1.9 in group 1, while in group2 haemoglobin level ranged from8.4-17.3g/dl with a mean of 11.2±1.9 with no statistical significance between the 2 groups as regard haemoglobin level.(p=0.212). In relation to our study, a study was done by Lai Y et al on 2013.(213) This retrospective cohort study was conducted in a university-affiliated teaching hospital in Taiwan. Patients who fulfilled the criteria of difficult weaning were enrolled which were patients who failed spontaneous breathing trials (SBT) two or more times or patients who required as many as 7 days from the first SBT to successful weaning.. Medical records were reviewed to obtain data on hemograms, biochemistry tests, transfusion records, comorbidities and weaning outcome. The association between hemoglobin levels and 30-day weaning outcomes was evaluated using a logistic regression model. A total of 751 patients received mechanical ventilation during the study period, 138 of whom fulfilled the criteria of difficult weaning. Compared with the patients whose hemoglobin was <8 g/dL, those with higher hemoglobin levels were more likely to be successfully weaned (odds ratio [OR], 3.69; 95% CI, 1.22–11.15 for hemoglobin 8–10 g/dL and OR, 4.16, 95% CI, 1.30–13.29 for hemoglobin >10 g/dL). Multivariate analysis showed that the odds ratio for weaning success remained significant for hemoglobin levels of 8–10 g/dL (adjusted OR, 3.3; 95% CI, 1.07–10.15) with borderline significance for hemoglobin level > 10 g/dL (adjusted OR, 2.95, 95% CI, 0.88–9.96). (213) In our study all patients have haemoglobin above 8 g/dL so, it was difficult to determine the exact effect of haemoglobin level on weaning.

On assessing the presence of cardiac arrhythmias (atrial fibrillation) we discovered that cardiac arrhythmias was present in 2 patients(6.1% of the total number of patients in group 1),while in group2 cardiac arrhythmias was present in3 patients (4.5% of the total number of patients in group2) with no statistical significance between the 2groups.(p=1). In relation to our study, a study was done by Marcelino et al on 2006.(214) In that study fifty nine patients with chronic respiratory failure were enrolled, with a mean age 74.7 +/- 9.7 years, mean length of ventilator support 10.8 +/- 12.6 days, and. Within the first 24 hours of admittance, cardiac chamber dimensions, inferior vena cava (IVC), and mitral transvalvular Doppler were evaluated using transthoracic echocardiography; the cardiac rhythm was recorded (presence of sinus rhythm or atrial fibrillation). Greater length of ventilation was observed in patients(n=28) presenting atrial fibrillation(15.6 +/- 8.7 days) (p=0.027), particularly when a dilated IVC(>20mm) (n=11) was also present (17.1 +/- 10.2 days)(p=0.004). Twelve patients died. Mortality was related to the presence of a dilated right ventricle(33%)(n=9) (p=0.03) and a ratio between right and left ventricle > 0. 6 (n=7)(29.2%)(p=0.04).So, that study concluded that patients submitted to mechanical ventilation due to exacerbation of chronic respiratory failure which present atrial fibrillation require a longer ventilation period, particularly if a dilated IVC is also present. Patients with dilated right cardiac chambers are at an increased risk of a fatal outcome. (214) As a comparison, atrial fibrillation was present in 5 patients in our study and 2 of them presented with failed weaning trial (40%) while 3 succeeded in the weaning trial(60%)

which suggests that AF may have an impact on weaning of patients presenting with respiratory failure but this issue needs assessment on larger number of patients.

As regarding systolic blood pressure in our study, it ranged from 100-140 mmHg with a mean of 124.5±12.8 in group1, while in group 2 it ranged from 100-150mmHg with a mean of 124.0±12.1 with no statistical significance between the 2 groups as regard systolic blood pressure.(p=0.868). In relation to our study, a study was carried out by Routsi C et al on 2010.(215) Twelve difficult-to-wean (failed ≥ 3 consecutive trials) chronic obstructive pulmonary disease patients, who presented systemic arterial hypertension (systolic blood pressure ≥ 140mmHg) during weaning failure and had systemic and pulmonary artery catheters in place, participated in this prospective, interventional, non-randomized clinical trial. Patients were studied in two consecutive days, i.e., the first day without (Control day) and the second day with (Study day) nitroglycerin continuous intravenous infusion starting at the beginning of the spontaneous breathing trial, and titrated to maintain normal systolic blood pressure. Hemodynamic, oxygenation and respiratory measurements were performed on mechanical ventilation, and during a 2-hour T-piece spontaneous breathing trial. Primary endpoint was hemodynamic and respiratory effects of nitroglycerin infusion. Secondary endpoint was spontaneous breathing trial and extubation outcome. Compared to mechanical ventilation, mean systemic arterial pressure, rate-pressure product, mean pulmonary arterial pressure, and pulmonary artery occlusion pressure increased [from (mean ± SD) 94 ± 14, 13708 ± 3166, 29.9 ± 4.8, and 14.8 ± 3.8 to 109 ± 20mmHg, 19856 ± 4877mmHg b/min, 41.6 ± 5.8mmHg, and 23.4 ± 7.4 mmHg, respectively], and mixed venous oxygen saturation decreased (from 75.7 ± 3.5 to 69.3 ± 7.5%) during failing trials on Control day, whereas they did not change on Study day. Venous admixture increased throughout the trial on both Control day and Study day, but this increase was lower on Study day. Whereas weaning failed in all patients on Control day, nitroglycerin administration on Study day enabled a successful spontaneous breathing trial and extubation in 92% and 88% of patients, respectively. So, they concluded that in this clinical setting, nitroglycerin infusion can expedite the weaning by restoring weaning-induced cardiovascular compromise. (215) In our study, all cases except 2 patients are within the normal range of systolic blood pressure and the cases suffered failed weaning were failed due to other causes discussed above.

On assessing heart rate as a predictor of weaning, heart rate ranged from65-130 beats/minute with a mean of 91.5±16.0 in group1, while in group 2 it ranged from 60-105 beats /minute with a mean of 84.3±9.4 with statistical significance between the 2 groups as heart rate was significantly lower in patients of group2.(p=0.017). Heart rate showed the lowest PPV 39.7%, accuracy 54% and AUC 0.646 and it showed a sensitivity of 75.8%, specificity 43.3% and NPV78.4% as a predictor of failure of weaning from MV. A cutoff value of 84 beats/min or more was identified to predict failure of weaning from MV.

In relation to our study, a study was done by Huang C et al on 2014.(216) This study included 101 consecutive patients recovering from acute respiratory failure. Frequency-domain analysis, including very low frequency, low frequency, high frequency, and total power of HRV was assessed during a 1-hour spontaneous breathing trial (SBT) through a T-piece and after extubation after successful SBT. Of 101 patients, 24 (24%) had SBT failure, and HRV analysis in these patients showed a significant decrease in total power (*P* = 0.003); 77 patients passed SBT and were extubated, but 13 (17%) of them required reintubation within 72 hours. In successfully extubated patients, very low frequency and total power from SBT to postextubation significantly increased ($P = 0.003$ and $P = 0.004$, respectively). Instead, patients with extubation failure were unable to increase HRV after extubation. [216]

As regarding integrative weaning index(IWI) we found that integrative weaning index(IWI) ranged from 56.9-421.2 ml/cmH2O/breaths/min/L with a mean of 148.2±94.7 in group1, while in group2 it ranged from58.1-818.1 ml/cmH2O/breaths/min/L with a mean of 206.6±155.7 with statistical significance between the 2 groups as IWI was significantly higher in patients of group2.(p=0.016). Integrative weaning index(IWI) showed the lowest specificity 30.3% and NPV 47.6% and it showed a sensitivity of 83.6%,PPV70.9% ,accuracy 66% and AUC 0.648 as a predictor of successful weaning from MV. A cutoff value of 96 ml/cmH2O/breaths/min/L or more was identified to predict successful weaning from MV.. In relation to our study, the study done by Gamal M et al[11] on 2010 which was disussed above in the issue of static compliance found that IWI presented with sensitivity (86.67%), specificity (94.55%), PPV (81.25%), NPV (96.30%), accuracy (92.86%) and AUC (0.934)..This study used a cut off value of 25 ml/cmH2O/breaths/min/liter. [11] As shown the 2 studies are similar as regard sensitivity, but the differences in specificity, PPV, NPV, accuracy and AUC between the 2 studies can be explained by that one of the main limitations in the study done by M.Gamal[11] is that IWI was measured with a fixed FiO_2 of 35% in order to avoid variations in SaO_2 due to FiO_2 variations. And that study recommended that further studies must be performed to test the IWI accuracy in a wide range of FiO_2 values and this what was done in our study as we used variable FiO2 values. Another explanation is that we calculated the value of static compliance in different grades of severity of COPD and GOLD staging was not applicable due to lack of facilities to measure FEV1 and this may also have affected the values of IWI.

Another study was done by Madani S et al on 2013.[217] This study was evaluated on 124 adult patients who were on mechanical ventilation for more than 24 hours in six ICUs (Surgery-Trauma-Medical-Poisoning) of selected hospitals in Tehran,. Inclusion criteria were: Patient 18 to 80 years old, none of them suffering from neurological and neuromuscular diseases, none or a minimal dose of sedative drugs being used, non-addict or heavy smokers. The study was conducted from November 2011 to December 2012. There were 80 successful patients and 44 unsuccessful patients according to successfulness of weaning trial. The area under the ROC curves for IWI was 0.967, with standard error of 0.020, 95% Confidence interval of 0.899 to 0.993 and Significance level of P = 0.001, SE = 94.59%, SP = 66.67%, PPV = 97.22%, NPV = 50%, DA = 92.5 %. [217]

Also a study was done by Nemer S et al[11] on 2009. Two hundred and sixteen patients mechanically-ventilated for more than 24 hours were evaluated. The predictive performance IWI was tested prospectively in all patients. The new integrative weaning index IWI (Cst,rs × arterial oxygen saturation/f/Vt ratio) were evaluated in all patients. The readiness for weaning and the decision to return to mechanical ventilation was made by the physician in charge, based on the signs of poor tolerance. The receiver operating characteristic (ROC) curves were calculated in order to evaluate the predictive performance of IWI. successful weaning was observed in 183 patients (84.7%) and weaning failure in 33 (15.27%). IWI presented area under the ROC curves (0.96). IWI presented a higher probability of successful weaning when the test was positive (0.99) and a lower probability when the test was negative (0.14). Measurement of Cst,rs during the weaning process was considered one of the study limitations. [11]

In our study rapid shallow breathing index(RSBI) ranged from23.8-80breaths/min/L with a mean of 46.6±14.2 in group1,while in group2 it ranged from13.3-80 breaths/min/L with a mean of 39.1±15.9 with statistical significance between the 2 groups as RSBI was significantly lower in patients of group2.(p=0.025).

Rapid shallow breathing index(RSBI) showed a sensitivity of 87.9%, specificity 43.3% ,PPV 43.3% , NPV 87.9% and accuracy 58% and it showed the highest AUC 0.658 as a predictor of failure of weaning from MV. A cutoff value of 33.5 breaths/min/Lor more was identified to predict failure of weaning from MV.

In relation to our study and again in the study done by Gamal M et al[11] on 2010 RSBI that presented sensitivity (73.33), specificity (81.82), PPV(52.38), NPV (91.48), accuracy (80), and AUC (0.878). One study was done by Yang et al the sensitivity of RSBI in their results was (87), specificity (64). [6] These 2 studies measured RSBI on CPAP with pressure support 10 and PEEP 5 and a cut off value of 100breaths/min/L was used to predict specificity and sensitivity. [6, 11]Another study was done by Boutou AK et al on 2011.[193] A consecutive population of patients with COPD who were intubated for hypercapnic respiratory failure during a 2-year period were studied prospectively. RSBI was measured by 2 investigators at minute 5 of the T-piece trial, whereas 2 other physicians evaluated the 30 minute T-piece trial as successful or unsuccessful, according to clinical criteria. Of 64 patients with COPD (53 male, 11 female) who constituted the study population, 42 patients (35 male, 7 female; aged 70 ± 9.2 years) completed the spontaneous breathing trial (SBT) and remained clinically stable. The remaining 22 patients (18 male, 4 female; aged 71.9 ± 4.7 years) had to return to ventilatory support by the end of the SBT because of clinical deterioration. RSBI had low specificity (38.1%), low sensitivity (63.6%), and low diagnostic accuracy (46.8%) in predicting a successful T-piece trial outcome. [193] This study used a cut off value of 105 breaths/min/L.[193] The sensitivity of RSBI in our study(87.9%) was similar to the sensitivity found in the study of Yang et al(87%) [6] and the specificity in our study (43.3%) was quite similar to the specificity found in the study of Boutou AK et al[193] (38.1%). and was also quite similar to it as regard accuracy(58%)vs.(46.8%) respectively. PPV was similar in our study and the study of Gamal M[11] (43.3%) vs.(52.38) respectively and NPV was also similar between our study and Gamal M [11]study(87.9%) vs.(91.48%) respectively. Our study identified a cut off value of 33.5 breaths/min/L or more for RSBI as a predictor of failure of weaning.

Tobin et al prospectively examined the pattern of breathing in patients being weaned from mechanical ventilation: one group (n = 10) underwent a successful weaning trial and were extubated, whereas another group (n = 7) developed respiratory failure and required the reinstitution of mechanical ventilation. During the period of ventilator support, minute ventilation (VE), tidal volume (VT), and respiratory frequency (f) were similar in the 2 groups. After discontinuation of the ventilator, VE remained similar in the 2 groups, but VT was lower and f was higher in the patients who failed the trial compared with those who were successful, 194 +/- 23 and 398 +/-56 ml ($p < 0.001$); respectively, and 32.3+/- 2.3 and 20.9+/- 2.8 breaths/min ($p < 0.001$), respectively. The failure group displayed a significant increase in $PaCO_2$, ($p < 0.005$) during spontaneous breathing, without a concomitant increase in the alveolar-arterial PO_2 difference. Eighty-one percent of the variance in PCO2, was accounted for by the pattern of rapid, shallow breathing. In summary, (1) patients who failed a weaning trial had a well-maintained VE but a low VT and a high f, (2) these patients developed a further increase in respiratory drive from the beginning to the end of the weaning trial, and (3) patients with a successful weaning outcome showed only transient changes In breathing pattern after extubation. These results indicate that the development of hypercapnia In patients who fail a weaning trial is due to the development of rapid, shallow breathing with consequent inefficient gas-exchange.[(218)]

On the other hand, Tobin and Yang on 1991[(6)] developed RSBI. They tested the predictive accuracy of RSBI in a convenience sample of 64 adult medical patients who were considered ready for weaning. RSBI was calculated at the first minute of t piece trial. Sensitivity of RSBI was 97%, specificity was 64%, PPV was 78%, NPV was 95%. The threshold value was established at 100 breaths /min/L or less as a predictive value for successful weaning. [(6)]

While we investigated the effect of respiratory rate as a predictor of weaning outcome we found that respiratory rate ranged from 14-30 breaths/minute with a mean of 21.3±5.4 in group1, while in group2 it ranged from10-28 breaths/minute with a mean of 18.6±4.4 with no statistical significance between the 2 groups.($p=0.086$). In relation to our study, also in the study done by Gamal M[(11)] et al on 2010 ,respiratory rate (f) in group 1 ranged from 28 to ,34 with a mean of (30.67 ± 2.02) while in group 2 it ranged from 19 to 33 with a mean of (25.53 ± 3.82). Respiratory rate in group 1 was significantly higher ($p < 0.001$). Respiratory rate had sensitivity (53.33%), specificity (80%), PPV (42.11%) ,NPV (86.27%), accuracy (74.29%) and AUC (0.866). This study used a cutoff value of $f \leq 30$ breaths/minute to best predict successful weaning. [(11)] Another study was done by Lima EJ on 2013[(219)] That study prospectively evaluated 166 patients scheduled for weaning from MV. RR was evaluated at an early stage of screening and was compared with the following outcomes: weaning success/failure or extubation failure. Weaning success was present in 76.5% and weaning failure in 17.5% of patients. There were 6% of reintubations. The predictive power for RR weaning failure, RR best cut-off point > 24 breaths per minute (rpm), was: sensitivity 100%, specificity 85%, and accuracy 88%.($p < 0.0001$). [(219)]

While we investigated the effect of tidal volume as a predictor of weaning we found that tidal volume ranged from330-800 ml with a mean of 483.0±149.4 in group1,while in group2 it ranged from280-850ml with a mean of 524.4±143.9 with no statistical significance between the 2 groups.($p=0.185$).In relation to our study, in the study done by Gamal M[(11)] et al, tidal volume (VT) ranged from 0.26 to 0.34 in group 1 with a mean of (0.30 ± 0.03) while ranged from 0.27 to 0.58 with a mean of (0.45 ± 0.10) in group 2. Tidal volume was significantly higher in group 2 ($p<0.001$). Tidal volume presented sensitivity (66.67), specificity (76.36), PPV (43.48), NPV (89.63), accuracy (74.29) and AUC (0.864). A cutoff value of ≥ 315 ml was used to best predict weaning in this study. [(11)] This difference in stastistical significance was explained by the fact that the study of Gamal M[(11)] et al was done on mechanically ventilated patients in general ,while our study was done on COPD patients. Also, GOLD staging could not be done in our study due to lack of facility to measure FEV1so, there was vide range in tidal volumes in the 2 groups.

We also tried to find out the effect of maximum inspiratory pressure as a predictor of weaning and we found that maximum inspiratory pressure(MIP) ranged from-35.5,-25cmH2O with a mean of -27.6±2.3 in group1,while in group2 it ranged from-33,-

25.3cmH2O with a mean of -27.3±1.4 with no statistical significance between the2 groups.(p=0.608). As a relation a study was done by Tzanis G et al on 2011.[220] Seventy-four patients were recruited in the study and prospectively evaluated in a multidisciplinary university ICU towards the appearance of ICU-AW(acquired weakness). ICU stay was 26 ± 18 days.. MIP was measured using the unidirectional valve method, independently of the patients' ability to cooperate. Patients that developed ICU-AW had a longer weaning period compared to non ICU-AW patients (12 ± 14 versus 2 ± 3 days, $p < 0.01$). A cut-off point of 36 cmH_2O for MIP was defined by ROC curve analysis for ICU-AW diagnosis (88% sensitivity,76% specificity). Patients with MIP below the cut-off point of 36 cmH_2O had a significant greater weaning period (10 ± 14 versus 3 ± 3 days, p = 0.004) Patients that developed clinically ICU-AW (51%) had a longer ICU stay (41 ± 19 versus 21 ± 11, days, p = 0.001), a lower MIP (28 ± 15 versus 49 ± 11, cmH_2O, $p < 0.001$), and a longer MV weaning period (12 ± 14 versus 2 ± 3, days, $p < 0.05$). In a prospective analysis of the 74 patients included in the study, patients with MIP < 36 cmH_2O suffered a longer ICU stay (37 ± 6 versus 28 ± 13, days, p = 0.001), and a longer MV weaning period (10 ± 14 versus 3 ± 3, days, $p < 0.01$). [220] The absence of statistical significance for MIP in our study can be explained by that in our study there was no patients suffering myopathy. So, there was no affection for the value of MIP in our study and this led to absence of statistical significance.

P0.1 ranged from2-6 cmH2O with a mean of 3.8±0.9 in group1,while in group2 it ranged from1.5-5 cmH2O with a mean of 3.6±0.8 with no statistical significance between the 2 groups.(p=0.346). In relation to our study, a study was conducted by Vargas F et al on 2009.[221] 35 COPD patients who had been weaned from mechanical ventilation and extubated were included in the study. P0.1 were recorded at the first hour of postextubation. They determined whether those patients who developed postextubation respiratory failure (failed extubation group) differed from those who did not (successful extubation group).

Fourteen patients presented a postextubation respiratory failure. P0.1 values in the failed extubation group were (4.3 +/- 1.7 cm H20) were significantly different (P <.05) from those observed in the successful extubation group (1.8 +/- 0.8 cm H20). The area under the receiver operating characteristic curve for diagnosing postextubation respiratory failure was 0.87 for P0.1.

Bedside evaluation of P0.1 helps to define COPD patients at high risk for postextubation respiratory failure. [221] In relation, our study showed that P0.1 was somewhat lower in the successful weaning group (1.5-5 cmH2O) compared with the failed weaning group (2-6cmH2O) but still without statistical significance.

As regard oxygenation parameters, in our study PaO2 ranged from 55-238mmHg with a mean of 106.8±46.1 in group1, while in group2 it ranged from 57-201mmHg with a mean of 106.2±37.2 with no statistical significance between the 2 groups (p=0.758) (PaO2 measured on different FiO2 variables). HI ranged from 122.2-460 with a mean of 241±90.8 in group1, while in group2 it ranged from 95-450 with a mean of 232.7±89.7 with no statistical significance between the 2 groups (p=0.956) (PaO2 measured on different FiO2 variables).

El Khoury MY et al on 2010[222] carriedout a retrospective chart review of 154 patients with HRF (hypoxaemic respiratory failure) requiring mechanical ventilation for

≥24 hours. The primary outcome was reintubation within 48 hours.142 (92%) patients were successfully extubated. Pre-extubation HI and RSBI values among reintubated and successfully extubated patients were similar. The areas under the curve of the receiver operating characteristic curves using RSBI and HI were 0.5 and0.62, respectively. A HI < 200 or RSBI ≥ 70 when the HI was ≥200 indicated a higher risk of reintubation, with 7% sensitivity and 56% specificity (area under the curve, 0.69).So,neither the HI independently nor the HI in combination with the RSBI accurately predicted successful extubation in patients with HRF(low specificity and sensitivity). (222) In our study we tried to use a cutoff value of 250 for hypoxic index instead of 200 but still this was without significance in predicting weaning outcome in COPD patients.

As regard alveolar arterial pressure gradient of oxygen (PAO2-PaO2) we found that the diffirence between alveolar and arterial pressure of oxygen (PAO2-PaO2)ranged from14.6-422.5mmHg with a mean 158.0±98.1 in group1,while in group 2 it ranged from40.1 – 310.9mmHg with a mean of169.4±78.5 with no statistical significance. (PaO2 measured on different FiO2 variables).

As regard arterial pressure of carbon dioxide Arterial pressure of carbon dioxide (PaCO2) ranged from25-72mmHg with a mean of 50.2±12.0 in group1, while in group2 it ranged from33-68mmHg with a mean of 50.3±8.5 with no statistical significance between the 2groups.(p=0.666). A study was done by Rialp G et al on 2014.(223) A retrospective study was carried out in two intensive care units on subjects with and without chronic obstructive pulmonary disease (COPD), at the beginning of weaning from mechanical ventilation. The CO2 response was evaluated by the re-inhalation of expired air method, measuring the hypercapnic ventilatory response (ΔVE/ΔPaCO2) and hypercapnic drive response (ΔP01/ΔPaCO2), where VE is minute volume and P0.1 is airway occlusion pressure 0.1s after the initiation of inspiration. (223)

A total of 120 patients in the non-COPD group and 48 in the COPD group were studied. COPD patients had higher mean [HCO3(-)] than non-COPD patients (33.2 ± 5.4 vs. 25.7 ± 3.7 mmol/l, p<0.001). In both non-COPD and COPD patients they observed a significant inverse linear relationship between [HCO3(-)] and pH change per mmHg of PaCO2 (p<0.001), ΔVE/ΔPaCO2 (p<0.001) and ΔP0.1/ΔPaCO2 (p<0.001). (223)

That study concluded that there is an inverse linear relationship between [HCO3(-)] and the variation of pH for a given change in PaCO2 and the CO2 response. (223) So, this could explain the absence of statistical significance in PaCO2 between the 2 groups in our study as weaning depends on plasma bicarbonate level , change in PH ,minute ventilation and P0.1 rather than PaCO2 only.

Finally, non invasive pressure support ventilation(PSV) was tried on the group of failed weaning trial (group1)whose number of patients was 33 to detect the effect of non invasive PSV as a weaning method and we found that non invasive PSV trial was successful in 17 patients(51.5%), while it failed in 16 patients(48.5%). So, non invasive PSV became a promising issue in weaning of patients with COPD with successful weaning in more than 50% of cases. PSV with pressure support 15 cmH2O was given to the patients. Patients were put on intermittent non invasive ventilation for 2 hours with rest for 1 hour with overnight non invasive ventilation. As a comparison between the 2 groups, duration of MV was 4.5 +/-2.4 days in the group who succeeded in the non invasive trial versus 7.1+/-2.2 days in the group who failed in the non invasive trial(as this group has to be returned to invasive ventilation). In relation to our study, a study was done Mishra M et al on 2014.[191] For that prospective randomized controlled study, they included 50 COPD patients with type II respiratory failure requiring initial invasive MV. Upon satisfying weaning criteria and failing a t-piece weaning trial, they were randomized into two groups: Group I (25 patients) weaned by NIPPV, and group II (25 patients) weaned by conventional PSV. They were compared in terms of duration of MV, weaning duration, length of intensive care unit (ICU) stay, occurrence of nosocomial pneumonia and outcome. Statistically significant difference was found between the two groups in terms of duration of MV(4.93+/-2.92 days vs. 6.9+/- 2.97 days), weaning duration(5.09+/-2.39 days vs.7.56+/-2.35 days), length of ICU stay(13.18+/-4.85 days vs.18.11+/-3.65days), occurrence of nosocomial pneumonia(8% vs 32%) and outcome(Fewer deaths occurred in the ICU at discharge among group I patients than among group II patients (2 patients-8% vs 8 patients-32%, respectively) and more patients were successfully discharged from the ICU in group I than in group II (23 patients-92% vs 17 patients-68%, respectively)). Weaning criteria used when giving an initial t-piece trial to patients were: An adequate mentation and cough reflex, clinical stability, and adequate oxygenation as reflected by SaO_2 of >90% at FiO_2 ≤0.4, after at least 48 hours of invasive MV. Criteria for failure of the t-piece trial were PH <7.35, PaO_2 <50 mm Hg at FiO_2 of 0.4, RR >35/min, HR >145/min, SB*P* >180 mm Hg or <70 mm Hg, severe cardiac arrhythmias, agitation/anxiety/diaphoresis. That study concluded that NIPPV appears to be a promising weaning modality for mechanically ventilated COPD patients and should be tried in resource-limited settings especially in developing countries. [191]

According to Cochrane database system review, they evaluated studies in which invasively ventilated adults with respiratory failure of any cause (chronic obstructive pulmonary disease (COPD), non-COPD, postoperative, nonoperative) were weaned by means of early extubation followed by immediate application of NPPV or continued IPPV weaning. The primary objective was to determine whether the noninvasive positive-pressure ventilation (NPPV) strategy reduced all-cause mortality compared with invasive positive-pressure ventilation (IPPV) weaning. Secondary objectives were to ascertain differences between strategies in proportions of weaning failure and ventilator-associated pneumonia (VAP), intensive care unit (ICU) and hospital length of stay (LOS), total duration of mechanical ventilation, duration of mechanical support related to weaning, duration of endotracheal mechanical ventilation (ETMV), frequency of adverse events (related to weaning) and overall quality of life. We planned sensitivity and subgroup analyses to assess (1) the influence on mortality and VAP of excluding quasi-randomized trials, and (2) effects on mortality and weaning failure associated with different causes of respiratory failure (COPD vs. mixed populations). They identified 16 trials, predominantly of moderate to good quality, involving 994 participants, most with chronic obstructive pulmonary disease (COPD). Compared with IPPV weaning, NPPV weaning significantly decreased mortality. The benefits for mortality were significantly greater in trials enrolling exclusively participants with COPD (risk ratio (RR) 0.36, 95% confidence interval (CI) 0.24 to 0.56) versus mixed populations (RR 0.81, 95% CI 0.47 to 1.40). NPPV significantly reduced weaning failure (RR 0.63, 95% CI 0.42 to 0.96) and ventilator-associated pneumonia (RR 0.25, 95% CI 0.15 to 0.43); shortened length of stay in an intensive care unit (mean difference (MD) -5.59 days, 95% CI -7.90 to -3.28) and in hospital (MD -6.04 days, 95% CI -9.22 to -2.87); and decreased the total duration of ventilation (MD -5.64 days, 95% CI -9.50 to -1.77) and the duration of endotracheal mechanical ventilation (MD - 7.44 days, 95% CI -10.34 to -4.55) amidst significant heterogeneity. Noninvasive weaning also significantly reduced tracheostomy (RR 0.19, 95% CI 0.08 to 0.47) and reintubation (RR 0.65, 95% CI 0.44 to 0.97) rates. Noninvasive weaning had no effect on the duration of ventilation related to weaning. [224]

SUMMARY

SUMMARY

Weaning from mechanical ventilation can be defined as the process of abruptly or gradually withdrawing ventilatory support.

COPD is a preventable and treatable disease with some significant extrapulmonary effects that may contribute to the severity in individual patients. Its pulmonary component is characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lung to noxious particles or gases.

In our study we compared between different weaning parameters in combination of the general condition of the COPD patients(neurological, electrolyte, respiratory, cardiovascular ,acid base status and body mass index) as predictors of weaning outcome and we studied the effect of usage of non invasive PSV in difficult weaning patients.

The study was conducted on 100 patients with COPD admitted to Alexandria main university hospital who fulfilled the inclusion and exclusion criteria , mechanically ventilated for more than 24 hours and were considered candidates for weaning judged by the physician in charge. All selected patients fulfilling the inclusion criteria were subjected to full history (including age, sex and preexisting underlying disease), full clinical examination and Laboratory investigations were done on admission and daily .

The following values were measured in all patients with COPD candidate for weaning: vital signs (systolic and diastolic blood pressures, temperature, heart rate and respiratory rate), tidal volume, rapid shallow breathing index, maximum inspiratory pressure, P0.1, compliance, PaO2,PaCO2, PEEP, hypoxaemic index, integrative weaning index(IWI) and P0.1/MIP ratio.

These parameters were considered with neurological and electrolyte status(presence of structural brain damage ,presence of electrolyte disturbances especially hypophosphataemia , GCS and presence of taking sedatives or hypnotics prior to the trial of weaning),respiratory status(presence of abnormal value of compliance or resistance and alveolar arterial oxygen gradient(PAO2-PaO2)),acid base status and body mass index (body mass index and presence of acid base disturbance)and cardiovascular status(prescence of ischemic heart disease, arrhythmias(namely atrial fibrillation) or heart failure and haemoglobin level). According to the success of the weaning trial patients were classified into 2 groups: **Group 1** : patients who failed to wean and **group 2** : patients who succeeded the weaning trial (success of weaning was determined by the ability to breath normally away from MV for 48 hours). Then all these weaning parameters in addition to parameters reflecting the neurological, electrolyte, respiratory, acid base and cardiovascular status of the patient in addition to body mass index together with vital signs of the patient were compared according to their specificity, sensitivity ,positive and negative predictive values and accuracy to detect their ability as a predictor of weaning from mechanical ventilator.

The study also included the effect of usage of non invasive PSV in difficult weaning patients. We found that:

1. The most important and significant data in our study in predicting weaning outcome of COPD patients from mechanical ventilator were integrative weaning index(IWI), rapid shallow breathing index(RSBI), glascow coma score(GCS), heart rate and presence of abnormal value of resistance. GCS had the best specificity ,positive predictive value and accuracy, while presence of abnormal resistance had the best sensitivity and negative predictive value.
2. There were other data in our study that may predict weaning of COPD patients from mechanical ventilator although they were statistically non significant as they should be studied on larger number of patients. They were presence of structural brain damage, presence of electrolyte disturbance especially hypophosphatemia, presence of taking sedation prior to weaning, presence of acid base disturbance, presence of ischaemic heart disease, presence of heart failure, presence of atrial fibrillation and BMI.
3. Haemoglobin level, systolic blood pressure, respiratory rate, tidal volume, static compliance, maximum inspiratory pressure, P0.1 were poor predictors of weaning outcome of COPD patients from mechanical ventilator in our study.
4. PaO2, HI, PaCO2 could not accurately predict weaning outcome of COPD patients from MV.
5. Non invasive PSV gave more than 50% chance of weaning of COPD patients from MV and it can also shorten the duration of weaning from mechanical ventilator.