OUTCOME OF ACUTE RESPIRATORY DISTRESS SYNDROME NETWORK PROTOCOL IMPLEMENTATION IN PATIENTS WITH ACUTE LUNG INJURY/ACUTE RESPIRATORY DISTRESS SYNDROME.

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ABSTRACT

Background: There is under-use of ARDS Network ventilatory protocol in managing ARDS patients. Hence the objective of this study was to assess the impact of implementing ARDS network protocol, as a ventilatory strategy in management of ALI/ARDS patients.

Design: retrospective-prospective comparative study.

Patients and Methods: This study was conducted on 40 mechanically ventilated patients with ARDS admitted at ICUs of Zagazig University Hospitals. Twenty newly admitted cases of ALI/ARDS (group I)(prospective group) that have been managed by ARDS Network protocol of mechanical ventilation were compared with another 20 patients who have not been managed by ARDS Network protocol of mechanical ventilation (group II) (retrospective group).

Results: Both groups were matched as regards age, sex,smoking habits, oxygenation ratio and SAPS II on admission .There were a significant statistical difference between both groups as regards tidal volume and plateau pressure on days 1,3 &7 with mortality (60% vs. 90% p= 0.028) , duration of MV(18.6 vs. 25.5 days p = 0.001), LOS in ICU among survivors (22.6 vs. 30.5 days p=0.001)and barotraumas (1 vs. 6 patients p= 0.037) in group I and group II respectively.

Conclusions: Application of ARDS Network ventilatory protocol as a ventilatory strategy in ARDS patients decreases the overall mortality, days on mechanical ventilation, the length of stay in ICU and the incidence of barotrauma.

Key words: ARDS, mechanical ventilation, low tidal volume, ARDS Network, ICU.

INTRODUCTION

Acute lung injury (ALI) and ARDS involve a heterogeneous process in the lungs that results in diffuse alveolar damage. The current characteristics associated with ALI include bilateral infiltrates on chest radiograph, PaO2 to FIO 2 ratio less than 300, no evidence of left ventricular failure evidenced by a pulmonary artery occlusive pressure less than 18 mm Hg or central venous pressure less than 14 mm Hg, and need for invasive mechanical ventilator support. ARDS is a subset of patients whose PaO2 to FIO 2 ratio is less than or equal to 200 [1].

ALI (or ARDS) is associated with a variety of causative factors, which can be grouped into two general categories: those associated with direct lung injury via the airways and those associated with indirect lung injury via the blood stream [2].

Regardless of whether injury originates within or outside of the lung, the lung injury is associated with a systematic inflammatory response. [1]

The only method of mechanical ventilation that has been shown in randomized controlled trials to improve survival in patients with ARDS is low tidal volume ventilation. [3]

In the last decade with the emergence of SARS, H5N1, and H1N1 pandemic globally, there was an increase in ARDS cases; and consequently the need for positive pressure invasive mechanical ventilation.[2]

In spite of using a low tidal volume in ventilation of ARDS cases, it was observed that some intensevists deviates from complete application of ARDS network ventilatory protocol, not taking into consideration P Plateau and/or PEEP-FIO2 combination to achieve target oxygenation and/or target PH .

In ARMA (Respiratory Management in Acute Lung Injury/ARDS, 2000), ventilation with low tidal volumes and plateau pressures resulted in a nearly 9% absolute reduction in the risk of death. Therefore, high tidal volumes and high plateau pressures should be avoided in patients with ARDS, and critical care clinicians should utilize low tidal volumes as part of a ventilatory protocol that also limits plateau pressure. Specifically, it is recommended that practitioners utilize the ventilatory protocol outlined by the ARDS Network investigators in an ARMA publication from 2000.

Since the publication of ARMA, low tidal volume ventilation has remained underutilized in the treatment of patients with ARDS. Common barriers to the initiation of low tidal volume ventilation include unwillingness to relinquish control of the ventilator, failure to recognize patients as having ALI/ARDS, and perceived contraindications to low tidal volume ventilation. Significant barriers to the continuation of low tidal volume ventilation include concerns regarding patient discomfort and tachypnea or hypercapnia and acidosis.

PATIENTS AND METHODS

The study was carried out at the Intensive Care Units of Chest and Anesthesiology departments, Zagazig University Hospitals in the period from November 2011 to November 2013.

Patients with ALI/ARDS, regardless the cause, have been recruited.

Patients of this study included two groups:

1. (Group A) ARDS Network clinical trial group(prospective group)(20 patients): Newly admitted cases of ALI/ARDS, upon them ARDS Network protocol of mechanical ventilation has been conducted aged 49.9 ± 11.33 years .They were admitted in the period from November 2011 to November 2013.They were (12) males , and (8) females.
2. (Group B) Non ARDS Network clinical trial control group(retrospective group) (20 patients):

Patients with ALI/ARDS, who have not be managed by ARDS Network protocol of mechanical ventilation aged 50 ± 12.3 years .Their data were collected from file archives.They were collected from the period of October 2009 to October 2011 they were (10) males , and (10) females.

Inclusion criteria:

1. Patients diagnosed as ALI/ARDS according to The American-European Consensus Conference (AECC) on ARDS in 1994:

ALI defined as respiratory failure of acute onset with a PaO2/FiO2 ratio of less than 300 mm Hg (regardless of the level of positive end-expiratory pressure, PEEP), bilateral infiltrates on frontal chest radiograph not attributable to atelectasis or effusions, and no evidence of left atrial hypertension. ARDS was defined identically except for a lower limiting value of less than 200 mm Hg for PaO2/FiO2.

2. Patients age > 18 years old.

3. Initiation of the ARDS Network protocol occurred (for prospective group) within 24 hours of meeting consensus conference criteria for ARDS.

Exclusion criteria:

1. Age < 18 yrs
2. Pregnancy.
3. Acute neurologic disease for which hypercapnia would be contraindicated
4. Severe chronic obstructive or restrictive respiratory disease
5. History of sickle cell disease
6. Lobectomy or pneumonectomy during the current hospitalization.

METHODS

For Group (I) the followings were done:

- Thorough medical history: History taking from the relative(s).
- Full clinical examination: including both general and local chest examinations.
- Plain Chest radiography (antero-posterior view): on admission, and when required.
- Blood glucose level.
- Complete blood count (White blood cells count, Red blood cells count, Hemoglobin and Platelets).
- Kidney function tests (Serum urea level, creatinine).
- Liver function tests including SGOT, SGPT, serum bilirubin and serum albumin.
- Prothomobin time (PT), Partial thromboplastin time (PTT).
- Arterial blood gas analysis (ABG): including the followings:
- Serum electrolytes (Na, K.Ca, Cl).
- Electrocardiography and Echocardiography
- Pulse oximetry, non-invasive and blood pressure, central venous pressure, and urine output.
- Ventilator data tabulation as long the patients stay on mechanical ventilation include; VT (in mL/kg PBW), end-inspiratory plateau pressure (Pplat), positive end-expiratory pressure (PEEP), , inspired oxygen fraction (FIO2), total respiratory rate (f), arterial pH, arterial carbon dioxide partial pressure (PaCO2), and arterial oxygen partial pressure (PaO2).
- Calculation of the Simplified Acute Physiology Score (SAPS) II on the first day of admission.[4]
- ARDS Clinical Network Mechanical Ventilation Protocol was applied as the following.[5]

- Predicted body weight was calculated as the following:
  Males : =50 +2.3 (Height (inches) -60)
  Females := 45.5 +2.3 (Height (inches) -60)
- VAC mode was chosen as a ventilator mode
- Tidal volume was firstly 8 ml/kg PBW and this was reduced by 1 ml/kg at intervals ≤ 2hours until Vt became 6ml /kg PBW
- Initial rate was set to approximate baseline minute ventilation(not exceeding 35 b/m
- VT & RR were adjusted to achieve a target PH & Pplat goals
- Oxygenation goal : Pao2 (55 -80 mmHg) or SPO2 (88-95%) by applying incremental FIO2 /PEEP combination using a minimum PEEP of 5 CmH2o
- Pplat goal: (≤ 30 CmH2o) .
  Check Pplat (.5 sec inspiratory pause), at least every 4 hs and after each change of PEEP or Vt.

If Pplat > 30 Cm H20: Vt was decreased by 1 ml/kg steps(minimum Vt 4ml/kg).

If Pplat < 25 Cm H2o and Vt is < 6ml /kg,Vt was increased until Pplat > 25 Cm H2o or Vt = 6 ml /kg.

If Pplat < 30 cmH2o and breath stacking or dys-synchrony occurs: Vt may be increased in 1ml/kg increment to 70r 8 ml /kg provided Pplat ≤ 30 Cm H2o

- pH GOAL: 7.30-7.45

Acidosis Management: (pH < 7.30)

If pH 7.15-7.30: Increase RR until pH > 7.30 or PaCO2 < 25 (Maximum set RR = 35). If pH < 7.15: Increase RR to 35.

If pH remains < 7.15, VT may be increased in 1 ml/kg steps until pH > 7.15 (Pplat target of 30 may be exceeded).

May give NaHCO3

Alkalosis Management: (pH > 7.45) Decrease vent rate if possible.

- I: E RATIO GOAL: Recommend that duration of inspiration be < duration of expiration.
- WEANING

A. Conduct a SPONTANEOUS BREATHING TRIAL daily when:

1. FiO2 ≤ 0.40 and PEEP ≤ 8 OR FiO2 < 0.50 and PEEP < 5.
2. PEEP and FiO2 ≤ values of previous day.
3. Patient has acceptable spontaneous breathing efforts. (May decrease vent rate by 50% for 5 minutes to detect effort.)
4. Systolic BP ≥ 90 mmHg without vasopressor support.
5. No neuromuscular blocking agents or blockade.

B-SPONTANEOUS BREATHING TRIAL (SBT):

If all above criteria are met and subject has been in the study for at least 12 hours, initiate a trial of UP TO 120 minutes of spontaneous breathing with FiO2 < 0.5 and PEEP < 5:

1. Place on T-piece, or CPAP ≤ 5 cm H2O with PS < 5
2. Assess for tolerance as below for up to two hours.

a. SpO2 ≥ 90: and/or PaO2 ≥ 60 mmHg
b. Spontaneous VT ≥ 4 ml/kg PBW
c. RR ≤ 35/min
d. pH ≥ 7.3
e. No respiratory distress (distress= 2 or more)

- HR > 120% of baseline
- Marked accessory muscle use
- Abdominal paradox
- Diaphoresis
- Marked dyspnea

3. If tolerated for at least 30 minutes, consider extubation.
4. If not tolerated resume pre-weaning settings.

For Group (II) the followings were done:

Data that have been gathered from file achieves included:

as in group I in addition to :

NON ARDS Clinical Network Mechanical Ventilation Protocol was observed : in which low tidal volume (inspite of being not as low as that of group A) was applied and /or there were a deviation from ARDS Clinical Network Mechanical Ventilation Protocol in the form of non respect of plateau pressure values ,target oxygenation, target FIO2 &PEEP.

Comparing outcome in both groups as regard:

- Survival at day 28.[6],[7]
- Days on mechanical ventilation .[6],[7]
- Lengths of ICU stay.[6],[7]

Statistical analysis: Statistical analysis was performed with SPSS version19 software package (SPSS, Inc.Chicago). P value <0.05 was considered significant.

RESULTS

(Table-1): Demographic characteristics of the studied groups (n=40)

Group		I(20)	II(20)	P
Age		49.9±11.33	50±12.3	0.83
gender	male	12(60%)	10(50%)	0.52
	Female	8(40%)	10(50%)	
smoking	yes	7(35%)	6(30%)	0.73
	no	13(65%)	14(70%)	

This table shows the characteristics of the studied patients. Mean age was(49.9±11.33 years)Vs (50±12.3 years)in group 1 & 2 respectively .60 % of patients were males , 40 % were females in group

1 while in group 2, 50 % were males & 50 % were females .The percentage of smokers was 35% in group 1 & 30 % in group 2 without any statistical significant difference .(P > 0.05).

(Table -2): Risk factors of ARDS in the studied patients

Etiology	Group I	Group II	P
Aspiration	2(10%)	2(10%)	0.36
Pneumonia	5(25%)	6(30%)	
Sepsis	6(30%)	5(25%)	
Trauma	5(25%)	4(20%)	
H1N1	0(0%)	3(15%)	
Drug Overdose	2(10%)	0(0%)	
Total	20(100%)	20(100%)	40(100%)

This table shows the different risk factors of ARDS in the studied patients. The most frequent risk factor in Group I was sepsis (30%) while in Group II was pneumonia (30%). Aspiration represents (10% & 10%), pneumonia represents (25% & 30%), trauma (25% & 20%), H1N1 (0% & 15%), drug overuse (10% & 0%) in Group I & II respectively, without any statistical significant difference. (P > 0.05).

(Table-3): Pao_2/FIO_2 & SAPS II in the studied patients on admission.

Group	I	II	P
Pao_2/FIo_2 ratio	131±33	118±29	0.2
SAPS II	41.7±3.89	39.3±5.25	0.1

This table shows that the mean Pao_2/FIO_2 on admission in Group I was (131±3.3) while in Group II was (118±2.9) without any significant statistical difference. (P > 0.05). Also, mean SAPS II on admission in Group I & II were (41.7 ±3.89 &39.3 ±5.25) respectively without any significant statistical difference. (P > 0.05).

(Table -4): Ventilatory parameters on days 1,3, 7 in the studied patients:

Parameter	Group I	Group II	P value
	Day 1		
VT ml/kg	5.7±0.57	7.5±0.5	0.000
$FIo_{2\,\%}$	66.5±6.3	70.5±7	0.066
P.Plateau Cm H2o	26.55±1.6	31.1±1.9	0.000
PEEP Cm H2o	11.1±1.5	10.5±2.7	0.35
	Day 3		
VT ml/kg	6±0	7.52±0.7	0.000
$FIo_{2\,\%}$	61.7±6.9	68.8±6.5	0.003
P.Plateau Cm H2o	25.7±2.14	32.76±4.1	0.000
PEEP Cm H2o	10.44±1.2	9.94±1.71	0.3
	Day 7		
VT ml/kg	6±0	7.3±0.48	0.000
$FIo_{2\,\%}$	55.9±11.5	66±11.25	0.04
P.Plateau Cm H2o	24.6±4	31.9±3.25	0.000
PEEP Cm H2o	9.5±2.4	10.9±2.07	0.1

This table shows the mean ventilatory parameters of both groups on the day1, 3,7.On day 1: VT was 5.7± 0.57 ml /kg in Group I & 7.5±0.5 ml /Kg in Group II with highly statistical significant difference. ($P < 0.05$). FIO_2 was 66.5±6.3% & 70.5 ±7 %in Group I & II respectively but without any statistical significant difference. ($P > 0.05$). P plateau was 26.55 ±1.6 CmH20 &31.1 ±1.9 CmH20 in Group I & II respectively with highly statistical significant difference. ($P < 0.05$). PEEP was 11.1±1.5 &10.5 CmH20 ±2.7 CmH20 in Group I & II respectively but without any statistical significant difference. ($P > 0.05$). On day 3: VT was 6 ± 0 in Group I & 7.52 ± 0.7 in Group II with highly significant statistical difference. ($P < 0.05$). FIO_2 was 61.7 ±6.9 & 68.8 ± 6.5 in Group I & II respectively highly significant statistical difference. ($P < 0.05$). P plateau was 25.7 ± 2.14 & 32.7 ±4.1 in Group I & II respectively with highly significant statistical difference. ($P < 0.05$). PEEP was 10.44 ±1.29 &9.94 ±1.71 in Group I & II respectively but without any significant statistical difference. ($P > 0.05$). On day 7: VT was 6 ± 0 in Group I & 7.3 ± 0.48 in Group II with highly statistical significant difference. ($P < 0.05$).FIO_2 was 55.9 ±11.5 vs. 66 ± 11.25 in Group I & II respectively with significant statistical difference. ($P > 0.05$).

P plateau was 24.6 ± 4 vs. 31.9 ±3.25 in Group I & II respectively with highly statistical significant difference. ($P < 0.05$). PEEP was 9.5 ±2.4 vs. 10.9 ±20.7 in Group I & II respectively but without any significant statistical difference. ($P > 0.05$).

(Table -5): Arterial blood gases on day 1,3,7 in the studied patients:

Day 1	Group I	Group II	P value
PH	7.35±0.03	7.34±0.02	0.12
PaCo2 mmHg	39.4±3.2	39.3±1.9	0.85
PaO2 mmHg	64.9±3.9	69.45±7.2	0.019
Day 3	Group I(18)	Group II(17)	P value
PH	7.39±0.026	7.36±0.03	0.02
$PaCo_2$	40.5±2.38	40.4±1.9	0.9
PaO_2	66.38±5.38	67.47±6.6	0.5
Day 7	Group I(16)	Group II(10)	P value
PH	7.39±0.003	7.37±0.03	0.02
$PaCo_2$	42±2.5	41.3±1.9	0.4
PaO_2	68.12±2.5	66±4.6	0.1

This table shows the difference between the values of (PH & Paco2 & Pao2) between both groups on day 1,3,7.

On day 1 (PH & Paco2 & Pao2) were (7.35 ±0.03 & 7.34 ±0.02) & (39.4 ±3.2 mmHg & 39.3 ±1.9 mmHg) & (64.9 ± 3.9 mmHg & 69.45 ± 7.2 mmHg) respectively but with only significant statistical difference in Pao2 .($P < 0.05$).

On day 3 (PH & Paco2 & Pao2) were (7.39 ±0.026 & 7.36 ±0.03) with significant statistical difference. ($P < 0.05$). & (40.5 ± 2.38 & 40.4 ±1.9) & (66.38 ± 5.38 & 67.47 ± 6.6) respectively but without any significant statistical difference. ($P > 0.05$).

On day 7 (PH & Paco2 & Pao2) were (7.39 ±0.03 vs. 7.37 ±0.03) with significant statistical difference. ($P < 0.05$). & (42 ± 2.5 vs. 41.3 ±1.9) & (68.12 ± 2.5 vs. 66.46) respectively but without any significant statistical difference. ($P > 0.05$).

(Table-6): The outcome of studied groups in relation to mortality

Outcome	Survived	Died	P value
Group I (20) n (%)	8(40%)	12(60%)	0.028
Group II (20) n (%)	2(10%)	18(90%)	

This table shows the percentage of survivors and deaths in both groups in which 40%of Group I survived and 60% died while 10% survived in Group II and 90 % died with significant statistical difference ($p<0.05$).

(Table-7): duration of mechanical Ventilation in survivors

survivor	**Group I(8)**	**Group II(2)**	**P value**
Days on MV(S)	**18.6±1.7**	**25.5±2.1**	**0.001**

In survivors the mean duration of mechanical ventilation was 18.6±1.7days in Group I and 25.5 ± 2.1 days in Group II with significant statistical difference $p <0.05$

(Table-8): Length of stay (LOS) in ICU in survivor

survivor	**Group I(8)**	**Group II(2)**	**P value**
LOS in ICU	**22.6±1.6**	**30.5±3.5**	**0.001**

This table shows that LOS in survivors in Group I and II was (22.6 ±1.6,30.5 ±3.5)respectively with significant statistical difference (<0.05).

(Table -9): frequency of complications in the studied group

Complication	Group I (20)	Group II(20)	P
Acute renal failure	25%	20%	1
VAP	15%	15%	1
Pneumothorax	5%	30%	.037
Arrhythmia	15%	35%	0.14
Bed sores	20%	5%	0.15
Upper GIT bleeding	10%	10%	1

This table shows the frequency of complications in the studied population in which acute renal failure was the most frequent complication in Group I (25%) compared to(20%) in Group II. arrhythmia was the most frequent complication in Group II 35% compared to 15% in Group I .other complications in Group I and II were VAP (15%, 15%) ,bed sores (20%,5%) upper GIT bleeding(10%,10)respectively.

Regarding pneumothorax frequency in Group I & II was (5%-30%) respectively with significant statistical difference.

DISCUSSION

As regard the etiology of ALI/ARDS (table 2), the most frequent etiology in both groups were sepsis (30% in group I) and pneumonia (30% in group II) without any significant statistical difference between the 2 groups, in agreement with **(Stewart et al.,1998)[8] and (Kallet et al., 2005)[9] .**

Other etiologies in group I and II include: aspiration (10% vs. 10%), trauma (25% vs. 20%), H1N1 (0% vs. 15%), drug overdose (10% vs. 0%) respectively in both groups (table 2).

In group II there were 3 cases of ARDS caused by H1N1 at the period from second half of 2009 and 2010 but in group I there were no cases of H1N1.

In March 2009 a novel influenza virus emerged in Mexico and the United States and quickly spread worldwide. The pandemic A (H1N1) virus originated from the triple-reassortment of swine influenza (H1) virus circulating in North American pigs. On June 11, 2009, WHO declared a world pandemic alert. By August 1, 2010, almost every country had reported laboratory-confirmed cases, with over 18,449 deaths. **(Hendrickson and Matthay , 2013)[2].**

The majority of H1N1-infected patients were children or adults aged < 60 years; most recovered uneventfully, and the overall mortality was not higher than that of seasonal influenza. Risk factors for more severe infection by pandemic H1N1 include extremes of age, underlying medical illness, obesity, and pregnancy. However, some previously healthy patients without co-morbidities developed rapidly progressive pneumonia, ARDS, multi-organ failure, and death. **(Louie et al, 2010)[10].**

As regards Pao_2/FIo_2 ratio and SAPS II score at admission (table 3) there was **no significant statistical difference** between group I and II, Pao_2/FIo_2 (131±33 vs. 118±20) and SAPS II (41.7±3.89 vs. 39.3±5.25) respectively and this was in harmony with ***Brochard et al. (1998)[7] and Kallet et al. (2005)[9].***

The SAPS II, based on a large international sample of patients, provides an estimate of the risk of death without having to specify a primary diagnosis **(Le Gall et al., 1993)[4].**

Pao_2/FIo_2 ratio was used by AECC definition of ARDS to discriminate between ALI and ARDS (ALI non-ARDS (200 mm Hg<Pao2/FIo2 ≤300 mm Hg) and ARDS alone (Pao2/FIo2 ≤200 mm Hg) **(Bernard et al., 1994)[12].**

The Berlin definition of acute respiratory distress syndrome used Pao2/FIo2 ratio with PEEP or CPAP ≥5 cm H2O to classify ARDS into 3 categories according to severity and consequently its impact on the outcome (200 < Pao2/FIo2 ≤ 300, 100 < Pao2/FIo2≤200, and Pao2/FIo2≤100) for (mild, moderate, and severe ARDS) respectively **(Ferguson et al.,2012)[13].**

By monitoring the venilatory parameters in group I and II in this study on days 1, 3, 7 in (table 4) respectively; there was a very significant statistical difference regarding tidal volume **(5.7±0.57 vs. 7.5±0.5)** on day 1, **(6±0 vs. 7.52 ±0.7)** on day 3, and **(6±0 vs. 7.3±0.48)** on day 7 respectively.

The use of this tidal volume was reflected on the plateau pressure as follows **(26.55±1.6 vs. 31.1±1.9)** on day 1, **(25.7±2.14 vs. 32.76±4.1)** on day 3, and **(24.6±4 vs.31.9±3.25)** on day 7; with a very significant statistical difference between the two groups.

This was in harmony with (**Kallet et al., 2005)[9] and (Villar et al., 2006)[14].**

However in this study with complete application of ARDS Network ventilatory protocol a lower FIo_2 in group I on day 3 was reached which continued till the end of the study with a significant statistical difference **despite of** non-significant statistical difference in PEEP and Pao_2 between the two groups.

This was in contrary to ***Kallet et al. (2005)[9]*** in which there was a highly significant difference in PEEP between the studied groups on day 1.

Also at **Villar et al. (2006)[14] study** there was also a high significant difference in PEEP between the studied groups all over the study.

This can be explained by the relative lower tidal volume in this study compared to the

aforementioned studies where the PEEP difference may affect FIo_2.

In one uncontrolled study of 53 patients with severe ARDS, the hospital mortality rate was significantly lower than that predicted by the Acute Physiology and Chronic Health Evaluation II scores (26.4% vs. 53.3%, *p* = .004) **(Hickling et al., 1994)[15].**

Several uncontrolled trials confirm that the technique of permissive hypercapnia is safe and leads to reasonable outcomes **(Gentilello et al., 1995)[16].**

At 1990 Lee et al. [17]conducted One randomized study of low tidal volume (VT = 6 mL/kg) vs. what was considered standard tidal volume (VT = 12 mL/kg) in all ventilated patients in a surgical intensive care unit (ICU); found decreased morbidity in the low tidal volume group; The incidence of pulmonary infection tended to be lower and duration of intubation and hospital stay tended to be shorter for non-neurosurgical and non-cardiac surgical patients randomized to low VT. The use of low VT was associated with a statistically significant but clinically irrelevant decrease in oxygenation.

Another four multicenter studies have compared limited volume and pressure ventilation (VT ,8 mL/kg or peak inspiratory pressure ,30 cm H2O) to a strategy with what was considered conventional ventilation (VT of 10 –15 mL/kg or peak inspiratory pressure ,50 cm H2O) (**Brochard et al., 1998[11], Stewart et al., 1998[8], and Ranieri et al., 1999[18]).**

In the study of ***Stewart et al. (1998)[8],*** 120 patients at high risk for ARDS had a mortality of 50% in the limited- ventilation group and 47% in the control group without any significant statistical difference.

In the study of ***Brochard et al. (1998)[11],*** a total of 116 patients with ARDS and no organ failure other than the lung were enrolled in 25 centers. Mortality at day 60 (low VT 46.6% vs. control 37.9%, p = 0.38), duration of mechanical ventilation (23.1 vs. 21.4 days, p =0.85), the prevalence of pneumothorax (14% vs. 12%, p =0.78).

An alternative lung protective ventilation strategy is the "open lung" technique conducted by ***Amato et al. (1998[19]).*** This technique aimed to maintain a level of positive end-expiratory pressure above the level at which alveoli collapse, clinically defined as the "inflection point" in a lung pressure-volume curve, and limiting distending pressure and volume. A total
of 53 patients with ARDS were randomized to receive conventional or protective mechanical ventilation. Protective ventilation involved end-expiratory pressures above the lower inflection point on the static pressure-volume curve, a tidal volume of < 6 mL per kilogram, driving pressures of <20 cm of water above the positive end-expiratory pressure value, permissive hypercapnia, and preferential use of pressure-limited ventilator modes. In the protective-ventilation group, the 28-day mortality was 38% as compared with 71% in the conventional-ventilation group **(p = 0.001)**.

However, the most definitive support for low volume/pressure ventilation has come from the National **Institutes of Health (NIH) ARDS Network trial** comparing 6 mL/kg vs. 12 mL/kg VT in patients with ALI and ARDS **(ARMA, 2000)[20]** The NIH ARDS Network is a clinical trial consortium of 10 clinical centers including 24 hospitals.The Data Safety and Monitoring Board stopped the trial early after a planned data analysis. There were 432 patients enrolled into the 6 mL/kg arm and 429 into the 12 mL/kg group. Mean tidal volume in the lower stretch group was 6.2 ± 0.8 mL vs. 11.8 ± 0.8 mL in the traditional group. Mean end-expiratory plateau pressures were 25 ± 6 and 33 ± 8 cm H2O, and the mortality before discharge in the two arms was 31.3% and 39.8% respectively (p = 0.01)

In this study there was an evidence that the adherence to ARDS Network ventilatory protocol with the low tidal volume based on predicted body weight and guarding against high plateau pressure was associated with a decrease in the overall mortality from 90% in the retrospective group to 60% in the intervention group with a significant statistical difference (*p value:* 0.028), and this reduction in mortality was independent of age , SAPS II , pH , Pao_2/FI_{O2} , other indices of disease severity , and the etiology of ALI/ARDS.

Although there is a mortality benefit in the intervention group it was noticed that the mortality in both groups is higher than in the aforementioned studies and other studies as ***Villar et al. (2006)[14],*** and this can be explained by the previously limited resources in locality and the lack of respiratory therapists, and also the very low nurse/bed ratio and possibly the differences in the etiology of ARDS patients (3 cases H1N1).

The ICU mortality in ***Villar et al. (2006)***[14] was 53.3% (24 of 45) in the control group vs. 32 % (16 of 50) in the intervention group with a significant statistical difference (*p value*: 0.04), in the randomized controlled study that was done by ***Villar et al.*** a control group of established ARDS were ventilated using a tidal volume of 9 – 11 ml/kg of predicted body weight and a PEEP ≥ 5 cm H_2o and an intervention group that was ventilated using a tidal volume of 5 – 8 ml/kg predicted body weight and a PEEP that was set on day 1 to be above the lower inflection point of the pressure volume curve of the respiratory system.

In kallet et al. (2005)[9] which was a retrospective uncontrolled study the patients managed with ARDS Network protocol had a lower hospital mortality compared with historical controls (32% vs. 51%, respectively; p = 0.004)

As regard the percentage of survivor and deaths at specific day intervals (table 6) ; In the first three days ,90% survival and 10% died in group I ,while 85% survived and 15% died in group II with total deaths 12.5 % in both groups from 3rd day to 7th day ,80% survived and 20% died in group I compared to 50% survived and 50% died in group II with total deaths 35% in both groups after the 7th day till the end of the study at 40% survived and 60% died in group I while in group II 10% survived and 90% died with statistical significant difference (p<0.05)with total deaths , 75% in both groups. This was in consistence with ***kallet et al. (2005)***[9] in which at the 1st 3 days there was 84% survived patients and 16% died patients in the lower tidal volume group, and 77% survived patients and 23% died ones in the higher tidal volume group with an overall mortality in both groups 19% ; by day 7 there was 60% survived patients and 40% died ones in the lower tidal volume group and 57.6% survived and 42.4 % died in the control group with an overall mortality in both groups 41%.

As regard duration of mechanical ventilation (table 7) In survivors the mean duration of mechanical ventilation was 18.6±1.7days in group I and 25.5 ± 2.1 days in group II with statistical significant difference p <0.05 this was in agreement with ***Amato et al. (1998)***[19] in which the duration of mechanical ventilation was expressed as weaning from mechanical ventilation at day 28 which was 19 cases of 29 ones (66%) in the lower tidal volume group vs. 7 cases of 24 (29%) in the higher tidal volume group with highly significant statistical difference (p= 0.005).

This also was in harmony with ***ARMA trial (2000)***[20] in which in which the duration of mechanical ventilation was expressed as ventilator-free days which was 12 ±11 in the lower tidal volume group and 10 ± 11 in the control group with significant statistical difference (p=0.007).

This was also in consistence with ***Villar et al. (2006)***[14] in which the duration of mechanical ventilation was expressed as ventilator-free days which was 10.9 ±9.4 in the lower tidal volume group and 6.0 ± 7.9 in the control group with significant statistical difference (p=0.008)

As regard length of stay in ICU (table 8) LOS in survivors in group I and II was (22.6 ±1.6 vs. 30.5 ±3.5) respectively with significant statistical difference (p<0.05).

This was not in consistence with ***Stewart et al. (1998***[8]***)*** in which the lenghth of stay in ICU was more in the limited tidal volume group than in the controlled group (19.9±39 vs. 13.7±15.8) respectively with no significant statistical difference (p<0.05).

The lenghth of stay in ICU was also more in the limited tidal volume group than in the controlled group also in ***Brochard et al. (1998***[11]***)*** (33.5±28.7 vs. 29.7± 19.4) with no significant statistical difference between the two groups.

This can be explained by the difference in defining ARDS patients in their studies, and also we used a much lower tidal volume in this study in group I which was less than 6 ml of predicted body weight; but in both ***Brochard et al. (1998***[11]***)*** and ***Stewart et al. (1998)***[8] the tidal volume was more than 7 ml per kilogram and was not based on predicted body weight

As regard frequency of complications in the studied group(table 9) the frequency of complications in the studied population in which acute renal failure was the most frequent complication in group I (25%) compared to(20%) in group II. arrhythmia was the most frequent complication in group II 35% compared to 15% in group I .other complications in group I and II were VAP (15%, 15%) ,bed sores (20%,5%) upper GIT bleeding(10%,10)respectively without any significant statistical difference .But regarding **pneumothorax** frequency in group I & II was (5%-30%) respectively with significant statistical difference and this was in consistence with ***Villar et al.(2006)***[14]**.**

Conclusions: Application of ARDS Network ventilatory protocol as a ventilatory strategy in

ARDS patients decreases the overall mortality, days on mechanical ventilation, the length of stay in ICU and the incidence of barotrauma.

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