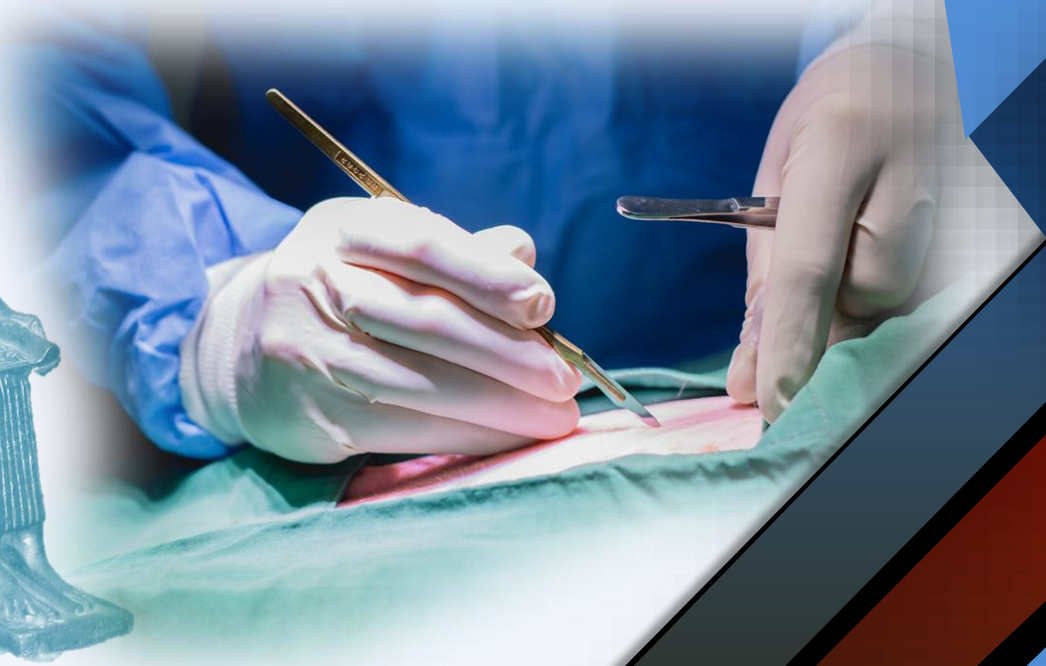


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## Original Article

# Comparative Study Between the Effect of Airway Pressure Release Ventilation and Synchronized Intermittent Mandatory Ventilation in Acute Respiratory Distress Syndrome

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## ABSTRACT

### Article information

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**Background:** Acute respiratory distress syndrome [ARDS] is a serious illness with a high fatality rate and a bleak prognosis. Mechanical ventilation [MV] is now regarded as one of the best methods for treating ARDS. In order to determine whether the breathing technique was safer and more effective for patients with acute ARDS.

**The aim of the work:** This study aimed to compare airway pressure release ventilation [APRV] mode and synchronized intermittent mandatory ventilation [SIMV] mode with lung protective strategy protocol.

**Patients and Methods:** This prospective study included 34 patients aged 20 to 75 years old, both sexes with ARDS. Patients were divided randomly into two equal groups: Group A: APRV mode and group B: SIMV mode with lung protective strategy protocol.

**Results:** Group A had substantially greater PaO<sub>2</sub>, PaO<sub>2</sub>/FiO<sub>2</sub> ratio and respiratory compliance at 12, 24, 36, 48, 72 and 96 hours than group B. Group A had considerably lower FiO<sub>2</sub> and plateau pressure at 12, 24, 36, 48, 72 and 96 hours than group B. Group A showed significantly shorter total ventilator days and intensive care unit [ICU] stay compared to group B [P<0.05]. Both groups had similar rates of ICU mortality and successful extubation. Both groups had a comparable heart rate, systolic blood pressure, diastolic blood pressure and mean arterial blood pressure.

**Conclusions:** In comparison to SIMV mode with the lung protective strategy protocol, APRV mode has a compatible effect and safer outcomes.

**Keywords:** Airway Pressure Release; Mechanical Ventilation; SIMV; Respiratory Failure.



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## INTRODUCTION

Insufficient oxygenation, lung infiltrates and sharpness of start without any indication of cardiogenic pulmonary edema are the hallmarks of acute respiratory distress syndrome [1]. Acute respiratory distress syndrome [ARDS] is determined by the ratio of the patient's partial pressure of oxygen [ $\text{PaO}_2$ ] to the fraction of inspiratory oxygen concentration [ $\text{FiO}_2$ ]. The patient's  $\text{PaO}_2/\text{FiO}_2$  ratio is less than 300. The ARDS definition, often known as the Berlin definition, underwent modification in 2012. The phrase "acute lung injury" was eliminated, the criterion of a wedge pressure of 18 was deleted and the condition of a continuous positive airway pressure [CPAP] or positive end-expiratory pressure [PEEP] of five or higher was introduced. These modifications distinguish it from the prior American European Consensus definition [2, 3]. The most popular way to provide breathing help is through invasive mechanical ventilation [MV]. In a significant North American randomized controlled trial, it was discovered that decreasing tidal volume [Vt] and restricting end-inspiratory plateau pressure [P-plat] improved the survival of ARDS patients [4]. Patients with ARDS often employ MV with a low Vt, limiting inspiratory pressure and PEEP to reduce overdistension and alveolar atelectasis [5, 6]. Controlled modalities of mechanical breathing are typically accompanied by lengthy weaning, hemodynamic impairment and high doses of sedation and neuromuscular blockers. Partial ventilatory support minimizes the necessity for muscle paralysis, sedation and respiratory muscle dysfunction during MV [7].

In contrast to conventional breathing techniques, airway pressure release ventilation [APRV] offers both intermittent release phases and continuous positive air pressure. This allows for the release of only a portion of the lung volume and enables spontaneous breathing at high-pressure levels. The use of the APRV technique, as opposed to low Vt [LTV], has been shown to enhance alveolar recruitment, improve gas exchange, promote homogeneity and reduce lung damage in ARDS [8]. As a result, APRV is still an experimental treatment for ARDS patients. In contrast to conventional LTV, we expected that the APRV technique would better increase oxygenation in ARDS patients and shorten the duration of MV.

## THE AIM OF THE WORK

The aim of this research was to evaluate the effectiveness and safety of APRV mode in comparison to SIMV mode with lung protective strategy protocol, in patients diagnosed with ARDS.

## PATIENTS AND METHODS

This research was conducted on 34 patients, ranging in age from 20 to 75 years old, of both sexes who had ARDS. The study design was prospective and randomized with a controlled group. The research was conducted with approval from the Ethical Committee of Al-Azhar University in Cairo, Egypt. The patient's family provided informed written permission. The exclusion criteria were patients exhibiting hemodynamic instability, cardiogenic pulmonary edema, recent unstable angina or myocardial infarction, chronic obstructive pulmonary disease, suspected or confirmed intracranial hypertension, severe barotrauma, anatomical abnormalities of the chest wall and pregnancy.

### Randomization:

During the stabilization phase of ARDS, patients underwent ventilation

using protective lung strategies with Volume Assist-Control Mandatory Ventilation [VACMV] mode. Prior to the study, participants were randomly assigned to either the SIMV mode with a lung protective strategy protocol or the APRV mode. An algorithmic random number generator was used to allocate the patients into two equitably sized groups. Each group adheres to a distinct process for safeguarding the lungs. Group A employs the APRV mode, whereas group B utilizes the SIMV mode along with a lung protective strategy protocol.

Complete blood count [CBC], serum sugar analysis, arterial blood gases [ABG], radiological investigations, trans-thoracic echocardiography to rule out cardiogenic pulmonary edema and a detailed medical history from family members were all part of the comprehensive assessment that all patients underwent. The assessment also included a comprehensive clinical examination.

### Group [A], APRV mode:

The prior VCV settings were used to determine the high airway pressure [ $\text{P}_{\text{high}}$ ], which was set at the  $\text{P}_{\text{plat}}$  and kept below 30  $\text{cmH}_2\text{O}$ . There were a 5  $\text{cmH}_2\text{O}$  setting for the low airway pressure [ $\text{P}_{\text{low}}$ ] [9, 10].

**Release phase duration [ $\text{T}_{\text{low}}$ ]:** Several authors have offered recommendations for the first APRV setting. In our investigation, we used a T-low range of 0.2 to 0.8 seconds. We fixed the release frequency at 10–14 cycles per minute. Based on the T-low and release frequency, we were able to indirectly calculate the duration of P-high [T-high] [9, 10].

**Weaning APRV:** Initially, we bring the  $\text{FiO}_2$  level down. Once  $\text{FiO}_2$  has decreased to 0.4-0.5, we reduced P-high. We are reducing P-high by 2  $\text{cmH}_2\text{O}$  every 2-6 hours while keeping  $\text{FiO}_2$  at 0.4-0.5. Hypoxemia necessitates a more gradual weaning process and an increase of 4  $\text{cmH}_2\text{O}$  in P-high. Once the P-high reached 20  $\text{cmH}_2\text{O}$ , we raised the T-high by one or two seconds each time the P-high was reduced. We swap to CPAP with a PEEP of 10 and a pressure support [PS] of 5-10  $\text{cmH}_2\text{O}$  once the patient's P-high and T-high had reached 10  $\text{cmH}_2\text{O}$  and 12-15 seconds, respectively. The evaluation of the patient's preparedness for extubation can only be done after that [11].

### Group [B], SIMV mode with lung protective strategy protocol group:

We used a technique called low-tidal volume breathing in order to safeguard the integrity of the lungs. The objective was to attain a volume-to-weight ratio [Vt] of 6  $\text{mL/kg}$  predicted body weight [PBW] and to maintain a plateau pressure [P-plat] below 30  $\text{cmH}_2\text{O}$ . If the plateau pressure exceeded 30  $\text{cmH}_2\text{O}$ , we decreased the Vt to 4  $\text{mL/kg}$  PBW. The first respiratory rate ranged from eighteen to twenty-two breaths per minute. The ratio of inhalation to exhalation ranges from 1:1 to 1:3. The target for  $\text{FiO}_2$  and PEEP was to achieve a  $\text{PaO}_2$  level between 55-100 mmHg or a  $\text{SaO}_2$  level between 88.0 - 95.0%. PEEP tables may serve as a useful point of reference, although strict adherence to them is not necessary. The World Health Organization [WHO] recommends using a high PEEP strategy, which aligns with the presently known knowledge on COVID-19. In our research, we used a strategy of greater PEEP and lower  $\text{FiO}_2$ . This choice was made since there is no observed benefit in terms of mortality when using low PEEP compared to high PEEP [12]. Then, in accordance with the ARDS net protocol, the respiratory rate and Vt were adjusted to get the desired pH and P-plat levels.

Each day, we discontinue the usage of sedation and use the Spontaneous Breathing Trials [SBT] safety screen in the morning to oversee the patients. Patients who successfully completed the SBT safety screening had a 30-minute SBT using pressure support ventilation with 5-7 cmH<sub>2</sub>O, positive end-expiratory pressure [PEEP] of 5 cmH<sub>2</sub>O, and a FiO<sub>2</sub> of 40.0% [13]. As recommended by current guidelines, both groups used the same procedures for pain management and sedation. In order to put the patients to sleep, we used midazolam and propofol, with the goal of getting their Richmond Agitation Sedation Scale [RASS] scores between -2 and -4, which is predicated on the analgesic effects of fentanyl. Fentanyl, midazolam and propofol were initially administered intravenously at dosages of 0.7–3 µg/kg, 0.03–0.3 mg/kg and 1-3 mg/kg, respectively. These were followed by infusions of 1-2 µg/kg/h, 1-4 mg/h, and 5-20 µg/kg/min, respectively. Every morning at 8:00 a.m., the patients were routinely awakened by interrupting their sedative infusions according to predetermined criteria. To accomplish a respectable level of spontaneous breathing during the P-high phase, we titrated the APRV and altered the settings and dosages of sedatives and analgesics in this study.

Hypoxic index [PaO<sub>2</sub>/FiO<sub>2</sub>] was the primary outcome. Main outcome variables [total ventilatory days, length of ICU stay, successful extubation and death during the ICU stay], the secondary outcomes included hemodynamic variables [heart rate, SBP, DBP and MAP] and respiratory variables [PH, PaCO<sub>2</sub>, PaO<sub>2</sub>, FiO<sub>2</sub>, plateau pressure and respiratory system compliance]. Except for the main outcome variables, data was taken at 0, 2, 4, 12, 24, 36, 48, 72 and 96 hours.

**Sample Size Calculation:**

Epidemiological Information [Epi Info] [version 7.2.5, Georgia, US] was used for power analysis to find a representative sample and guarantee the finding's validity. A 95.0% confidence level, 90.0% power and 5.0%  $\alpha$  error were taken into consideration. The minimum representative sample size would be 30 cases [n] based on the data from recent research by Zhou et al. [14], which showed that the PaO<sub>2</sub>/FiO<sub>2</sub> ratio was lower in the lung-protective ventilation group compared to the APRV group [180.5 ±68.6 Vs. 280.3±83.9]. There would be a total of 34 instances [N] if we estimate a 10.0% drop-out during follow-up [f].

**Statistical analysis:**

Software created by IBM Inc. of Chicago, IL, USA, known as SPSS v26, was used to perform a statistical significance analysis. To determine whether the data was normally distributed, we used histograms and the Shapiro-Wilks test. An unpaired Student's t-test was used to compare the two groups and obtain the means and standard deviations [SD] of quantitative parametric variables. The quantitative non-parametric data, which were shown using the IQR and median, were evaluated using the Mann-Whitney U-test. A Chi-square test or Fisher's exact test was used to assess the qualitative variables. Data were represented using frequencies and percentages. With a two-tailed P value less than 0.05, the statistical significance was determined.

**RESULTS**

Out of 45 people who were assessed for appropriateness, 3 patient's relatives decided not to participate in the study and 8 patients did not meet the criteria. There were 17 patients in each of the two remaining groups that were randomly allocated. Statistical approaches were used to track and evaluate each allocated patient [Figure 1].

There were no significant differences in age, sex, weight, height and BMI between both groups [Table 1]. Heart rate, SBP, DBP and MAP were insignificantly different at baseline, 2h, 4h, 12h, 24h, 36h, 48h, 72h and 96h between both groups [Figure 2]. pH and PaCO<sub>2</sub> were insignificantly different at baseline, 2h, 4h, 12h, 24h, 36h, 48h, 72h and 96 hours between both groups. PaO<sub>2</sub>, FiO<sub>2</sub>, PaO<sub>2</sub>/ FiO<sub>2</sub>, plateau pressure and respiratory compliance were insignificantly different at baseline, 2h and 4h between both groups. PaO<sub>2</sub>, PaO<sub>2</sub>/FiO<sub>2</sub> and respiratory compliance were significantly higher at 12h, 24h, 36h, 48h, 72h and 96h in group A than in group B. FiO<sub>2</sub> and plateau pressure were significantly lower at 12h, 24h, 36h, 48h, 72h and 96h in group A than group B [Figure 3]. Group A had a considerably lower number of ventilator days and shorter duration of stay in the ICU compared to group B [P<0.05] [Table 2]. Successful extubation and death during the ICU stay were insignificantly different between both groups [Table 2].

**Table [1]: Demographic data of the studied groups**

Variable		Group A [n=17]	Group B [n=17]	P
Age [years]		44.24±15.08	50.53±15.23	0.2349
Sex	Male	9 [52.94%]	7 [41.18%]	0.4984
	Female	8 [47.06%]	10 [58.82%]	
Weight [kg]		73.82±12.3	80.18±12.22	0.1407
Height [m]		1.68±0.08	1.68±0.07	0.8621
BMI [kg/m <sup>2</sup> ]		26.32±4.69	28.42±4.53	0.1937

**Table [2]: Outcome among study groups**

Variable	Group A [n=17]	Group B [n=17]	P
Total ventilator days [days]	10.88 ± 3.94	15.24 ± 5.29	<b>0.0104*</b>
Length of ICU stay [days]	13.41 ± 4.99	17.47 ± 5.9	<b>0.0378*</b>
Successful extubating	12 [70.59%]	10 [58.82%]	0.4795
Death during the ICU stay	5 [29.41%]	7 [41.18%]	0.4795

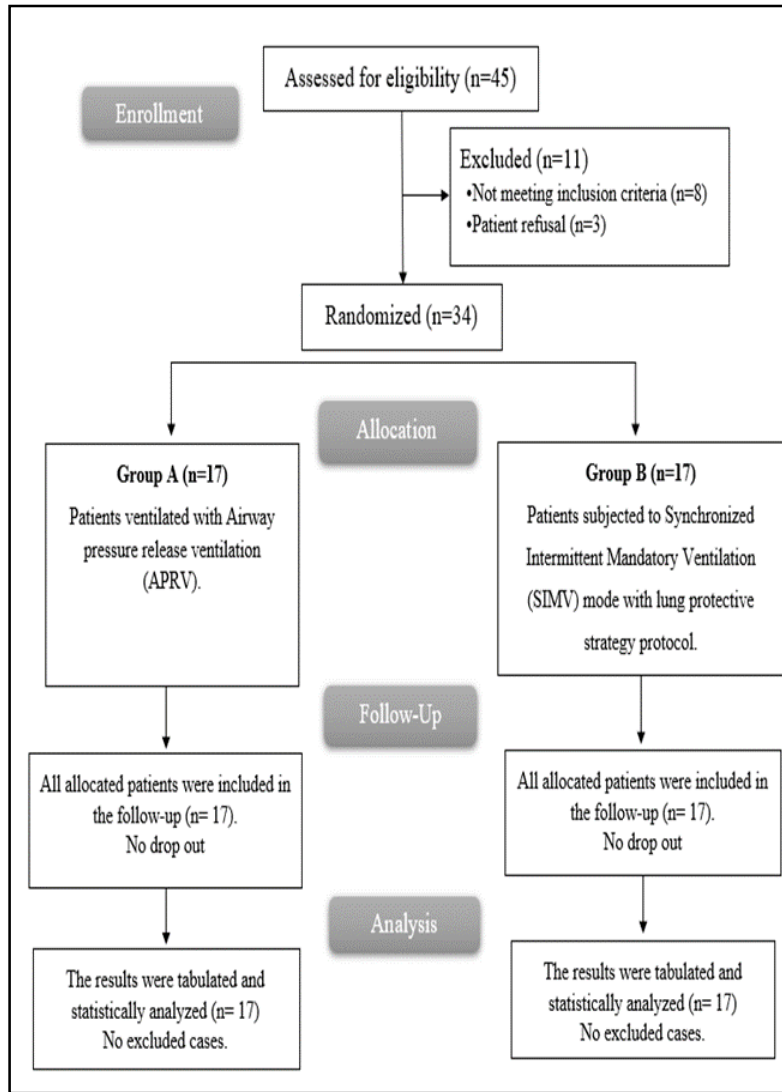


Figure [1]: CONSORT flowchart of the enrolled patients

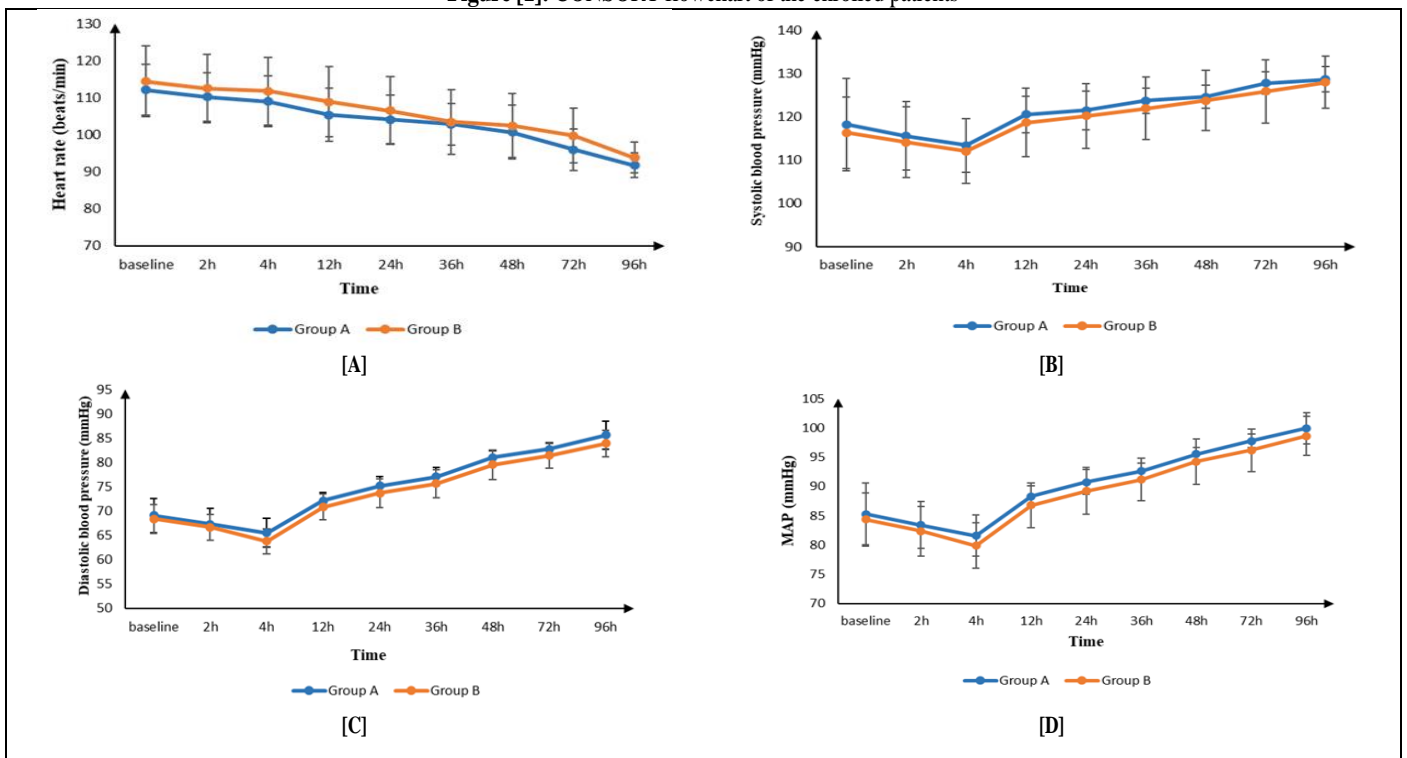


Figure [2]: [A] Heart rate, [B] systolic blood pressure, [C] diastolic blood pressure and [D] mean arterial blood pressure of the studied groups

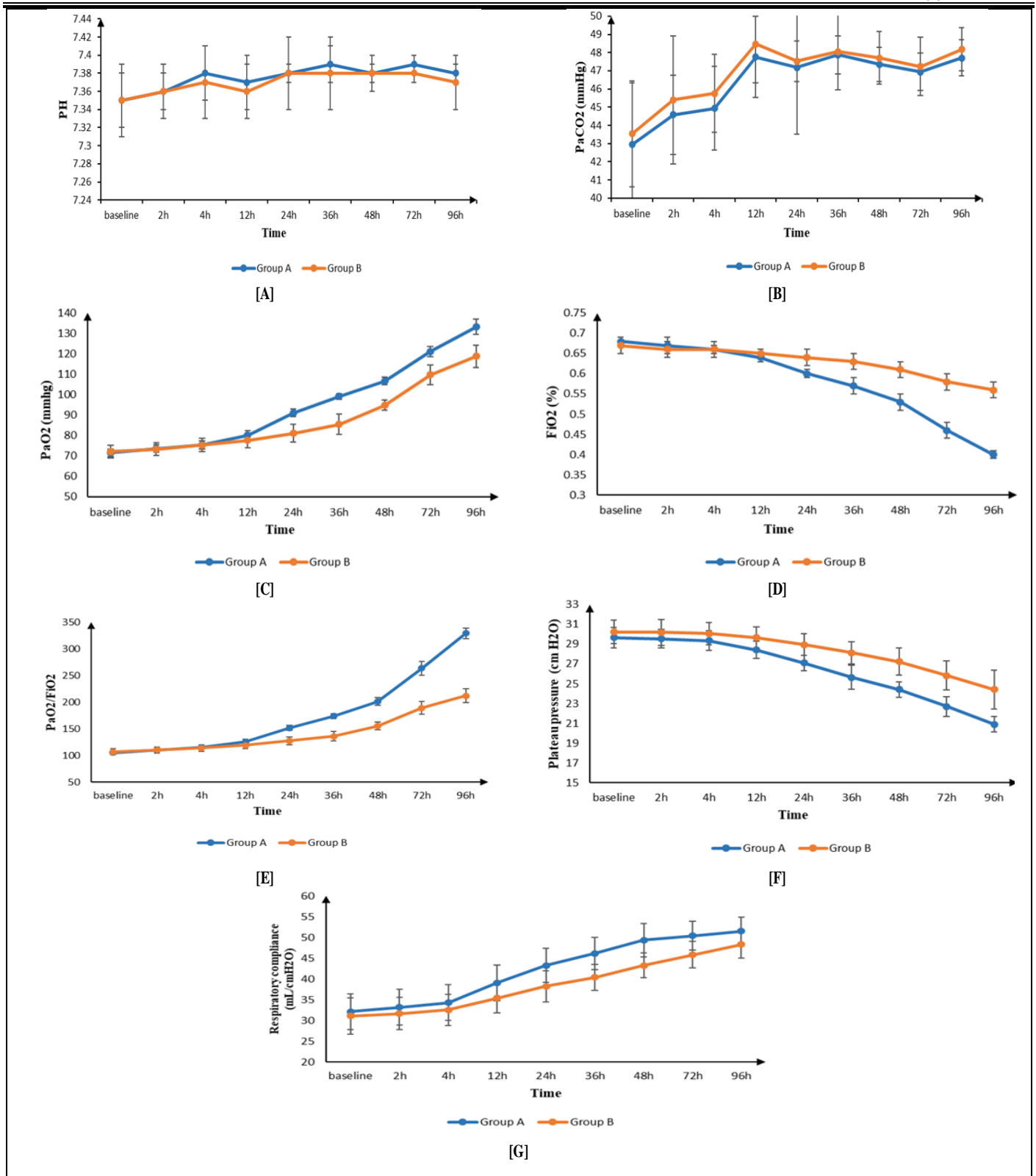


Figure [3]: [A] Potential of hydrogen, [B] partial pressure of carbon dioxide, [C] PaO<sub>2</sub>, [D] FiO<sub>2</sub>, [E] PaO<sub>2</sub>/FiO<sub>2</sub>, [F] plateau pressure and [G] respiratory compliance of the studied groups

### DISCUSSION

ARDS is a grievous medical condition that is distinguished by a poor prognosis for recovery and a high rate of mortality. MV is now *thought* to be among the best methods for managing ARDS [15]. Our research demonstrated that APRV was significantly associated with increased PaO<sub>2</sub>, PaO<sub>2</sub>/FiO<sub>2</sub> and respiratory compliance, as well as decreased FiO<sub>2</sub> and plateau pressure at 12h, 24h, 36h, 48h, 72h and 96h. Additionally, the patient group who had APRV exhibited a significant decrease in both the amount

of time spent on the ventilator and the length of time spent in the intensive care unit. Patient's demographics, hemodynamic variables [such as HR, SBP, DBP and mean arterial blood pressure], pH value, PaCO<sub>2</sub>, rate of successful extubation and rate of death during the ICU stay were not different between the study groups. Our research findings align closely with the conclusions stated by **Putensen et al.**[16], **Roy et al.**[13] and **Kollisch-Singule et al.**[17] on the evaluation of the hypoxic index and respiratory mechanics, who documented that when compared to LTV ventilation, APRV resulted in a considerable improvement in oxygenation and

respiratory system compliance, as well as a marked drop in plateau airway pressure and an increase in mean airway pressure in ARDS patients. In contrast to the SIMV and LTV procedures, **Sun et al.** [15] discovered that the APRV technique significantly improved the PaO<sub>2</sub>/FiO<sub>2</sub> ratio, indicating that it is safe and effective. **Liu et al.** [18] found that when APRV is used in ARDS patients, oxygenation improves and there is a tendency for ICU mortality to decline.

The findings indicate that sustaining spontaneous respiration at elevated mean airway pressure might stop the decline in pulmonary gas exchange, even among patients who MV. Conversely, every *breathing* attempt is augmented to guarantee a steady influx of air into the alveoli when SIMV with pressure support is used [18].

However, when compared to CPPV or LTV, the study results from **Maxwell et al.** [19], **Varpula et al.** [20] and **Song et al.** [21] indicated that the advantages of APRV on pulmonary function showed similarities. For example, research by **Maxwell et al.** [19] revealed that the physiological characteristics of adult trauma patients experiencing acute respiratory failure on APRV or LTV were similar. However, the study's APRV methodology was out of date; P-high's *maximum* limit was 40 cmH<sub>2</sub>O, while the most recent data suggests keeping the inspiratory end plateau pressure below 30 cmH<sub>2</sub>O [9], there may be dynamic variability between inhalation and exhalation if the T-low is less than 50.0% of the PEFR, which was determined to be 25.0-75.0% of the PEFR [17]. Pressure and time should regulate the recruitment and de-recruitment of lung units, according to **Bates and Irvin** [22].

By elevating CPAP pressure levels, extending the duration of hypertension and elevating the oxygen concentration [FiO<sub>2</sub>], APRV improves *oxygenation*, according to **Li et al.** [23]. Furthermore, providing sufficient PEEP during the P-high phase of APRV by permitting a moderate spontaneous breath level promoted lung recruitment, enhanced ventilation/perfusion matching and enhanced lung homogenous aeration, all while reducing pendelluft and the harm it causes [10, 24, 25].

**Yoshida et al.** [26] and **Fan et al.** [27] found no differences in HR and MAP between various conventional ventilator modes and APRV mode, which is in agreement with our study's findings when it comes to analyzing hemodynamics. According to **Kollisch-Singule et al.** [17], **Habashi** [10] and **Fan et al.** [27], when APRV is used in ventilation, spontaneous breathing is allowed while concurrently lowering intrathoracic pressure. As a result, circulatory function and systematic venous return are enhanced, while sedation and neuromuscular blockers are reduced. Therefore, this may reduce the negative effects on the cardiovascular system from increased airway pressures. Furthermore, **Hering et al.** [28] reported that spontaneous breathing improves organ perfusion more than complete MV control.

Results from our research corroborate those of **Walkey et al.** [29] and **Sharaf et al.** [30] when it comes to evaluating acid-base balance. When comparing several traditional ventilator modes with APRV *mode* in individuals with ARDS, they found no alterations in pH or serum bicarbonate levels.

When it comes to assess CO<sub>2</sub> partial pressure levels, our research agrees with the results of both **Walkey et al.** [29] and **Sharaf et al.** [30]. They found no differences in carbon dioxide partial pressure readings between various conventional ventilator modes and APRV mode among those with acute lung injury [ALI] or ARDS. According to our findings, CO<sub>2</sub> emissions occur

through [i] Allow hypercapnia if the pH is more than 7.25 and acidosis is not harmful [permissive hypercapnia]. [ii] Attempt to reduce the usage of sedatives until the patient is actively breathing on their own. [iii] Make sure there aren't any secretions or excess moisture in the ventilator circuit or the heat and moisture exchanger filter. [iv] Reduce T-high by 0.2 seconds, bringing it down to a minimum of 3 seconds. [v] Think about increasing P-high to maximize recruitment and minimize dead space.

Our results corroborate those of **Putensen et al.** [16] when calculating the amount of time, the patient spends in the ICU and the total number of days they need ventilatory assistance. What they discovered was that patients at risk for ARDS who used APRV had shorter ventilatory support durations and *shorter* ICU stays. Both **Kambhampati et al.** [31] and **Sundar et al.** [32] postulated that APRV's ability to improve early respiratory performance and boost organ perfusion is the primary reason for its ability to reduce MV time and ICU stays. Consequently, early recovery is made possible by lowering the time of sedative treatment while maintaining spontaneous breathing. Another study by **Maung et al.** [33] found that APRV could make patients use the ventilator for longer than necessary. However, the *research* did not employ a comprehensive weaning protocol and the APRV parameters used were outdated.

In evaluating successful extubation and death during ICU stay the findings of our study align with those of the study that **Liu et al.** [18] concluded. Stated there is no statistically significant correlation between the usage of APRV and decreased ICU mortality. **Sun et al.** [15] concluded that when comparing APRV to SIMV, no significant disparities were seen in mortality or length of ICU stay.

Several limitations were found in the research. First, the research was a hospital-based study, so there weren't a lot of instances and the sample size wasn't that big in comparison to the results and the possibility of publication bias is further increased *since* the research was not multicentric. Secondly, blinding was not used in this study due to the obvious differences in ventilator settings. Finally, in our sample, there were several patients, but they were all of Egyptian heritage, so that's something to keep in mind. This is why we need to broaden our search to include people of different ethnicities in the local database.

**Conclusions:** In comparison to SIMV mode with the lung protective strategy protocol, APRV mode has a compatible effect and safer outcomes, including better oxygenation and respiratory system compliance, reduced plateau pressure, fewer ventilatory days and a shorter length of ICU stay.

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