

# Impact of airway pressure release ventilation mode on vasopressors and sedation in patients with Septic Shock

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## ABSTRACT

**Introduction:** Generally, airway pressure release ventilation (APRV) simply is defined as a pressure-controlled manner that permits natural breathing through the ventilation set. It enhances significantly organ perfusion through increasing in both venous return and cardiac index. The primary outcome of the current study is to assess the valuable of using APRV in cases of septic shock patients returns hemodynamics constancy earlier than the controlled mechanical ventilation (CMV) method. The secondary outcome is to validate whether the application of APRV improves the survival in the ICU, decrease the length of ICU stay; decrease the ventilator days and whether it decrease the need for sedation and neuromuscular blockers (NMBS) compared to CMV mode. **Methods:** We prospectively evaluated the clinical documents of forty septic shock patients who given invasive mechanical ventilation from November 2014 to August 2015 at Department of Critical Care, Faculty of Medicine, Cairo University, Egypt. Patients were randomized into two groups according to the mode of ventilation (APRV and CMV groups). All included patients were subjected to resuscitation for septic shock for control of septic shock in patients depending on the instructions of surviving sepsis campaign international guidelines (2013), full clinical evaluation, routine microbiological and laboratory investigations. Patients were followed up daily to assess their clinical course, length of ICU stay, duration of mechanical ventilation, dosages and duration of vasopressors, dosage and duration for sedation and if needed NMBS and their final outcome. **Results:** The initial time to start recovery from septic shock was significantly earlier in APRV compared to CMV patients ( $13.7 \pm 4.6$  hours versus  $21.3 \pm 8.5$  hours,  $P < 0.001$ ). The need for sedation or NMBS was statistical significantly higher in CMV compared to APRV patients with a  $P$ : 0.010 and 0.028 respectively. CMV patients had statistical insignificantly longer ICU length of stay and duration of mechanical ventilation. APRV mode did not reduced mortality compared to CMV. **Conclusion:** The application of APRV mode in patients with septic shock to return hemodynamic constancy former than the CMV manner, decreases the need of sedation and NMBS.

**Keywords:** airway pressure release ventilation, controlled mechanical ventilation, Septic shock, Hemodynamics.

## Introduction

Septic shock is a major healthcare problem, affecting millions of individuals around the world each year; In fact; in the United States, septic shock is the main frequent reason of mortality in intensive care units [1]. In addition to mortality rate of 30–50% in adults, septic shock carries a substantial morbidity from secondary organ failure, which occurs in over one-third of patients. The most common organ failure is the

respiratory system [2].

The definition of septic shock generally is known as a response of body systems to inflammatory reactions resulting from a usually localized disease with new or acute onset leads to lesions or even dysfunction in affected organ and or malfunction with refractory hypotension which need vasopressors in spite of adequate fluid resuscitation and or elevated lactate [3].

Microbial infections or sepsis is considered one of the main etiologies of acute respiratory distress syndrome (ARDS) and acute lung injury (ALI), where the lungs are wounded due to the presence of inflammatory mediators circulating in the body particularly in the lungs, leading to harshly impaired exchange of gas which frequently needs invasive mechanical ventilation. Therefore, the aim of mechanical ventilation is to sustain oxygenation of tissues and keep away from elevated acidosis with high level, In the same time reducing additional lung deterioration, which subsequently extend to multiorgans ending with dysfunction or failure [4].

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One of the disadvantages of mechanical ventilation is that it induces high positive pressure, which obligates the air to enter inside the lungs, which consequently elevate an intra thoracic pressure<sup>15, 61</sup>. The elevation in the intrathoracic pressure will be accompanied by induction of physiological impacts that are directly contrary to usual natural ventilation.

The impacts of high (+ve) pressure ventilation on hemodynamic comprises a diminish in venous return of the left and right ventricle, reductions in the interaction of ventricles, a raise in the resistance of pulmonary blood vessels, is associated with an elevation in central venous pressure and a reduction in left ventricular after loading with the net effect that ending with a fall in cardiac output and systolic blood pressure<sup>15-81</sup>. The impacts of mechanical ventilation on hemodynamic are relative to the quantity of high pressure, inspiratory size and rate of positive end-expiratory pressure<sup>17, 9, 101</sup>. A drop in preload and blood pressure depends on the capacity condition of the patient and are more distinct in conditions of dropped venous return (hypovolemia, vasodilatation)<sup>17, 101</sup>.

The drop in preload and blood pressure will moreover be larger with controlled tools of mechanical ventilation with high airway pressure and high tidal volume, therefore the using of assisted spontaneous mechanical ventilation modalities (BiPAP, APRV, PSV, CPAP) are favored<sup>17, 101</sup>.

The most current mode of ventilation used in septic shock is CMV mode with lung protective strategy for ARDS. However, currently there is an increasing use of non-conventional ventilator modes in intensive care units, one of which is APRV.

APRV simply is a pressure-controlled mode that allows spontaneous breaths, Stock and Downs in 1987<sup>111, 121</sup> definite APRV as a constant positive airway pressure (CPAP) with an intermittent discharge period. APRV permits impulsive breathing all over the ventilation cycle. It maintains cardiac index and venous come back, which will appreciably recover organ perfusion which is essential in septic shock individuals to avoid extra thoracic organ system failure resultant from reduced perfusion.

APRV mode is characterized by the average inspiratory pressure is highest and the end-expiratory pressure is according to intentional auto-PEEP, this differs from traditional modes of APRV<sup>113</sup>.

Profit of APRV with cardiovascular alterations have been observed in subjects with ALI and ARDS.<sup>114</sup>

Our aim in this study was to evaluate the usefulness of APRV mode in restoring hemodynamics in patients with septic shock and decreasing need for vasopressors and inotropes.

## Materials and Methods

This current study was conducted on forty patients (26 males and 14 females with their ages ranging between 35 to 72 years) diagnosed as having septic shock and required invasive mechanical ventilation and admitted to the critical care

department, faculty of medicine, Cairo University from November 2014 to August 2015. Patients were randomized into two groups: APRV group and CMV group according to the mode of mechanical ventilation. Exclusion criteria for all participants selected for the study included: patients not capable of breathing spontaneously, patients with neuromuscular disease, obstructive lung disease, conditions that may worsen with the elevation of the mean airway pressure such as patients with unmanaged increase of intracranial pressure (e.g. head injury) and large bronchopleural fistulas.

All patients were followed up for a total of 28 days (4 weeks) from study day 1, till the day of discharge or demise.

## Ventilators mode parameters:

- All patients were ventilated using Dragger Evita4 ventilator. Assist control ventilation (ACV) was used as the initial ventilation mode in CMV group patients with an initial FiO<sub>2</sub> of 1, positive end expiratory pressure (PEEP) of 5-15 cm H<sub>2</sub>O; a rate of 15-25 breaths per minute.
- The primary goal is to achieve arterial oxygen saturation greater than 90% and PH greater than 7.25 while the secondary goals include FiO<sub>2</sub> 0.6 or less, peak airway pressures of less than 40 cm H<sub>2</sub>O and plateau pressures of less than 30 cm H<sub>2</sub>O. Patients should receive tidal volumes of 6 ml/kg of ideal body weight and end-inspiratory plateau pressures of less than 30 cm H<sub>2</sub>O to minimize additional lung dysfunction according to ARDS net protocol<sup>115</sup>.

## Initial ventilator settings in APRV group patients:

P high and T high are set to increase end-inspiratory lung volume, recruitment, and oxygenation. P low and T low regulate end-expiratory lung volume, and their settings should prevent derecruitment but ensure adequate alveolar ventilation.

P high; it is better to be  $\leq 30$  cm H<sub>2</sub>O to minimize peak alveolar pressure and reduce the risk of lung over distention. P low is set at 0 cm H<sub>2</sub>O.

T high is set at 4 seconds and is then adjusted if necessary. We usually start with a T low of 0.6 to 0.8 seconds.

All included patients were subjected to resuscitation for septic shock according to approved international guidelines of surviving sepsis campaign 2013.<sup>116</sup> Full clinical evaluation and routine laboratory investigations were done including arterial lactate (on admission and 6 hours later) as a prognostic tool for improvement in hemodynamics or outcome and microbiological studies. Hemodynamic parameters had been assessed on admission to ICU and continuously according to ICU protocol; including heart rate, mean arterial pressure (MAP) measured invasively, central venous pressure (CVP),

central venous oxygen saturation (ScVO<sub>2</sub> %) and urine output hourly.

Dosages and duration of vasopressors drugs.

The need for and doses of sedatives as midazolam and neuromuscular blockers as tracium is evident. In both groups the length of ICU stays, duration of mechanical ventilation, time required for reversal of shock and mortality was monitored and reordered.

## Statistical methodology:

Data was analyzed using IBM SPSS advanced statistics version 22 (SPSS Inc., Chicago, IL). Numerical data were expressed as mean and standard deviation or median and range as appropriate. Qualitative data were expressed as frequency and percentage. Chi-square test or Fisher's exact test was used to examine the relation between qualitative variables. For not normally distributed quantitative data, comparison between two groups was done using Mann-Whitney test (non-parametric t-test).

The final outcome and the reversal of septic shock were analyzed using survival analysis. Survival analysis was done using Kaplan-Meier method and comparison between two survival curves was done using log-rank test. All tests were two-tailed. A p-value  $\leq 0.05$  was considered significant.

## Results

### A. Descriptive data:

- Our study was conducted on forty patients; 26 males (65%) and 14 females (35%). Their ages were ranged from 35 -72 years old with mean age of  $59.4 \pm 9.5$ .
- Different co-morbidities were encountered during the study as shown in figure (1).

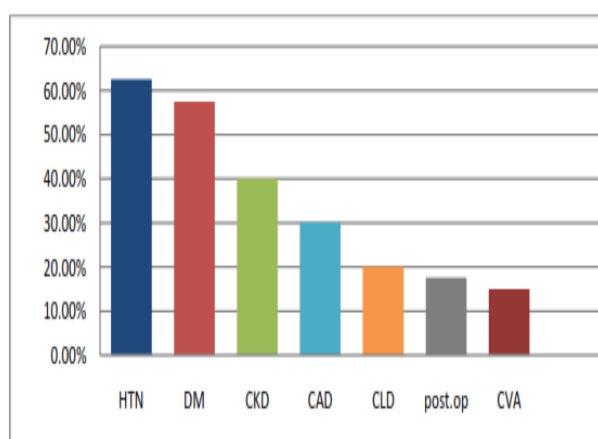


Figure 1: Incidence of different Co-morbidities in all patients of study groups

DM (diabetes), HTN (hypertension), CVA (cerebrovascular strokes), CKD (chronic kidney diseases), CLD (chronic liver diseases), CAD (coronary artery diseases), postoperative (post.op).

- Patients showed several sources of infection as abdominal sepsis, urinary tract infection, blood septicemia, skin and soft tissue infections but chest infection comprised 70 % of whole sources of sepsis in the studied patients as table (1) is showing.

Table 1: Different sources of infection in all patients of study groups

| Source of infection                    | Number (%) |
|--|------------|
| Isolated Chest                         | 19 (47.5%) |
| Isolated Abdomen                       | 7 (17.5%)  |
| Isolated urinary tract infection (UTI) | 1 (2.5%)   |
| Isolated Skin & soft tissue            | 2 (5%)     |
| Isolated Blood stream infection        | 2 (5%)     |
| Combined infection*                    | 9 (22.5%)  |

NB: Combined infection\* means; chest and UTI infections which represent 15% (six patients), chest and skin & soft tissues infections which represent 2.5% (one patient), chest and blood stream infections represented 5% (two patients).

- There were 18 mortalities (45 %) from the total of 40 patients (seven patients of APRV group versus eleven patients in CMV group); cause of most mortalities was septic shock and multiple organ dysfunctions.

### B. Correlative data

#### Hemodynamics

- The two groups showed no significant difference on admission regarding the mean arterial blood pressure (MAP), P value 0.056, also regarding temperature, respiratory rate and central venous pressure (CVP), while CMV group patients had significantly higher heart rate (HR) compared to APRV group (P. value 0.004), table (2).

Table 2: Difference in vital signs on admission of both groups

| Parameter                                    | APRV        | CMV         | P value |
|--|-------------|-------------|---------|
|  | (n=20)      | (n=20)      |         |
|  | (Mean + SD) | (Mean + SD) |         |
| MAP (on admission) (mmHg)                    | 55.2 ± 5.3  | 51.4 ± 6.2  | 0.056   |
| Temperature (Celsius degree)                 | 38.7 ± 0.3  | 38.8 ± 0.3  | 0.640   |
| Heart Rate (bpm)                             | 116.5 ± 7   | 123.6 ± 7.1 | 0.004   |
| Resp. Rate (Cycle/min)                       | 24.2 ± 3.2  | 25.6 ± 2.1  | 0.068   |
| Central venous pressure (cmH <sub>2</sub> O) | 5 ± 3.8     | 3.9 ± 3.4   | 0.192   |

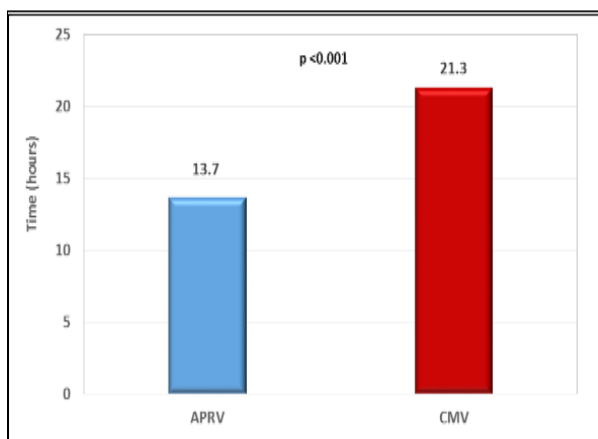
### Parameters reflecting recovery from septic shock:

1. The initial time to start recovery signs from septic shock:

It was significantly earlier in APRV group patients compared to CMV group (13.7 ± 4.6 hours versus 21.3±8.5 hours) with p value<0.001; table (3) and figure (2).

**Table 3: Initial time to start signs of recovery from shock on mode**

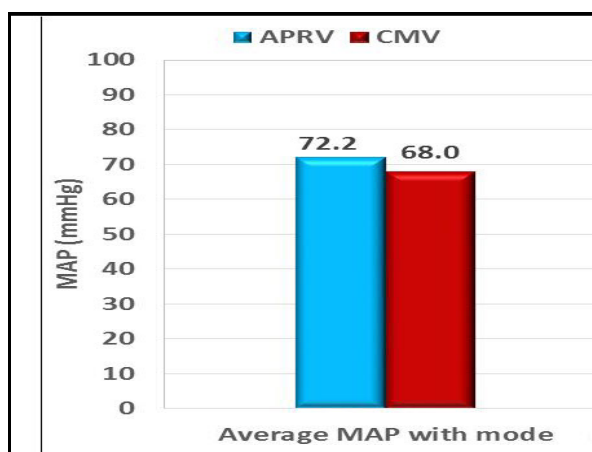
| Parameter   | APRV<br>(Mean + SD) | CMV<br>(Mean + SD) | P<br>value |
|---|---------------------|--------------------|------------|
| Initial time to start recovery signs of shock (hours) | 13.7 ± 4.6          | 21.3±8.5           | < 0.001    |



**Figure 2: Initial time to start signs of recovery from shock on mode**

2. Mean arterial blood pressure during both modes of ventilation:

The average MAP during period of using APRV mode was significantly higher compared to CMV mode. P: 0.049, figure (3) and table (4).



**Figure 3: Average MAP during the period of using each mode in both groups**

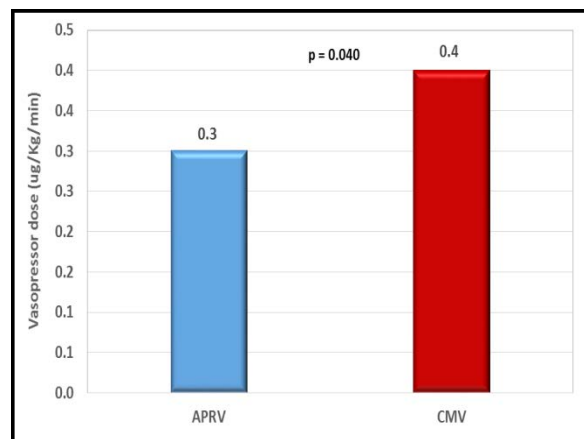
**Table 4: The average MAP during period of using each mode in both groups**

| Parameter MAP      | APRV(n=20)<br>(Mean + SD) | CMV(n=20)<br>(Mean + SD) | P<br>value |
|--------------------|---------------------------|--------------------------|------------|
| Average MAP (mmHg) | 72.2 ± 6                  | 68.0± 8                  | 0.049      |

3. CMV group patients required significantly higher mean infused dosage of vasopressors daily during using CMV mode compared to patients on APRV mode with p value of 0.040, table (5) and figure (4).

**Table 5: Mean infused dosage of vasopressors required daily during period of each mode**

| Parameter                                      | APRV<br>(n=20) | CMV<br>(n=20) | P<br>value |
|--|----------------|---------------|------------|
| Mean infused dosage (ug/Kg/min)<br>(Mean + SD) | 0.3 ± 0.1      | 0.4 ± 0.1     | 0.040      |



**Figure 4: Mean infused dosage of vasopressors required daily during period of each mode**

### I I-Duration of mechanical ventilation:

CMV group patients had insignificantly longer duration of mechanical ventilation compared to APRV group with p value 0.327, table (6).

**Table 6: Whole duration of mechanical ventilation in both groups**

| Parameter                              | APRV<br>(n=20) | CMV<br>(n=20) | P<br>value |
|--|----------------|---------------|------------|
| Whole duration of MV(days) (Mean + SD) | 5.8 ± 3.6      | 7.4 ± 5.1     | 0.327      |

### I II- Sedation and neuromuscular blockers

1) On evaluating the need for sedation, it was significantly higher in CMV group patients compared to APRV group (60% versus 20%) with p value 0.010, table (7).

**Table 7: Need of sedation during using each mode in both groups**

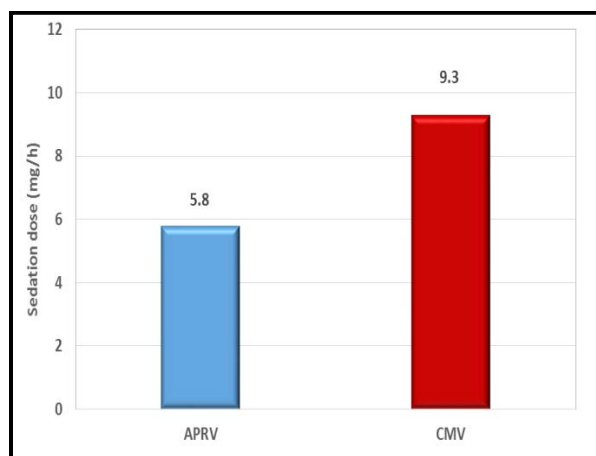
| Parameter     | APRV (n=20) |            | CMV (n=20) |            | P<br>value |
|---------------|-------------|------------|------------|------------|------------|
|               | number      | Percentage | number     | percentage |            |
| Sedation need | 4           | 20%        | 12         | 60%        | 0.010      |

2) The need for neuromuscular blockers (NMBS) were significantly higher in CMV group patients compared to APRV group (40% versus 10%) with p value 0.028, table (8).

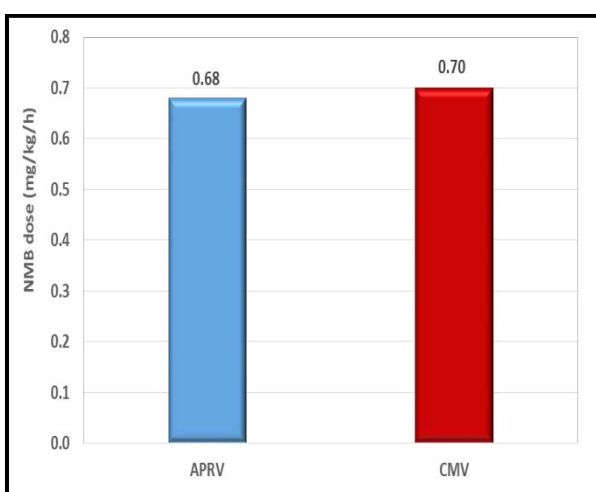
**Table 8: Need of neuromuscular blockers during using each mode in both groups**

| Parameter | APRV (n=20) |            | CMV (n=20) |            | P value |
|-----------|-------------|------------|------------|------------|---------|
|           | number      | Percentage | number     | percentage |         |
| NMBS need | 2           | 10%        | 8          | 40%        | 0.028   |

- 3) The mean dose of sedation on mode was higher in CMV group patients compared to APRV group ( $9.3 \pm 3$  mg/h versus  $5.8 \pm 1$  mg/h); the mean duration of sedation was longer in CMV group patients compared to APRV group ( $3.4 \pm 1.6$  days versus  $2.5 \pm 1.3$  days) as figure (5) is showing.

**Figure 5:** Mean dose of sedation during using each mode in both groups

- 4) The mean dose of NMBS on mode was higher in CMV group patients compared to APRV group ( $0.70 \pm 0.25$  mg/kg/h versus  $0.68 \pm 0.25$  mg/kg/h); the mean duration of NMBS was longer in CMV group patients compared to APRV group ( $3.1 \pm 1.5$  days versus  $2.5 \pm 0.7$  days) as figure (6) is showing.

**Figure 6:** Mean dose of NMBS during using each mode in both groups

### C. Laboratory finding

- 1) Arterial lactate level.

Arterial lactate after 6 hours of admission was significantly higher in CMV group patients compared to APRV group (P: 0.003), table (9).

- 2) during period of ventilation with APRV, the mean serum bicarbonate level and central venous oxygen saturation (ScVO<sub>2</sub> %) were significantly higher with P: 0.005, P: 0.002 respectively compared with CMV group.

**Table 9: Arterial lactate after 6 hours of admission, the mean serum bicarbonate and central venous oxygen saturation during period of ventilation on each mode in both groups**

| Parameter                           | APRV(n=20)<br>(Mean + SD) | CMV(n=20)<br>(Mean + SD) | P value |
|-------------------------------------|---------------------------|--------------------------|---------|
| Art. Lactate (after 6h)<br>(mmol/L) | 2.8 ± 0.9                 | 3.6 ± 1                  | 0.003   |
| Mean serum Bicarb (mEq/L)           | 15.7 ± 2.4                | 12.7 ± 3.4               | 0.005   |
| MeanScVo2 (%)                       | 65.3 ± 6.9                | 58.5 ± 7.3               | 0.002   |

### D. Final outcome

- 1) The total length of ICU stay:

CMV group patients had insignificantly longer ICU length of stay compared to APRV group, with p value 0.28, table (10).

**Table 10: Total length of ICU stay in both study groups**

| Parameter  | APRV(n=20)<br>(Mean + SD) | CMV(n=20)<br>(Mean + SD) | P value |
|------------|---------------------------|--------------------------|---------|
| LOS (days) | 7.4 ± 4                   | 8.9 ± 5.4                | 0.28    |

- 2) Percentage of recovered cases from septic shock:

Percentage of APRV group patients recovered from septic shock (complete withdrawal of vasopressors) within 72 hours was insignificantly higher compared to CMV group (61.5% vs. 27.3%), while the percentage of CMV group patients recovered from septic shock after 72 hours was insignificantly higher compared to APRV group (72.7% vs. 38.5%) with p value 0.093, table (11).

**Table 11: Percentage of septic shock recovery in both APRV and CMV groups before and after 72 h.**

| Percentage of septic shock recovery (complete withdrawal of Vasopressors) | APRV (n=13)  | CMV (n=11)   | Total (24=100%) | P. value |
|---|--------------|--------------|-----------------|----------|
| ≤ 72 h  | 8<br>(61.5%) | 3<br>(27.3%) | 11<br>45.8%     |          |
| After 72 h  | 5<br>(38.5%) | 8<br>(72.7%) | 13<br>54.2%     | 0.093    |

- 3) Scoring system

A. The mean and the highest SOFA scores were near significant higher in CMV group patients compared to APRV group with p value 0.056 and 0.052 respectively, figure (7) and table (12).

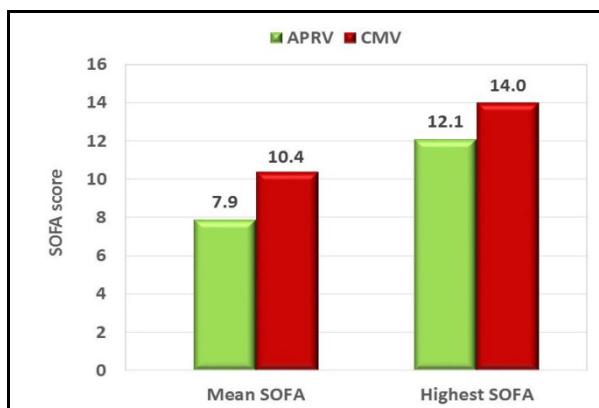


Figure 7: Mean and highest SOFA score in APRV and CMV groups

Table 12: Mean and highest SOFA score in APRV and CMV groups

| parameter (Mean ± SD) | APRV(n=20) | CMV(n=20)  | P value |
|-----------------------|------------|------------|---------|
| Mean SOFA             | 7.9 ± 4.6  | 10.4 ± 4.3 | 0.056   |
| Highest SOFA          | 12.1 ± 3.1 | 14.0 ± 3.1 | 0.052   |

B. There was insignificant correlation between the actual length of ICU stay in all patients and estimated length of ICU stay measured by APACHE IV score with correlation coefficient 0.075 and p value 0.648, figure (8).

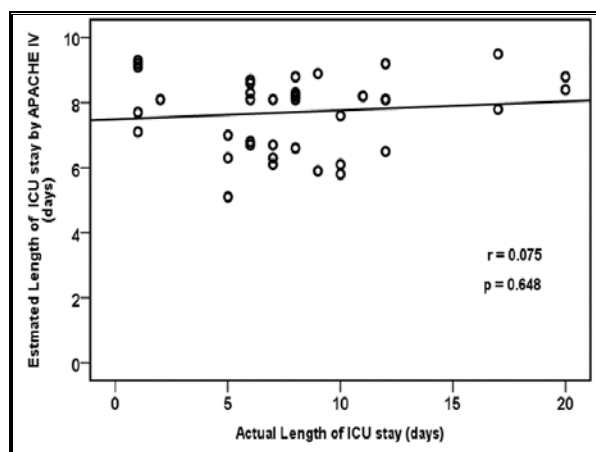


Figure 8: Correlation between actual and estimated ICU length of stay (days) measured by APACHE IV score.

C. There was significant correlation between (the median estimated lengths of ICU stay and the median estimated mortality) measured by APACHE IV in non-survivors versus survivors group patients and the actual mortality in both groups, P < 0.001, table (13).

Table 13: Correlation between the median estimated lengths of ICU stay and the median estimated mortality measured by APACHE IV in non-survivors versus survivors' group patients and the actual mortality

| Parameter   | Survivors (n=22) | Non- survivors (n=18) | P value |
|---|------------------|-----------------------|---------|
| Median estimated LOS measured by APACHE IV (days) | 6.8              | 8.3                   | < 0.001 |

| Median estimated mortality measured by APACHE IV (%) | APRV | CMV | P       |
|--|------|-----|---------|
|  | 21.6 | 45  | < 0.001 |

4) The time needed for complete withdrawal of vasopressors was near significantly longer in CMV group patients compared with APRV group (P: 0.055), table (14).

Table 14: Time needed for complete withdrawal of vasopressors in both groups

| Parameter  | APRV |             | CMV |             | P value |
|--|------|-------------|-----|-------------|---------|
|  | N    | (Mean + SD) | N   | (Mean + SD) |         |
| Time needed for complete withdrawal of vasopressors (days) | 13   | 4.3 ± 2.6   | 11  | 7.1 ± 2.9   | 0.055   |

## Discussion

The application of airway pressure release ventilation (APRV) in the intensive care units is dependable with lung protection protocols that attempt to restrict lung wounds accompanied with mechanical ventilation. The benefits of APRV mode comprise decrease in tiny ventilation and induce negligible side impacts on the function of cardio-circulatory system, and decrease in airway pressures. It is capable to depend completely the whole time on spontaneously breathing from ventilatory cycle; this will reflect the condition of patient and decrease the dependency on sedatives for calming and enhance the elimination period of neuromuscular blockade [17].

In our present study, forty patients were admitted to the critical care department, faculty of medicine, Cairo University between November 2014 and August 2015.

All these patients were diagnosed as having septic shock and needed invasive mechanical ventilation:

In the present work, on evaluating the source of sepsis, chest infection was the main source of primary infection that comprised 75% of the sources of sepsis in APRV group and 65% in CMV group, this goes hand in hand with Lewis, et al [18] who found that chest and abdominal sepsis represent 67% of all sources of infection in their study which was done on twelve patients for evaluation the effect of APRV mode on cardiac performance of subjects complaining from ALI and ARDS.

In the present work during first 48h of admission, the APRV group patients had significantly higher mean urine output (UOP) in day 1 and day 2 compared to CMV group (P: 0.001 and 0.002 respectively).

This copes with Kaplan, et al [19] who found a significant improvement in urine output and glomerular filtration rate in their study which was done on twelve patients had ALI on APRV mode as compared to pressure controlled ventilation (PCV) mode. Moreover, Daoud (2007) [20] found that APRV mode had improved the hemodynamics and organ perfusion (urine output and mesenteric circulation) in their study compared to conventional ventilation.

In the current study, CMV patients had insignificantly longer duration of mechanical ventilation compared to APRV patients ( $7.4 \pm 5.1$  days versus  $5.8 \pm 3.6$  days) during the whole period of ventilation ( $P: 0.327$ ).

This goes hand in hand with Rathgeber, et al. <sup>[21]</sup> who found that APRV reduced the time spent on mechanical ventilation in their study which was done on 596 post-operative cardiac patients on comparing CMV and SIMV modes versus APRV mode.

Similarly, Putensen, et al <sup>[22]</sup> found that APRV mode improved oxygenation, hemodynamics and reduced the time on mechanical ventilation on comparing with pressure control ventilation (PCV) mode (15 days versus 21 days) in their study which was done on thirty critically ill trauma patients.

Our study found that the initial time to start recovery signs from septic shock was significantly longer in CMV group patients compared to APRV group ( $21.3 \pm 8.5$  hours versus  $13.7 \pm 4.6$  hours),  $P < 0.001$ . Consequently, the time needed for complete withdrawal of vasopressors was near significantly longer in CMV group patients compared to APRV group ( $7.1 \pm 2.9$  days versus  $4.3 \pm 2.6$  days),  $P: 0.055$ .

These results was against Hamed, et al. <sup>[23]</sup>, who did not demonstrate any significant change in the hemodynamics variables between APRV and CMV modes of ventilation in their comparison study which was done on twenty patients with acute lung injury (ALI),  $P > 0.05$ . The difference between the results of the present study and Hamed, et al.<sup>[23]</sup> study regarding the hemodynamics variables may be attributed to more hours of ventilation of APRV used for the patients in our study compared to short observational study done by Hamed, et al. <sup>[23]</sup> for twelve hours only.

In the current study, we found that the average MAP during the period of using APRV mode was significantly higher when compared to the period of using CMV mode ( $P: 0.049$ ). This matches the explanation given by Habashi, et al. <sup>[24]</sup> who found that the negligible side effects of APRV on the functions of cardiovascular function is possibly due to the presence of controlled system ventilation and spontaneous breathing module. Moreover, Pinsky, et al. <sup>[10]</sup>, Daoud, et al. <sup>[25]</sup> and McMullen, et al <sup>[26]</sup> found that the apparent explanations for the improved cardiac performance with diminished pressure necessities branch from decreased peak and average airway pressures.

In the current study, the percentage of APRV group patients needed vasopressors one week or less was insignificantly higher versus CMV group (65% versus 45%), while the percentage of CMV group patients whom needed vasopressors more than one week was insignificantly higher versus APRV group (55% versus 35%),  $P: 0.204$ .

This relatively goes with Abdul Muthalib, et al <sup>[27]</sup> who found that 75% of CMV group patients in their study required inotropic support till day 7 versus 45% in APRV.

In the current study, we found that the need for sedation (Midazolam) during using each mode was significantly higher in CMV group patients versus APRV group (60% versus 20%,  $P: 0.010$ ). Moreover, the need for NMBS (Atracurium) was

significantly higher in CMV group patients versus APRV group (40% versus 10%,  $P: 0.028$ ). The present study matches also with Hamed, et al <sup>[23]</sup>, Burchardi, et al. <sup>[28]</sup>, Grasso, et al. <sup>[29]</sup>, Putensen, et al. <sup>[22]</sup> and Kaplan, et al. <sup>[19]</sup> who found that diminished period of mechanical ventilation and the duration of stay in ICU and less negative effect on hemodynamics this will lead to decrease in the dependency on sedatives and neuromuscular blockers.

The present study had found also that CMV group patients needed higher doses and longer duration of sedation and NMBS drugs versus APRV group patients. This goes hand in hand with Hamed, et al <sup>[23]</sup> who found that the doses of sedative propofol decreased significantly ( $P: 0.0001$ ) to  $0.7 \pm 0.8$  mg/kg/hr after application of APRV, instead of  $1.6 \pm 0.5$  mg/kg/hr when CMV were used.

The present study found that the arterial lactate on admission and its follow up after six hours were significantly higher in CMV group patients compared to APRV group ( $P: 0.011$  and  $0.003$  respectively). Elevated arterial lactate on admission in CMV group patients compared to APRV can be explained by randomized base of our study. Improvement in arterial lactate clearance after 6 hours of admission in APRV group versus CMV group ( $2.8 \pm 0.9$  mmol/l in APRV versus  $3.6 \pm 1$  mmol/l in CMV;  $P 0.003$ ) copes with Kaplan, et al. (2001) <sup>[19]</sup> who found a significant improvement in lactate levels in APRV (PCV  $2.2 \pm 0.4$  mmol/l versus APRV  $1.8 \pm 0.3$  mmol/l;  $P < 0.01$ ).

Our current study showed that CMV group patients had insignificantly longer ICU length of stay compared to APRV group ( $8.9 \pm 5.4$  days versus  $7.4 \pm 4$  days),  $P: 0.28$ . This agrees with Putensen, et al. <sup>[22]</sup> who found that the total length of ICU stay was shorter in APRV compared to pressure controlled ventilation (PCV) (23 days versus 30 days).

In the present study, we found that 45% of all patients in both groups died versus 55% were recovered from septic shock.

This matches with Hamed, et al. <sup>[23]</sup> who found that mortality represent 60% of all patients of their comparison study.

In our present study, the proportion of survival after beginning of ventilator treatment was elevated in APRV (65%) than CMV (45%) group. This agrees with Abdul Muthalib, et al. <sup>[27]</sup> who found that the proportion of survival after beginning of ventilator treatment was elevated significantly ( $P < 0.0001$ ) in APRV (71%) than CMV (49%) group in their study which was done on 129 patients with septic shock.

In the current study, seven patients of APRV group (35%) died versus eleven patients in CMV group (55%), which was not of statistical clinical significance. This agrees with Gonza, et al. <sup>[30]</sup> and Varpula, et al. <sup>[31]</sup> studies which was done on 1462 and 58 patients respectively and found no decreasing in mortality with APRV use compared to controlled mechanical ventilation.

On evaluating the mean and the highest SOFA scores in the present study we found that they were weak significantly higher in CMV group patients compared to APRV group ( $P: 0.056$  and  $0.052$  respectively). This can be explained by reported improvement in our current study results regarding SOFA score items like oxygenation, hemodynamics, renal

perfusion and functions in APRV group compared to CMV group.

## Conclusion

APRV mode had shown to decrease the need of sedation and NMBS and restores hemodynamics stability earlier in septic shock patients as compared to CMV mode.

## Recommendations

We recommend using APRV mode in patients with septic shock needing mechanical ventilatory support, and owing to its favorable impact on hemodynamics and its sparing effect on vasopressors, sedatives and neuromuscular blockers are needed. However adequate experience is required for implementing this ventilatory mode effectively.

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