ORIGINAL ARTICLE

Different patterns of lung recruitment maneuvers in primary acute respiratory distress syndrome: effects on oxygenation and central hemodynamics

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ABSTRACT

Aim. The aim of this study was to test if different recruitment maneuver (RM) patterns that achieve the same maximum pressure for the same length of time in humans have a similar efficacy on alveolar recruitment, intrathoracic vascular pressures and flows, and on cardiac function and ventricular filling.

Methods. Forty patients were randomly allocated to undergo different RM patterns: sustained inflation (SI) or pressure controlled ventilation (PCV). The RM methods tested are as follows: SI was achieved by raising peak inspiratory pressure to 45 cmH_2O and sustaining it for 40 seconds. The PCV was set to obtain a 45 cmH_2O peak inspiratory pressure for 2 minutes, I:E 1:2, PEEP 16 RR 8/min. During the study period, patients were mechanically ventilated to obtain a volume of 6 mL/kg, FiO_2 0.7, PEEP 14, RR 14, Pplateau ≤30 cmH_2O according to the ARDSnet trial. All patients were sedated and paralyzed during the study period. All patients were given i.v. norepinephrine. Heart rate, pulse oxymetry, blood pressure, pulmonary artery catheter data (C.I. PVRI, MPAP, PAOP, SvO_2, CVP), and arterial and right heart side venous blood gas analysis data (Ph, PaO_2, $PaCO_2$, $SatO_2$, HCO_3^-, SvO_2) were recorded before and immediately after the lung recruitment maneuver. The static compliance of the respiratory system (CRS) was recorded. Echocardiographic spot evaluations before and after RM were obtained in all cases.

Results. Central venous pressure increased during RM. Mean pulmonary artery pressure, pulmonary capillary wedge pressure and pulmonary vascular resistance index (PVRI) were reduced during PCV RM compared to SI RM ($P<0.05$). The right ventricle stroke work index decreased to a major extent during PCV RM ($P<0.05$). The P/F ratio was significantly increased after PCV RM compared to SI RM ($P<0.05$). $PaCO_2$ levels were similar in the two groups. Compared to baseline, the Qs/Qt decreased significantly after the PCV recruitment maneuver. Ventricular end-diastolic and end-systolic areas decreased during both RM protocols, but they were decreased to a greater extent after SI RM than after PCV RM ($P<0.05$). The eccentricity index increased from baseline after the SI RM ($P<0.05$).

Conclusion. Given its comparable, or even superior, performance over the SI RM, we favor the PCV technique over the time-honored SI maneuver.

Key words: Respiratory distress syndrome, adult; Pneumonia; Respiration, artificial.

Recruitment maneuvers (RMs), which are intermittent application of high distending pressures, are intended to gain patency of refractory lung units in order to improve gas exchange while allowing acceptable peak tidal pressures and hemodynamic impairment. The patency of injured lung units that tend to collapse during expiration can be maintained by positive end-expiratory pressure (PEEP).[1-4] However, these unstable units must first be opened for PEEP to be effective.[5, 6] Without

recruitment, PEEP may hyperinflate functional airspaces, misdirect blood flow, and increase the risk of barotrauma.[7]

Lung RMs reduce the amount of lung collapse, decrease intra-pulmonary shunt and improve arterial oxygenation in early forms of this condition, as well as in lung collapse induced by anesthesia or surgery.[8-14] High airway pressures may be required to establish the patency of consolidated collapsed lung units.[15]

Thus, in recent years, many studies have shown that cardiovascular side effects of lung recruitment maneuvers are present in both clinical and experimental settings.[16-24]

The response to RM varies with the nature and extent of the lung injury, the characteristics of the recruiting technique and the tidal volume and PEEP settings after recruitment.[25-29]

Precise indications pointing to the necessity of RM in ARDS do not exist because there is no conclusive evidence about their efficacy on clinical outcome, and data homogeneity is missing due to the diversity of techniques used in published works and to differences in lung mechanics between human and animal studies.

The aim of this study was to test if different RMs that achieve the same maximum pressure for the same length of time in humans have similar efficacies on alveolar recruitment, intrathoracic vascular pressures and flows, as well as on cardiac function and ventricular filling.

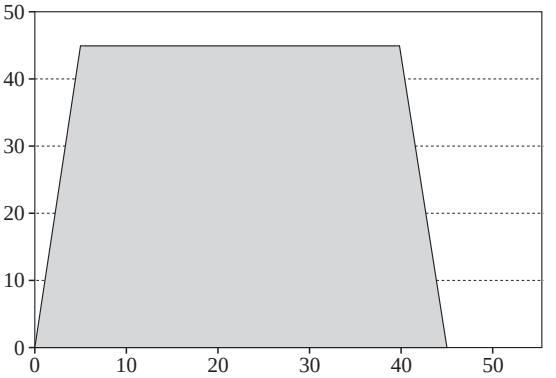

Figure 1.—Pressure-time product of sustained inflation (SI) recruitment maneuver. X axis: time (seconds); Y axis: pressure (cmH_2O).

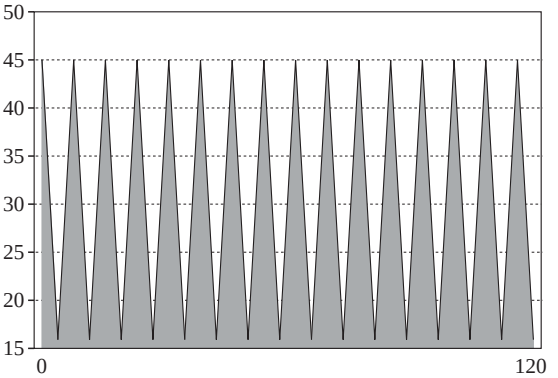

Figure 2.—Pressure-time product of pressure controlled ventilation (PCV) recruitment maneuver. X axis: time (seconds); Y axis: pressure (cmH_2O).

Materials and methods

The study design was approved by the Ethical Committee and complied with the Declaration of Helsinki. All patients gave written informed consent before being enrolled in the study. The majority of written informed consents were obtained from in-hospital patients upon signs of pneumonia during a three-year period. All patients reported primary ARDS due to hospital-acquired bacterial pneumonia. Forty patients were enrolled after ARDS criteria of the American/European Consensus Conference on ARDS were met within 48 hours of Intensive Care Unit admission. Patients were randomly allocated to undergo different RM patterns by means of a closed envelope technique. The two different patterns were sustained inflation (SI) and pressure controlled ventilation (PCV). The RM methods tested are as follows: SI was achieved by raising peak inspiratory pressure to 45 cmH_2O and sustaining it for 40 seconds (Figure 1). The PCV was set to obtain a 45 cmH_20 peak inspiratory pressure for 2 minutes I:E 1:2 PEEP 16 RR 8/min (Figure 2).

As previously demonstrated by Lim *et al*., peak pressure and inspiratory duration of the PCV-RM were selected so that the cumulative product of inspiratory pressure and inflation time (pressure time product) matched that of the SI maneuver (pressure time product: SI and PCV=1800, Intrathoracic Pressure=approximately 6690 cm H_2O s; mean pressure: SI=45 cmH_2O, PCV=26 cm H_2O).[30] The cumulative pressure time product was made equivalent for the SI and PCV

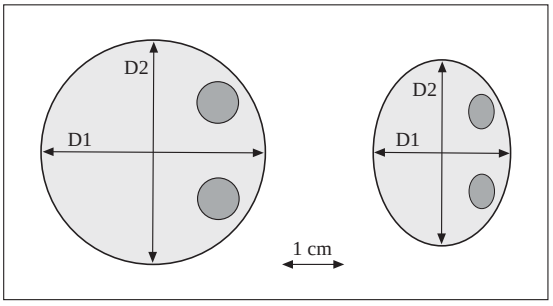

Figure 3.—Left ventricle at end-diastole before (circle) and after (oval) a lung recruitment maneuver. D1 The midmitral diameter; D2 diameter orthogonal to D1. Eccentricity index (EI) was calculated as D2/D1. A high EI represents a flatter intraventricular septum, indicating raised right ventricular pressure.

maneuvers, with each achieving a pressure of 45 cmH_2O. Given that pressure and time may be determinant factors influencing recruitment efficacy, we used a similar pressure time product when comparing the two maneuvers (PT product =1 800).

During the study period, patients were mechanically ventilated (Dräger Evita™ Ventilator; Lübeck, Germany) with a tidal volume of 6 mL/kg, FiO_2 0.7, PEEP 14, RR 14, Pplateau $\leq$30 cmH_20, according to the ARDSnet trial.[31] All patients were sedated with a midazolam/fentanyl infusion and paralyzed with cisatracurium during the study period. All patients were under continuous i.v. norepinephrine infusion, with the maximum dose never exceeding 0.25 mcg/kg/min (mean dose= 0.18±0.07 mcg/kg/min).

Routine monitoring included continuous monitoring of heart rate by electrocardiogram, arterial oxygen saturation by pulse oxymetry, urine output and temperature. An arterial catheter was placed in the radial artery for continuous invasive blood pressure monitoring and for intermittent arterial blood sampling (1-1/2" QuickFlash® Arterial Catheter Kit – Arrow International). A 7.0-French fiberoptic pulmonary artery flotation catheter (CCOmboV™; Edwards Lifesciences, Critical Care Division, Irvine, CA, USA) was inserted into the proximal pulmonary artery through the internal jugular vein. The catheter was connected to a Continuous Cardiac Output monitor (Vigilance; Revision 4.4, Baxter Healthcare).

Pulmonary artery catheter data (C.I. PVRI, MPAP, PAOP, SvO_2, CVP), arterial and right heart side venous blood gas analysis data (Ph, PaO_2, $PaCO_2$, $SatO_2$, HCO_3^-, SvO_2) were recorded before and immediately after the lung RM.

The static compliance of the respiratory system (C_{RS}) was computed using the occlusion technique before and after the RM. During measurement of C_{RS}, patients were mechanically ventilated with a tidal volume of 6 mL/kg, PEEP 14 cm H_2O. Echocardiographic spot evaluations before and after the RMs were obtained in all cases. Echocardiography was performed using a Vivid 7 echocardiograph (GE VingMed Ultrasound, Horten, Norway). A transthoracic subcostal approach was obtained with a M4S transducer, and the probe was maintained in this position throughout the study. Images were digitally stored as loops containing one cardiac cycle both before and at the end of each RM. An investigator blinded to the intervention measured left ventricular end-diastolic and end-systolic diameters and areas. The midmitral diameter (D1) and a diameter orthogonal to it (D2) were measured. The eccentricity index (EI=end-systolic D2/end-systolic D1) was calculated from these measurements [32] (Figure 3). A high EI represents a flatter intraventricular septum, indicating raised right ventricular pressure.

Statistical analysis

All values are reported as means ± standard deviation unless otherwise specified. The level of significance was set at 5%. A repeated analysis of variance was used to determine the effects of RM pattern (independent variable) on oxygenation and hemodynamic variables (dependent variables). Mean values were compared by simple t test. Analysis was performed with SPSS Software Version 10.1 Windows XP.

TABLE I.—*Population characteristics data. Values are presented as mean values /SD or range in brackets.*

	PCV RM	SI RM
Age (years)	53.6 (39-63)	45.8 (28-60)
Weight (kg)	71.7±12.5	74.1±6.4
Gender (Male/female)	12/8	13/7

TABLE II.—*Hemodynamic variables before and after recruitment maneuvers (RM).*

Author	Pre-RM SI group	Post-SI RM group	Pre-PCV RM Group	Post-PCV RM
PaO_2 (mmHg)	86.3±23.7	105.2±31.5	88.2±20.2	157.6± 61.5*
P/F	141.8±40.7	165.7±44.4	155±30.8	238.8±86.5*
$PaCO_2$ (mmHg)	58±3.2	62±1.3	55±2.1	55±3.4
CRS	32±11.1	48±5.1	30±9.4	62±12.5*
Qs/Qt (%)	28.4± 5.8	23.5± 3.2		
	28.0± 5.8	17.3±9.7		
C.I. (L/min)	3.3±0.9	2.0±0.8*	3.2±0.5	3.4±0.8
PAOP (mmHg)	21.4±2.5	28.4±2.7*	20.4±2.3	19.7±2
MPAP (mmHg)	40.4±7.8	49.6± 2.8	40.2±5.7	30.2±3.5*
PVRI (dyne. sec. m^2/cm^5)				
	460.5± 64	848.6±12.4*	505 ±20.1	247±15.2
RVSWI (g.m/m2)				
	12±1.4	9.4±0.5	10.6 ±0.7	5.7±0.9*
CVP (mmHg)	17.4±2.5	20.4±2.7	18.1±1.8	19.7±2
Sys/Dia (mmHg)	108.5±14.3/53.5±12.4	89±6.5*; 49.5±9.2	105.5±15.5/58.2 ±10.4	106.5±13.1; 55.7±10.3
HR (bpm)	85.1±15.4	84.3±14.3	86±10.5	84.5±13.1

*P<0.05. SI: sustained inflation; PCV: pressure controlled ventilation; P/F: PaO_2 FiO_2 ratio; C.I.: cardiac index; PVR: pulmonary vascular resistance; CVP: central venous pressure; Sys/Dia: Systolic / Diastolic; HR: heart rate.

TABLE III.—*Echocardiographic evaluations before and after recruitment maneuvers (RM).*

	Pre-SI RM	Post-SI RM	Pre-PCV	Post-PCV RM
LVEDA	19.0 (14.2 to 25.6)	7.4 (2.6-10.5)*	18.7 (13.2 to 24.2)	11.7 (7.5 to 19.2)*
LVESA	9.2 (5.2 to 16.1)	5.4 (2.2 to 7.4)*	9.4 (5.5 to 13.3)	7.1 (3.2 to 15.4)*
EI	1.15± 0.1	1.44±0.26	1.18±0.2	1.21± 0.1

*P<0.05. LVEDA: left ventricular end diastolic area; LVESA: left ventricular end systolic area; EI: eccentricity index.

Results

Population characteristics are shown in Table I Lung Injury Severity Score (LISS) was ≥2.5 in all cases.

Oxygenation and hemodynamic data before and after different RM patterns are shown in Table II. Heart rate prior to RM was similar in all groups and did not change after RM. Arterial pressure decreased more at the end of the SI RM compared to the PCV RM (P<0.05). Central venous pressure increased during RM. Mean pulmonary artery pressure, pulmonary capillary wedge pressure and pulmonary vascular resistance index (PVRI) were reduced during PCV RM compared to the SI RM (P<0.05). Right ventricle stroke work index decreased to a large extent during PCV RM (P<0.05). PaO_2/FiO_2 ratio presented a major increase after PCV RM compared to SI RM (P<0.05). $PaCO_2$ levels were lower in the PCV RM group (P>0.05). Compared to baseline, the Qs/Qt decreased significantly after the PCV recruitment maneuver, as shown in Table II.

Ventricular end-diastolic and end-systolic areas decreased during both RMs, but the decrease was greater after SI RM than after PCV RM(P<0.05). The eccentricity index increased from baseline after the SI RM (P<0.05). (Table III).

Discussion and conclusions

In this setting, the PCV-RM method caused a major increase in PaO_2 and less adverse hemodynamic effects than the SI RM. Our data show the superiority of PCV RM to SI RM, suggesting that despite equivalent peak pressure and pressure-time product, the pattern in which airway pressure is applied is not always of secondary importance. Multiple high-pressure breaths may be needed to achieve the full benefit from step changes in PEEP, and airway opening may proceed in a series of avalanches. Such sequential behavior might help to

explain why several identical RMs may be needed for full effect.

Thus, there are multiple explanations for the reduction of cardiac output induced by lung RMs: the transmission of the airway pressure to the pleural space; the increase in intrapleural pressure hampers venous return and the filling of the right ventricle; lung distension due to the increase in transpulmonary pressure compresses the small alveolar vessels and increases right-ventricular outflow impedance; or the increase of intrathoracic pressure can compress the right atrium and the caval veins, increasing venous pressures. Increased intrathoracic pressure might, by this mechanism, temporarily impede venous return and thereby right ventricular filling. High intrathoracic pressure may induce a decrease in left ventricular afterload, which can contribute to reduced left ventricular end-diastolic area.

Upon echocardiographic examination, it is clear that impaired filling is a dominant mechanism, but that increased outflow impedance, as indicated by a right ventricular dysfunction and paradoxical movement of the septum, is the major cause for reduced cardiac output.

In the present study, we found that LRMs markedly changed the left ventricle eccentricity index, indirectly demonstrating right ventricular pressure overload. A leftward septal shift, indicating an acute right ventricular pressure overload, was first demonstrated in humans by Brinker *et al.*[33] One year later, leftward septal shift was also seen in acute respiratory distress syndrome patients mechanically ventilated with PEEP, thus explaining the poor efficacy of volume loading in correcting the drop in CO produced by PEEP implementation.[34] More recent studies showed that cyclic changes in right ventricular afterload produced by cyclic delivery of tidal volume are a major determinant of the drop in CO produced by mechanical ventilation.[35-37]

It is our opinion that in the present study, the restoration of lung volume to normal values by PCV RMs and (PEEP) reduced PVR by reversing hypoxic pulmonary vasoconstriction (HPV). The relationship between lung volume and PVR played a major role in favoring PCV RM. PCV RM led to a higher grade of lung recruitment compared to SI RM and consequently produced a decrease in pulmonary vascular resistance, favoring right heart function. On the other hand, PCV generated less hyperinflation compared to SI RM, which passively compresses the alveolar vessels increasing PVR and hampering right heart function.

Improvement in oxygenation is commonly used to detect recruitment, although gas exchange is also influenced by many other factors, like ventilation-perfusion distribution, pulmonary blood flow and regional vascular regulation.[38-43]

What clinicians want to know is whether a certain improvement in oxygenation can predict the amount of recruitment. Improvements in gas exchange after recruitment are attributed mainly to two basic mechanisms: first, by redirection of blood flow from non-aerated to aerated lung regions and reduction of venous admixture and secondly, through an increase in alveolar ventilation.[36] In our study, the PCV RM group had increased PaO_2 levels, whereas the $PaCO_2$ levels were unaffected in both groups.

A PCV pattern that attained the same plateau pressure and cumulative inspiratory PT product with a low mean airway pressure was better tolerated than a sustained inflation maneuver.

One caveat of the current study is that we could not directly measure lung volumes by means of the He dilution technique, aerated/non aerated lung ration on CT scan or by 3He MRI.

However, in the most severe ARDS patients, RMs have to be considered in association with high levels of PEEP and low tidal volume to assure an open lung approach.[44, 45]

We also believe that in future clinical practice, an important role in lung recruitment will be played by transpulmonary pressure computed by means of esophageal pressure measurement.[46]

In our experience, given its comparable or superior performance over the SI RM, we favor the PCV technique over the time-honored SI maneuver. In conclusion, in hemodynamically stable and adequately volume-loaded patients, RM significantly reduced CO and left ventricular end diastolic area, suggesting that the indication for such maneuvers should be very strict, tailored to the patient and should be applied judiciously.

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