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Respiratory and Hemodynamic Effects of a Stepwise Lung Recruitment Maneuver in Pediatric ARDS: A Feasibility Study

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Summary. Background: Little is known about the efficacy and safety of recruitment maneuvers (RMs) in pediatric patients with acute respiratory distress syndrome (ARDS). We therefore assessed the effects on gas exchange and lung mechanics and the possible detrimental effects of a sequential lung RMs and decremental positive end-expiratory pressure (PEEP) titration in pediatric ARDS patients. Methods: We enrolled patients <15 years of age with ARDS, progressive hypoxemia, <72 hr of mechanical ventilation, and hemodynamic stability. A step-wise RM and decremental PEEP trial were performed. Safety was evaluated as the occurrence of hypotension and low pulse oxymeter oxygen saturation during the maneuver and development of airleaks after. Efficacy was evaluated as changes in lung compliance (C_{dyn}) and gas exchange 1, 12, and 24 hr after the RM. Results: We included 25 patients, of median age 5 (1–16) months, median weight 7.0 (4.1–9.2) kg, median PaO_2/FIO_2 117 (96–139), and median C_{dyn} 0.48 (0.41–0.68) ml/cmH_2O/kg at baseline. Thirty RM were performed, with all completed successfully. No airleaks developed. Mild hypotension was detected during four procedures. Following RM, C_{dyn}, and PaO_2/FIO_2 increased significantly ($P < 0.01$ each), without changes in $PaCO_2$ ($P = 0.4$). A >25% improvement in lung function (C_{dyn} or PaO_2/FIO_2) was observed after 90% of the RM procedures. Gas exchange worsening over the next 24 hr resulted in HFOV use in 36% of patients, while the remaining subjects sustained improvements in oxygenation at 12 and 24 hr. The 28-day mortality rate was 16%. Conclusions: Sequential RMs were safe and well tolerated in hemodynamically stable children with ARDS. RMs and a decremental PEEP trial may improve lung function in pediatric patients with ARDS and severe hypoxemia. **Pediatr Pulmonol. 2013; 48:1135–1143.**

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INTRODUCTION

Acute respiratory distress syndrome (ARDS) is the clinical manifestation of many diseases that produce widespread alveolar damage, fluid leakage across the alveolar–capillary barrier, and alveolar edema.[1] These processes are responsible for variable degrees of flooding and collapse of alveolar spaces, producing severe gas exchange abnormalities and loss of lung compliance.[2–4] The loss of aerated lung volume is the cardinal tomographic feature of ARDS.[5–7]

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Conflict of interest: None.

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Recruitment maneuvers (RMs) can be defined as a transient increase of transpulmonary pressure with the goal of opening or recovering alveolar units with high critical opening pressure, thus increasing end expiratory lung volume.[8] RMs have been shown to improve oxygenation and restore lung volume and may reduce the heterogeneity of the distribution of tidal volume (V_T) in patients with ARDS.[9] These effects may be temporary, but, over time, alveolar stability may be preserved, with maintenance of an adequate positive end-expiratory pressure (PEEP) after RM administration.[10–13]

Since RMs may have some detrimental hemodynamic and respiratory effects in adults,[14] current recommendations limit RMs to early rescue of severe ARDS, following evaluation of the potential risks and benefits of these maneuvers. Less is known about these maneuvers in pediatric ARDS patients, although a recent study in 21 pediatric patients with acute lung injury (ALI), using Open Lung Tool® commercial software, showed that RMs may safely improve oxygenation.[15] However, mechanical ventilators with this software are not available in all pediatric ICUs. We have therefore designed this feasibility study of a sequential manually performed lung recruitment maneuver in hemodynamically stable children with early ARDS. Our primary objective was to assess the possible detrimental effects of RMs, particularly on hemodynamics and air leak development. Our secondary objective was to determine the efficacy of RM, registering the effects on gas exchange and lung mechanics. We hypothesized that a stepwise RM can improve gas exchange and pulmonary mechanics, being safe in hemodynamically stable children with ARDS.

METHODS

Patients and Monitoring

We evaluated consecutively intubated pediatric patients fulfilling American European Consensus Conference criteria for ARDS.[16] For definitive selection, we selected subjects <15 years of age with $PaO_2/FIO_2 < 100$ mmHg or $PaO_2/FIO_2 < 200$ mmHg plus progressive deterioration of oxygenation in two evaluations performed at least 1 hr apart. All patients had a PEEP of $\geq$8 cmH_2O and hemodynamic stability, with the latter defined as mean arterial pressure (MAP) >50th percentile, pulse pressure variation <15%, superior cava vein oxygen saturation ($ScvO_2$) > 70% and constant doses of vasopressors over the previous 4 hr. Exclusion criteria were mechanical ventilation (MV) for >72 hr, previous barotrauma (pneumothorax, pneumomediastinum or subcutaneous emphysema), signs of intracranial hypertension, cyanotic congenital cardiac disease, pre-existing clinically significant or palliated/uncorrected cardiac disease and limitations of life support.

The study protocol was approved by the Ethics Committee of Hospital Padre Hurtado, and written informed consent was obtained from the parents or legal guardians of each patient according to the guidelines of the Declaration of Helsinki.

Demographic parameters, comorbidities, factors predisposing to the development of ARDS, Pediatric Index of Mortality 2 (PIM2) score,[17] Paediatric logistic organ dysfunction (PELOD) score,[18] rescue treatments for ARDS (prone position, high frequency oscillatory ventilation [HFOV] and inhaled nitric oxide), 28-day ventilator free days, and mortality were recorded. Ventilatory parameters, expiratory tidal volume (V_T), dynamic lung compliance (C_{dyn}), PaO_2/FIO_2, and $PaCO_2$ were measured before and after RM administration. The patients were intubated with cuffed tubes as is the routine practice for patients developing ARDS in our unit. C_{dyn} was measured as the median of 10 consecutive breaths [19].

Experimental Protocol

Heart rate, invasive arterial pressure, pulse oximetry-oxygen saturation (SaO_2), and respiratory mechanics were monitored. All patients were continuously infused with midazolam (1.5–5 μg/kg/min) and fentanyl (1–3 μg/kg/hr), to achieve a COMFORT sedation scale between 17 and 26 points.[20] Before the RM, subjects were pre-oxygenated with 100% FIO_2 for 5 min. Each was administered vecuronium (0.1 mg/kg) while maintaining the previous decubitus position (prone or supine). Basal ventilatory and gasometric parameters were recorded before pre-oxygenation and muscle relaxation. Before and after the interventions, FIO_2 was adjusted to $SaO_2 \geq 90\%$.

RM Procedure

In control pressure modality, PEEP was set at 10 cmH_2O and driving pressure (peak inspiratory pressure minus PEEP) at 15 cmH_2O, without modifying other parameters. Sequential RM was performed, increasing PEEP by 5 cmH_2O every 2 min to a PEEP of 25 cmH_2O. Optimal PEEP was set according to the best C_{dyn} during the decremental phase of the maneuver (decremental PEEP trial; Fig. 1), although a minimum PEEP of 10 cmH_2O was considered according to lung disease severity. If C_{dyn} was equal between 2 steps (i.e., 10 cmH_2O vs. 15 cmH_2O of PEEP), the optimal PEEP was set at the lower PEEP plus 2 cmH_2O. During the RM, patients were maintained at their previous RR and at FIO_2 of 100%. The maneuvers were manually performed with EVITA XL® (Dräger Medical, Lübeck, Germany) or AVEA® (Vyasis, San Diego, California) ventilators, depending on availability. After

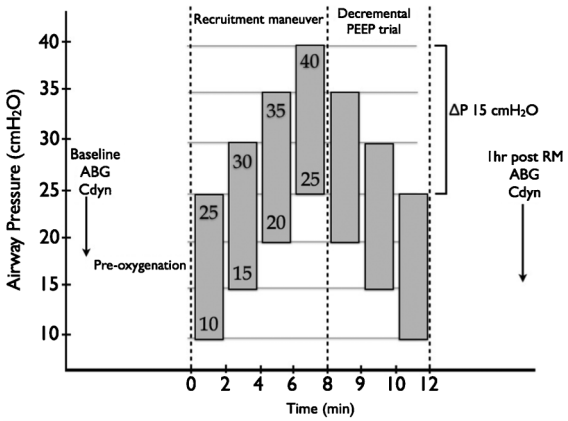

Fig. 1. Sketch of pressure–time tracings illustrating the ventilation protocol we utilized. The recruitment strategy was performed under pressure-controlled ventilation with an initial PEEP of 10 cmH_2O and a fixed driving pressure of 15 cmH_2O. A sequential RM was performed, increasing PEEP by 5 cmH_2O every 2 min until PEEP reached 25 cmH_2O. During the decremental phase of the maneuver, PEEP was optimized to achieve better C_{dyn} (decremental PEEP trial) (ABG: arterial blood gases; C_{dyn}: dynamic compliance; ΔP: driving pressure; RM: recruitment maneuver).

the RM, patients were maintained in the same ventilatory mode.

Patients with a post-RM PaO_2/FIO_2 increment $\geq$50%, but a 24-h oxygenation reduction of >30% were subjected to a second maneuver using the same protocol.

Safety: Immediate RM interruption criteria included sustained $SaO_2 < 85\%$ for 1 min, hypotension or bradycardia adjusted for age (defined by pediatric advanced life support guidelines).[21] MAP was recorded at the end of each step of the maneuver. If MAP was reduced >20% relative to baseline, but interruption criteria were not fulfilled, a 10 ml/kg bolus of normal saline solution was administered during RM. If hypotension persisted, RM was interrupted. A <20% decrease of MAP relative to baseline was categorized as not clinically relevant, and no further interventions were performed. Chest radiographs were obtained 1, 24, and 48 hr after RMs to evaluate the presence of pneumothorax, pneumomediastinum, and subcutaneous emphysema.

Efficacy

C_{dyn} and arterial blood gases were measured 1, 12, and 24 hr after RM, and compared with measurements made before RM. In the absence of lung CT scans, recruitment potential (RP) was evaluated by gas exchange and lung mechanics, grouping subjects with an increment of PaO_2/FIO_2 or C_{dyn} $\geq$25% (RP25%) and $\geq$50% (RP50%) for analysis.

Statistical Analysis

Sample size and power for means with repeated measures was performed based on PaO_2/FIO_2 ratio and C_{dyn} of previous studies of da Silva et al.[22] and Curley et al.[23] We estimated a sample size of 30 measurements would detect changes greater than 25% in these variables after the RM with 80% power and alpha error of 0.05. The Anderson Darling test was performed to evaluate normal distribution of data. Continuous data were expressed as median and interquartile range (IQR). Percentage changes after the RM were expressed as mean and 95% confidence interval (CI). Related samples Friedman's two-way analysis of variance by ranks test was performed to determine significant changes in hemodynamics and lung mechanics during the maneuver and in gas exchange at 12 and 24 hr after the maneuver. The Wilcoxon signed-rank test was performed to analyze paired pre-RM versus post-RM data. Spearman's rank correlation was performed to determine the relationship between baseline data and percentage changes (Δ) in C_{dyn} and PaO_2/FIO_2 after RM. All statistical analyses were performed with the SPSS 20.0 software program (SPSS, Chicago, IL). Significance was set at a P-value < 0.05.

RESULTS

Patient Characteristics

From January 2008 to December 2010, 270 children were screened, and 25 (16 males, 9 females) were enrolled. Their median age was 5 months (1–16 months), their median weight was 7 kg (4.1–9.2 kg), and 22 (88%) had primary ARDS. Comorbidities were present in six patients (24%), with three having chronic lung disease, two having a genetic condition (one each with Larsen and Down syndrome), and two having immunodeficiency. Median PaO_2/FIO_2 ratio was 117 mmHg (96–139 mmHg) and median oxygenation index was 11.4 (9.4–13.5) at baseline. Predicted mortality by the PIM_2 and PELOD scoring systems were 8.4 ± 6.3% and 18.2 ± 31.7%, respectively. The baseline characteristics of the patients are shown in Table 1.

Nineteen patients (76%) were in the supine position. Of the 25 patients, five required two bouts of maneuvers, resulting in 30 RMs. Of these, 22 maneuvers were performed during the first 24 hr after meeting ARDS criteria and the remaining eight were performed between 24 and 48 hr. Before the maneuver, subjects were ventilated in pressure control (n = 26, 86.7%) or double control (n = 4, 13.3%) mode.

Safety of RMs

All RMs were successfully completed, and none of the patients met RM termination criteria during the

TABLE 1— Clinical Characteristics and the Predisposing Factor for ARDS Diagnosis of the Patients Included in the Study

N	Age (Mo)	Weight (kg)	Sex	Predisposing factor	Co-morbidities	Outcome
1	1	4.1	M	RSV pneumonia superinfected		Alive
2	1	4	F	Bacterial pneumonia		Alive
3	24	12.3	M	ADV pneumonia	Larsen Synd CLD	Exitus
4	12	10	M	ADV pneumonia	Preterm CLD	Alive
5	3	7.5	M	RSV pneumonia superinfected		Alive
6	1	4	M	Pneumonia		Alive
7	2	4.5	M	Pneumonia		Alive
8	5	6.7	M	CMV pneumonia	Pancytopenia Suspected ID	Exitus
9	12	10	F	RSV pneumonia superinfected	Preterm	Alive
10	36	20	F	Pneumonia *H. influenzae*	IAC	Alive
11	12	8	M	Myocarditis/pneumonia		Alive
12	4	7	M	Pneumonia		Alive
13	1	3.5	M	RSV pneumonia superinfected		Alive
14	4	7.5	M	RSV pneumonia superinfected		Alive
15	1	5.8	M	Bacterial pneumonia		Alive
16	2	5.6	F	Severe pertussis		Alive
17	16	9	M	Pneumonia *H. influenzae*	Suspected ID	Exitus
18	23	5	F	Pneumonia		Alive
19	16	9	M	Pneumonia		Alive
20	1	4.1	F	Pneumonia		Alive
21	1	4	M	Pneumonia *E. coli*	Down Synd	Alive
22	3	4.5	M	RSV pneumonia superinfected	Preterm CLD	Alive
23	36	14	F	TTP		Exitus
24	13	10.5	F	Pneumonia *H. influenzae*		Alive
25	2	4	F	Myocarditis/pneumonia		Alive

Mo, months; M, male; F, Female; Synd, syndrome; IAC, interatrial communication; RSV, Respiratory Syncytial Virus; ADV, Adenovirus; CLD, Chronic Lung Disease; CMV, Cytomegalovirus; ID, Immunodeficiency; TTP, Thrombotic thrombocytopenic purpura.

procedures. During all but two procedures, MAP decreased, with a median decrease of 9.2% (5.8%–12.7%). A >20% decrease relative to baseline MAP occurred during four procedures (range, 21–28%), but RM was not halted, because these patients had not fulfilled the hypotension criteria for interruption.

Patients received support with vasoactive drugs during 21 of the 30 RMs (70%), but the infusion rate was not modified during or after RM delivery. None of the patients developed air leaks during the observation period.

Efficacy of RMs

After the RM, C_{dyn} increased a median 31% (95% CI, 20.7–41.8%, $P < 0.01$) and PaO_2/FIO_2 ratio increased a median 47.1% (95% CI, 31.9–62.1%, $P < 0.01$), whereas $PaCO_2$ decreased a median 2.2% (95% CI −9.1 to 4.7%, $P = 0.4$) (Table 2). At 12 hr, median PaO_2/FIO_2 was 166 (95% CI, 152–201, $P = 0.013$) and median $PaCO_2$ was 50 (95% CI, 41.5–55, $P = 0.015$), whereas, at 24 hr, median PaO_2/FIO_2 was 183 (95% CI, 145–199, $P = 0.016$) and median $PaCO_2$ was 41 (95% CI, 39–47.3, $P = 0.046$).

TABLE 2— Ventilatory Parameters at Baseline and 1 hr After RM (RM-1 hr)

	Baseline	RM-1 hr	
PaO_2/FIO_2, median (IQR)	117 (96–139)	164 (141–197)	$P < 0.01$
$PaCO_2$ (mmHg), median (IQR)	57 (41–66)	54 (39–66)	$P = 0.4$
C_{dyn} (ml/cmH_2O/kg), median (IQR)	0.48 (0.41–0.68)	0.6 (0.49–0.80)	$P < 0.01$
V_T (mL), mean ± SD	8.2 ± 2.5	9.6 ± 2.5	$P < 0.01$
PEEP (cmH_2O), Mean ± SD	8.4 ± 1.1	10.0 ± 0.3	$P < 0.01$
Driving pressure (cmH_2O), Mean ± SD	17.5 ± 2.0	16.3 ± 2.9	$P = 0.15$
FIO_2 (%), Mean ± SD	71 (54–100)	60 (50–84)	$P = 0.036$

C_{dyn}, dynamic lung compliance; V_T, tidal volume; PEEP, positive end-expiratory pressure.

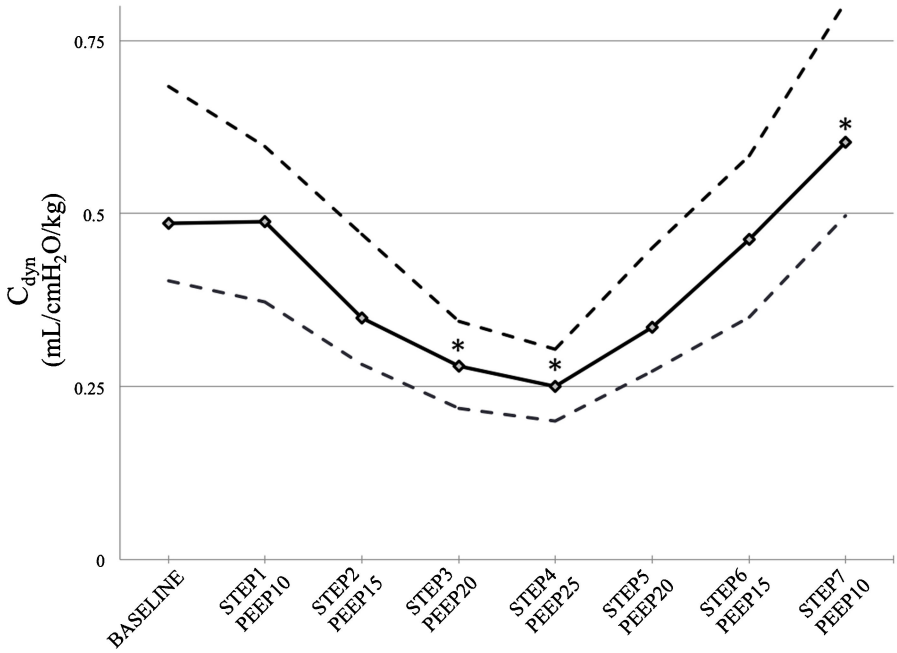

Fig. 2. Dynamic compliance (C_{dyn}) at baseline and at each step of the RM. The solid line represents the median and the dotted lines represent the interquartile range. $^{*}P < 0.05$ compared with baseline. (PEEP: Positive End Expiratory Pressure, cmH_2O)

After performance of the RMs, 90.0% of the subjects were classified as RP25% and 46.6% as RP50%.

All subjects showed a transient decrease in C_{dyn} during the steps with higher PEEP (Fig. 2). An >25% increase in C_{dyn} was observed after 60.7% of the maneuvers and a >50% increase was observed after 25% of the maneuvers. Only two of the patients experienced a mild decrease in C_{dyn} after the maneuver. There was an inverse correlation between baseline C_{dyn} and ΔC_{dyn} (Rho $= -0.54$, $P = 0.002$).

Increases in PaO_2/FIO_2 ratio in excess of 25% and 50% were observed after 64.3% and 46.4% of the maneuvers, respectively. There was an inverse correlation between baseline PaO_2/FIO_2 and $\Delta PaO_2/FIO_2$ (Rho $= -0.4$, $P = 0.03$), but no correlations between baseline C_{dyn} and PaO_2/FIO_2 and $\Delta PaO_2/FIO_2$ ratio and ΔC_{dyn} were observed. A >20% decrease in $PaCO_2$ was observed after 28.6% of maneuvers, though a >20% increase was observed after 7.1% of maneuvers.

A histogram of the distribution of C_{dyn} and gas exchange percentage variations after RMs is presented in Figure 3. Decremental PEEP titration after RMs resulted in a mild increase in PEEP and V_T following 89.2% of the procedures, without significant changes in driving pressure (Table 2).

Percentage variations in C_{dyn} and gas exchange were similar prone and supine groups (Table 3).

Outcome

Gas exchange deterioration during the 24-h post-RM period resulted in HFOV use in nine patients (36%), including four with persistent hypoxemia, two with severe respiratory acidosis, and three with both conditions. The percentages of patients requiring HFOV were similar in RM responders and nonresponders, being 37.0% and 33.3% respectively, in patients achieving RP25% ($P = 0.72$) and 35.7% and 37.5%, respectively, in patients achieving RP50% ($P = 0.61$). No others rescue therapies were employed.

The median number of ventilator free days was 22 (21–24). The median PICU stay was 9 days (7–12 days) and the median overall hospital stay was 13 days (10–15 days). The 28-day mortality rate was 16.0%. Outcome rates were similar in RM responders and nonresponders. PaO_2/FIO_2 ratio at baseline was significantly lower in patients who died than in survivors [74 (48–105) vs. 124 (103–169), $P = 0.02$].

DISCUSSION

Two main findings emerged from this evaluation of early respiratory and hemodynamic effects of a stepwise manually performed lung recruitment maneuver in children with ARDS and severe hypoxemia. First,

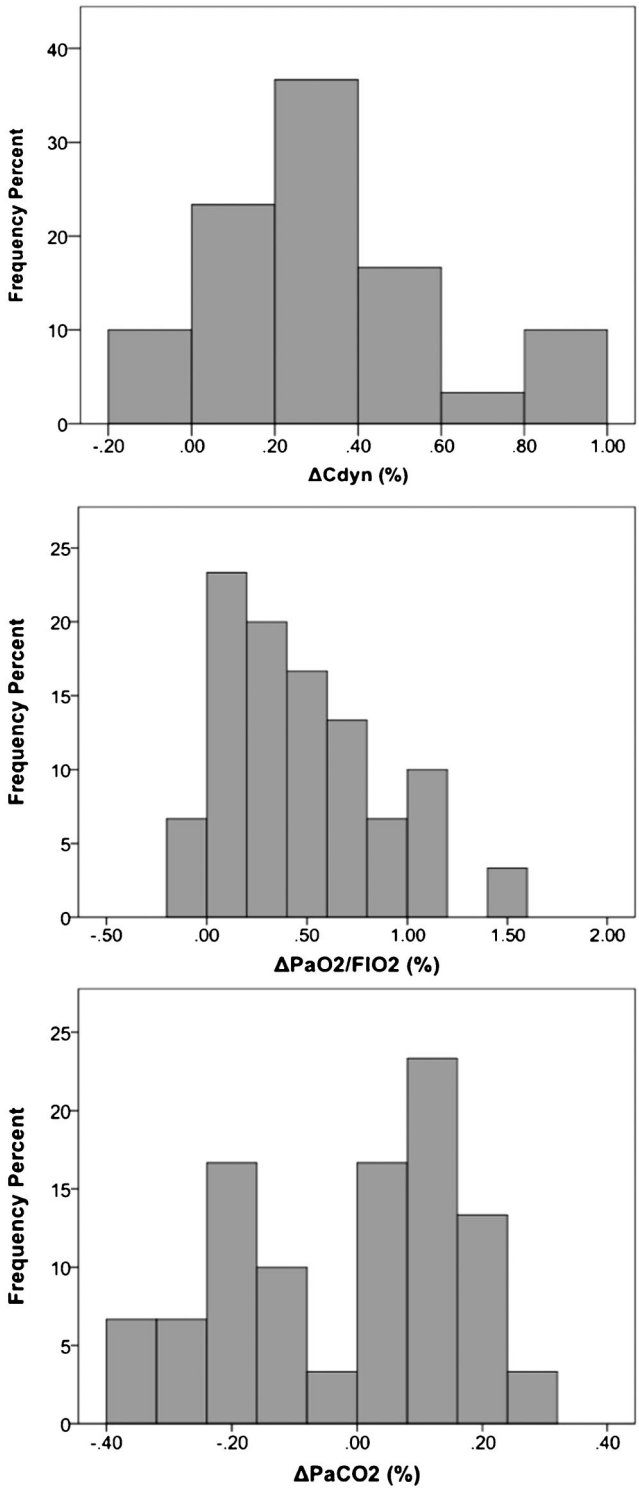

Fig. 3. Histogram of the distribution of dynamic compliance (C_{dyn}), PaO_2/FIO_2 ratio and carbon dioxide ($PaCO_2$) percentage variations (Δ) after the RM.

the RM procedure was safe and well tolerated in hemodynamically stable children, and second, RM and decremental PEEP trial was able to improve lung compliance and gas exchange.

TABLE 3— Dynamic Compliance (C_{dyn}), PaO_2/FIO_2 Ratio, and Carbon Dioxide ($PaCO_2$) Percentage Variations (Δ) After the RM According to Decubitus Position

	Supine	Prone	*P*-value
C_{dyn}	32% (19–44%)	31% (6–55%)	0.965
$\Delta PaO_2/FIO_2$	45% (23–64%)	51% (22–81%)	0.689
ΔCO_2	−3% (−12–6%)	−1% (−15–12%)	0.979

Data showed as mean and 95% confidence interval.

In assessing the safety of RM, we observed transient mild hypotension during most of the maneuvers. Although a moderate decrease (>20%) in MAP occurred occasionally, it was not clinically relevant. This finding may be due to our selection of patients and the RM used. Patients were included after initial resuscitation with fluids and titration of vasoactive drugs and after hypovolemia was ruled out. RMs performed 36–72 hr after ARDS diagnosis has been reported to be less detrimental in adults than RMs performed later.[24] The mild cardiovascular impact we observed may have been due to the characteristics of our RM protocol: a progressive, step-wise increase in airway pressure with a fixed driving pressure of 15 cmH_2O and a limitation on peak alveolar pressure of 45 cmH_2O.[25] Nonsequential sustained increases in airway pressure and peak inspiratory pressure > 45 cmH_2O have shown higher rates of adverse effects. In our cohort, there were no other adverse events related to RMs (e.g., airleaks and severe hypoxemia). The incidence of these complications was also low in other series.[26]

The efficacy of RM we observed was in accordance with those of clinical studies in critically ill adults. That studies found improvements in gas exchange associated with the reopening of collapsed lung areas following RM during the early phase of ARDS,[26–32] although the usefulness RMs is still controversial.[33–35] In addition, the PEEP selected during the decremental PEEP trial after the RM may reduce the fraction of collapsed lung tissue and limit cyclical recruitment and de-recruitment, interfering with the results attributed to the RM itself. Decremental PEEP trial is based on the presence of alveolar units with heterogeneous critical opening pressures and hysteresis, defined as the difference between the pressure required to open the lung and the pressure required to keep it open.[36]

Surprisingly, we found that the effects of RMs on gas exchange were sustained in two-thirds of subjects at 12 and 24 hr; the remaining patients required HFOV within 24 hr of receiving RMs. Despite our study not being designed to test this outcome, we believe that this result may increase the clinical relevance of RMs in pediatric patients with ARDS. Additionally we found a reduction in $PaCO_2$ at 12 and 24 hr in the group of patients that

were kept on conventional mechanical ventilation. This may be interpreted as sustained alveolar recruitment over time. We think that dead space ventilation due to regional overdistension post maneuver may be responsible for the heterogeneity of changes of early $PaCO_2$ measurements (1 hr after the procedure).

We observed large variations in lung mechanics and oxygenation response among our patients, a pattern similar to that reported in adults.[37] The magnitude of the response to the maneuver and the high response rate, with 90% showing a $\geq$25% improvement and almost half showing a $\geq$50% improvement in lung function, may be due to the application of RM during early stages of ARDS. Indeed, RM shows better clinical responses when applied within 48 hr of the development of ARDS.[24] Despite their initial positive response to RMs, however, about one-third of our patients required HFOV during the 24-h period immediately following RMs due to gas exchange deterioration. This need may have resulted from an insufficient level of PEEP to keep open the recruited lung. Our post-RM PEEP was equal to or higher than that previously reported to be used in pediatric ARDS,[15,38,39] but was lower than that used in adults with ARDS.[26,29,31] The variations of gas exchange and dynamic compliance cannot be exclusively explained by the moderate increase in PEEP (about 2 cmH_2O) after the RM. Because PEEP is applied in an expiratory setting, it should be more clinically relevant to tailor its level after lung recruitment. Titration of PEEP during the decremental phase of the maneuver has the effect of maintaining alveolar stability for a prolonged period of time.[30,31,40] On the other hand an insufficient PEEP after the RM might promote derecruitment (loss of aerated lung tissue), counteracting the initial effect of the RM.[27,41] The step changes of PEEP by 5 cmH_2O during the decremental PEEP trial may be too large and may have precluded the identification of the optimal PEEP levels. In a recent study de Matos et al.[41] found that careful selection of PEEP after the RM can maintain a PaO_2/FIO_2 ratio to high levels (>300) for days (even weeks) in selected patients with ARDS. Interestingly the decremental PEEP trial used in that study was similar to ours (changes by 5 cmH_2O).

The inverse relationship between PaO_2/FIO_2 ratio and C_{dyn} and their change after the maneuver suggest that patients with more severe ARDS experience a greater response to RMs. These results are consistent with a prior tomographic study reporting that patients with a higher percentage of potentially recruitable lung had poorer oxygenation and respiratory-system compliance.[27] Moreover, there was an association between the percentage of potentially recruitable lung and the risk of death, indicating that patients with a greater recruitment potential are more severely ill and are at higher risk of death.[27] Our finding of a lack of correlation between PaO_2/FIO_2 ratio and C_{dyn} may reflect the heterogeneity of lung involvement in our patients. This issue may be clarified in future tomographic studies of pediatric ARDS patients.

Although RMs may be performed using various methods, the optimal method, target pressures, and frequencies have not been determined. The RM technique we employed combines a moderate level of pressure, progressive increase in airway pressurization, and prolonged application time. This protocol was based on clinical observations and experimental evidence suggesting that hemodynamic tolerance of sequential (progressive) RMs is better for sustaining inflation, whereas the benefits of pressures above 40 cmH_2O and durations longer than 2 min are marginal.[42,43] A recent meta-analysis of RM use in adults with ALI/ARDS found that RMs could be used on patients with severely hypoxemic ARDS.[40,44] Thus, RM should be used only as a rescue therapy in patients with life-threatening hypoxemia and not prophylactically or systemically (i.e., once or twice daily).

Some studies have assessed intermittent RMs in anesthetized children without lung disease[45–47] and in ventilated pediatric patients without ALI/ARDS.[48,49] Although improvements in lung function were observed after the RMs, the clinical settings were very different from that of our acutely ill children with severe lung injury. A recent study assessed the effects of an RM procedure similar to ours using modified Open Lung Tool® commercial software (Servo-I; Maquet Critical Care, Solna, Sweden) in pediatric ALI/ARDS patients selected according to criteria comparable to ours.[15] Since their objective was to determine the critical opening pressure (functional goal), fixed upper and lower pressures were not set, although peak pressure was set at 35 cmH_2O and driving pressure at 15 cmH_2O. They achieved good hemodynamic tolerance and improvements in oxygenation, similar to our findings, although we did not use a specific ''open lung system'' to perform RMs. Interestingly, their optimal post-RM PEEP settings were similar to ours, but lower than those reported for adults with ARDS, suggesting that critical alveolar opening pressures may be lower in children than in adults or that the current methods to identify optimal PEEP in children are not adequate. Future studies in pediatric patients should determine the frequency of distribution of critical opening pressure as a function of airway pressures by quantifying the percent of collapsed tissue on imaging modalities, such as computed tomography or electric impedance tomography. These new technologies might help to define the optimal PEEP in children and might have an impact in outcome, especially in patients with a large nonaerated lung compartment, reducing cyclic alveolar collapse/reopening,

and preventing secondary systemic inflammatory response (biotrauma).

In summary, we found that sequential RMs were safe and well tolerated in hemodynamically compensated children with ARDS, and that their use was associated with improvements in lung compliance and gas exchange after implementation of RMs and decremental PEEP. These interventions should be considered in children with early ARDS and severe hypoxemia, although their effects may be transitory in a subset of patients.

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