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REVIEW

Recruitment maneuvers in acute respiratory distress syndrome and during general anesthesia

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ABSTRACT

The use of low tidal volume ventilation and low to moderate positive end-expiratory pressure (PEEP) levels is a widespread strategy to ventilate patients with non-injured lungs during general anesthesia and in intensive care as well with mild to moderate acute respiratory distress syndrome (ARDS). Higher PEEP levels have been recommended in severe ARDS. Due to the presence of alveolar collapse, recruitment maneuvers (RMs) by causing a transient elevation in airway pressure (*i.e.* transpulmonary pressure) have been suggested to improve lung inflation in non-inflated and poorly-inflated lung regions. Various types of RMs such as sustained inflation at high pressure, intermittent sighs and stepwise increases of PEEP and/or airway plateau inspiratory pressure have been proposed. The use of RMs has been associated with mixed results in terms of physiological and clinical outcomes. The optimal method for RMs has not yet been identified. The use of RMs is not standardized and left to the individual physician based on his/her experience. Based on the same grounds, RMs have been proposed to improve lung aeration during general anesthesia. The aim of this review was to present the clinical evidence supporting the use of RMs in patients with ARDS and during general anesthesia and as well their potential biological effects in experimental models of acute lung injury.

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Invasive mechanical ventilation is routinely used to support patients during general anesthesia and with acute respiratory distress syndrome (ARDS). However mechanical ventilation has the potential to induce a iatrogenic form of acute lung injury named ventilator-induced lung injury (VILI).[1] Thus it now clearly stated that the main target of mechanical ventilation in ARDS is not only to improve gas exchange but to minimize VILI as much as possible.[2] The current mechanical ventilation strategy for minimizing VILI is to apply relatively low tidal volume (VT) and positive end-expiratory pressure (PEEP) in order to maintain plateau pressure below the 30 cmH_2O threshold. However, low VT and/or inadequate PEEP levels promote alveolar derecruitment.[3] Recruitment maneuvers (RMs), aimed to reopen not aerated lung regions through a transient elevation in transpulmonary pressure has been proposed.[4]

Although several experimental data showed that RMs could reduce or prevent the VILI, clinical studies did not report homogenous data. In addition three recent systematic reviews and meta-analysis were discordant: one concluded that RMs could improve the survival [5] while the two others stated that there is no evidence that RMs could reduce mortality [6] and concluded that, at the moment, RM cannot be recommended or discouraged.[7]

Lung derecruitment may also occur during general anesthesia though with different mechanisms than in ARDS. Since several years RMs have been suggested to improve lung aeration during general anesthesia.[8]

Aim of this clinical review is to revise the role of RMs (if any) during general anesthesia and in ARDS patients.

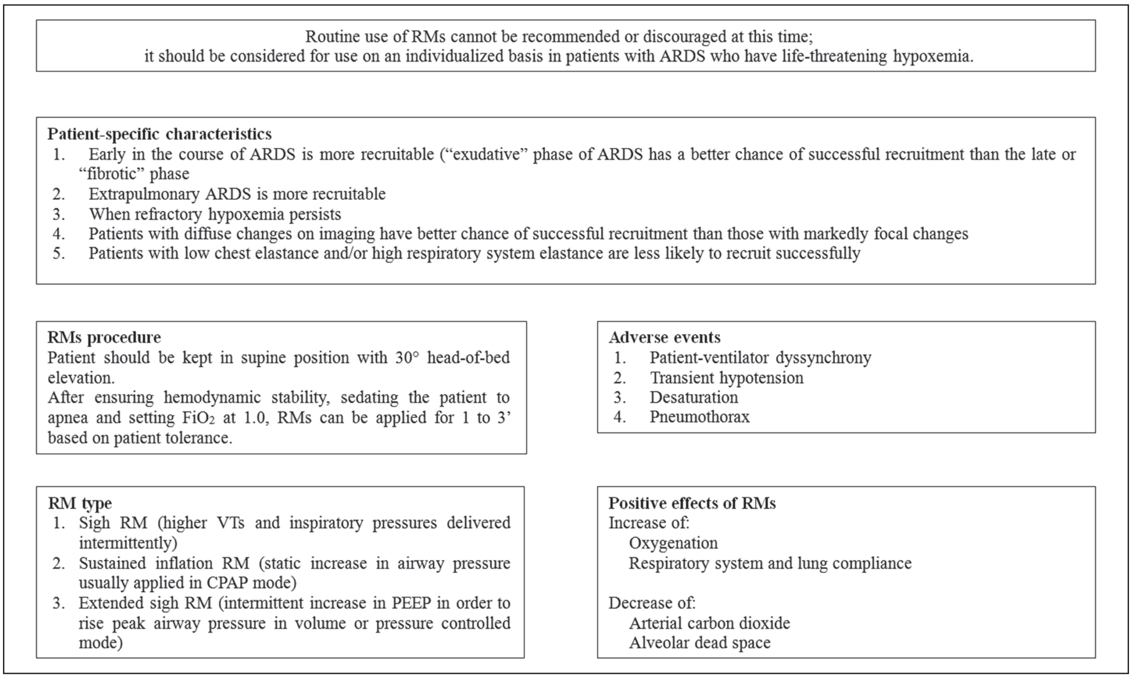
Acute respiratory distress syndrome

The most frequently reported RMs are (Table I): 1) the sigh RM in which higher VTs and inspiratory airway pressures are intermittently delivered; 2) the sustained inflation RM in which a static increase in airway pressure (usually in CPAP mode) is transiently applied (20-40 s); 3) the extend sigh RM, where a stepwise PEEP increases is applied in order to increase airway pressure in volume or pressure controlled mode.

In Figure 1 is a suggested flow chart for lung recruitment.

Sigh RM

In a small group of ARDS patients, a sigh RM based on three consecutive higher VTs per minute, able to reach 45 cmH_2O of plateau airway pressure, lead to a significant improvement in arterial oxygenation, lung aeration and elastic properties of the respiratory system.[9] Of note after only 30 minutes from sigh interruption, all these physiological beneficial effects were lost. Pelosi *et al.* showed that a sigh RM applied in the prone position could provide greater lung recruitment in the early stage of ARDS, as compared to supine position.[10] In a larger population of ARDS patients, Villagrà *et al.* investigated the effect of sigh RMs in patients with early and late ARDS.[11] Despite arterial oxygenation was not affected, the RMs



Routine use of RMs cannot be recommended or discouraged at this time;
it should be considered for use on an individualized basis in patients with ARDS who have life-threatening hypoxemia.

Patient-specific characteristics
1. Early in the course of ARDS is more recruitable (“exudative” phase of ARDS has a better chance of successful recruitment than the late or “fibrotic” phase
2. Extrapulmonary ARDS is more recruitable
3. When refractory hypoxemia persists
4. Patients with diffuse changes on imaging have better chance of successful recruitment than those with markedly focal changes
5. Patients with low chest elastance and/or high respiratory system elastance are less likely to recruit successfully

RMs procedure
Patient should be kept in supine position with 30° head-of-bed elevation.
After ensuring hemodynamic stability, sedating the patient to apnea and setting FiO_2 at 1.0, RMs can be applied for 1 to 3’ based on patient tolerance.

Adverse events
1. Patient-ventilator dyssynchrony
2. Transient hypotension
3. Desaturation
4. Pneumothorax

RM type
1. Sigh RM (higher VTs and inspiratory pressures delivered intermittently)
2. Sustained inflation RM (static increase in airway pressure usually applied in CPAP mode)
3. Extended sigh RM (intermittent increase in PEEP in order to rise peak airway pressure in volume or pressure controlled mode)

Positive effects of RMs
Increase of:
Oxygenation
Respiratory system and lung compliance

Decrease of:
Arterial carbon dioxide
Alveolar dead space

Figure 1.—Suggested flow chart for lung recruitment.

TABLE I.—*Clinical studies evaluating recruitment maneuvers.*

Author, year	N.	Diagnosis	Study type	Ventilation strategy	RM type	Gas exchange	Mortality	Complications
Pelosi (1999)[9]	10	ARDS	Observational	VT 6-8 mL/kg PEEP 14±2.2 cmH$_2$O	Sigh	PaO$_2$ significantly increased; reduction of PaCO$_2$	Overall mortality N.=5 (50%)	No data
Pelosi (2003)[10]	10	ARDS (early)	Observational	VT 7 mL/kg ABW PEEP 14±3 cmH$_2$O	Sigh	PaO$_2$ significantly increased in both supine and prone	Overall mortality N.=4 (40%)	No major complication
Villagrà (2002)[11]	17	ARDS (early: 8 patient were also studied in late phase)	Observational	VT <8 mL/kg PEEP 14±1 cmH$_2$O	Sigh	PaO$_2$ not increased during RM. PaCO$_2$ increased and pH decreased significantly. Values returned to baseline 15 min after RM in early but remained altered in late ARDS group	No data	No major complication
Lapinski (1999)[12]	14	ARDS (early)	Observational	VT 12 mL/kg PEEP mean 10.4 cmH$_2$O	Sustained inflation	SpO$_2$ significantly increased by 10 min after RM	No data	No major complication
Oczenski (2004)[13]	30	ARDS (early)	Randomized	VT 6 mL/kg IBW PEEP, RM group 15.1±1.2 cmH$_2$O, no-RM group: 14.5±1.3 cmH$_2$O	Sustained inflation	PaO$_2$ significantly increased at 3 min after RM, baseline values were reached again within 30 min	No data	No major complication
Xi (2010)[14]	110	ARDS	Randomized	VT, RM group 6.6±0.9 mL/kg, no-RM group 6.8±1.1 mL/kg PEEP, RM-group 10.5±3.2 cmH$_2$O, no-RM group 9.7±2.4 cmH$_2$O	Sustained inflation	No differences in PaO$_2$ between two groups	No differences in hospital and 28-day mortality. ICU mortality significantly lower in RM group	Hypotension: in one instance RM was terminated early
Brower (2003)[15]	96	ALI/ARDS (only in patients with high PEEP)	Crossover study	VT 6.0±0.8 mL/kg PBW PEEP 13.8±3.0 cmH$_2$O	Sustained inflation	SpO$_2$ were greater within 10 and 60 mins after RMs than after sham RMs; no significant differences at the other time points	No data	Hypotension and low SpO$_2$: in three instances RMs were terminated early. Barotrauma after one RM and after one sham RM
Grasso (2002)[16]	22	ARDS	Observational	VT, RM-responding group 6.1±0.1 mL/kg, RM-non-responding group 6.0±0.2 mL/kg PEEP, RM-responding group 9.4±2.2 cmH$_2$O, RM-non-responding group 9.1±2.7 cmH$_2$O	Sustained inflation	PaO$_2$ significantly increased in RM-responding group than in non-responding; 20 min after values of PaO$_2$ tended to return toward baseline values in both groups	No data	Hypotension (transitory) in PEEP non-responding group
Meade (2008)[17]	27	ALI/ARDS	Observational	VT 8.4±3.0 mL/kg PEEP 10±4 cmH$_2$O	Sustained inflation	PaO$_2$ not significantly increased following the first or subsequent RMs. Augmenting the inflation pressure or duration had no significant effect	No data	Barotrauma: 4 (3.2%), ventilator asynchrony: 5 (4%), appeared uncomfortable: 3 (2.4%), experienced transient hypotension: 2 (1.6%)
Foti (2000)[18]	15	ARDS (only PEEP responders)	Observational	VT 7.9 mL/kg PEEP 13.3±27.7 cmH$_2$O	Extended sigh	PaO$_2$ and SaO$_2$ significantly increased after RMs, no difference in PaCO$_2$	No data	No major complication

TABLE I.—*Continues from previous page.*

Author, year	N.	Diagnosis	Study type	Ventilation strategy	RM type	Gas exchange	Mortality	Complications
Johannigman (2003) [19]	12	ARDS (early)	Observational	VT (study) 6.3 mL/kg IBW PEEP 12.3±3.2 cmH_2O	Extended sigh	PaO_2 significantly increased 3 mins after RM. Two hours after the RM, oxygenation fell below 30-min values but remained greater than pre-RM values	No data	No major complication
Borges (2006) [20]	26	ALI/ARDS (early)	Observational	VT 6 mL/kg PBW PEEP 5-10 cmH_2O	Extended sigh	PaO_2 significantly increased	Overall ICU mortality: 11 (42.3%), hospital death 14 (57.7%)	No major complication
Moràn (2011) [21]	13	ALI/ARDS (early)	Observational	VT 7.8 mL/kg IBW PEEP 15±4 cmH_2O	Extended sigh	PaO_2 significantly increased and remained greater than pre-RM values	No data	Transitory hypotension
Katsiari (2012) [22]	25	ARDS (early)	Observational	VT 8.5±1.4 mL/kg IBW PEEP 10±3 cmH_2O	Sigh Sustained inflation Three consecutive sighs	PaO_2 significantly improved after all RMs. In patients with BMI>27 kg/m^2 only sustained inflation induced a longer improvement	Overall ICU mortality: 8 (32%)	No major complication
Lim (2003) [23]	47	ARDS (early)	Randomized	VT 8 mL/kg PEEP of 10 cmH_2O	Extended sigh	PaO_2 significantly increased in RM+PEEP group. PaO_2 in RM-only and in PEEP-only group did not differ. Patients with extrapulmonary ARDS showed greater increase in PaO_2 after RM	RM+PEEP 10 (50%); RM 10 (52.6%); PEEP-only group 7 (87.5%)	No major complication
Constantin (2008) [24]	19	ARDS (early)	Randomized	VT 6 mL/kg PEEP 14±2 cmH_2O	Sustained inflation Extended inflation	Both RMs increased oxygenation; increase in PaO_2 was significantly higher with extended sigh than sustained inflation RM at 5 and 60 min	Overall mortality: 6 (31%); CPAP 2 (22%), extended sigh 4 (40%)	Hypotension: in two instances RM was terminated early
Iannuzzi (2010) [25]	40	ARDS	Randomized	VT 6 mL/kg PEEP 14 cmH_2O	Sustained inflation Extended inflation	PaO_2 significantly increased after extended inflation; $PaCO_2$ levels were lower compared to sustained inflation group	No data	Hypotension: more during sustained inflation RM
Amato (1998) [26]	53	ARDS (early)	Randomized	VT, protective ventilation 6 mL/kg, control group 12 mL/kg PEEP, protective ventilation 16.4±0.4 cmH_2O, control group 6.2±0.5 cmH_2O	Sustained inflation	PaO_2 significantly increased in protective ventilation group; $PaCO_2$ higher in protective group	28 days-mortality: 11 (38%) in protective ventilation group *vs.* 17 (71%) in control group (P=0.001)	Barotrauma: 2 (7%) in protective-ventilation *vs.* 10 (42%) in control group (significantly lower)
Meade (2008) [27]	983	ALI/ARDS	Randomized	VT, LOV group 6.8±1.4 mL/kg, control group 6.8±1.3 mL/kg PEEP, LOV group 14.6±3.4 cmH_2O, control group 9.8±2.7 cmH_2O	Sustained inflation	LOV group had lower rates of refractory hypoxemia and lower mortality rates with refractory hypoxemia; no difference in $PaCO_2$	Hospital mortality: 36.4% in LOV group and 40.4% in the control group	Hypotension: 4.5%, desaturation: 4.2%, bradycardia or tachycardia: 1.8%, cardiac arrhythmia: 0.3%, new air leak through an existing thoracostomy tube: 0.3%; barotrauma: LOV 53 (11.2%) control 47 (9.1%)

TABLE I.—*Continues from previous page.*

Author, year	N.	Diagnosis	Study type	Ventilation strategy	RM type	Gas exchange	Mortality	Complications
Huh (2009)[28]	57	ARDS	Randomized	VT, experimental group 7.9±1.9 mL/kg, control group 8.0±1.4 mL/kg PEEP, experimental group 8.4±3.1 cmH_2O, control group 7.0±3.7 cmH_2O	Extended sigh	PaO_2 significantly increased in decremental PEEP titration group than in control group. $PaCO_2$ was higher in decremental PEEP titration group than in control group on day 1. Improvement of PaO_2 and $PaCO_2$ level were not different between two groups during follow-up	Overall mortality 37%. 28 and 60-day mortality did not differ between two groups	Barotrauma: 3 (11%) in experimental *vs.* 3 (11%) in control group
Hogdson (2011)[29]	20	ARDS	Randomized	VT 6 mL/kg in both groups PEEP, experimental group 15±1 cmH_2O, control group 10±0.5 cmH_2O	Extended sigh	PaO_2 significantly increased in experimental group than control group over the first 24 hours and over 7 days	Any difference in hospital mortality between two group	Desaturation in three instances at maximum PEEP of 40 cmH_2O (no lasting adverse effects)
Park (2009)[30]	53	Total laparoscopic hysterectomy	Randomized	VT 10 mL/kg and ZEEP	Sigh	PaO_2 increased during pneumoperitoneum in RM group than in no-RM group	No data	No data
Cinnella (2013)[31]	29	Elective gynecologic laparoscopic surgery	Observational	VT 8 mL/kg IBW PEEP 5 cmH_2O	Extended sigh	PaO_2 increased during and after RM	No data	No major complication
ProVHILO (2014)[32]	900	Elective open abdominal surgery, with intermediate or high risk for postoperative pulmonary complications	Randomized	VT 8 mL/kg PBW in both groups PEEP, experimental group 12 cmH_2O with RMs, control group ≤2 cmH_2O without RMs	Extended sigh	SpO_2 significantly higher in the higher PEEP group	No difference at day 5 (<1%) or in-hospital (2%)	Intraoperative hypotension in higher PEEP group
Futier (2013)[33]	400	Elective laparoscopic or open major abdominal surgery and intermediate to high preoperative risk for pulmonary complications	Randomized	VT, control group 6 to 8 mL/kg PBW, control group 10 to 12 mL/kg PBW PEEP, experimental group 6-8 cmH_2O and RMs repeated every 30 mins, control group ZEEP and no RM	Sustained inflation	No differences between groups	No difference in mortality at 30 days between the two groups	No difference between the two groups
Severgnini (2013)[34]	56	Elective open abdominal surgery	Randomized	VT, experimental group 7 mL/kg IBW, control group 9 mL/kg IBW PEEP, experimental group 10 cmH_2O, control group ZEEP	Extended sigh	PaO_2 higher in patient ventilated protectively at days 1, 3, and 5	None of the patients died	Hypotension: 9 (33.3%); bradycardia: 2 (7.4%)

RM: recruitment maneuver; ABW: actual body weight; IBW: ideal body weight; PBW: predicted body weight; ALI: acute lung injury; ARDS: acute respiratory distress syndrome; VT: tidal volume; PEEP: positive end-expiratory pressure; ZEEP: zero end-expiratory pressure.

induced a significant increase in the lung gas volume only in the early ARDS group.

Sustained inflation RM

Lapinsky *et al.* evaluated sustained inflation RMs (CPAP; inflation pressure between 30 and 45 cmH_2O sustained for 20 seconds) in patients with hypoxemic respiratory failure. The arterial saturation significantly increased significantly after 10 minutes.[12] The beneficial effect of the RM in terms of oxygenation lasted at least 4 hours in the majority of the patients. Patients with pulmonary and extrapulmonary ARDS presented a similar change in oxygenation. Oczenski *et al.* studied a group of patients with early ARDS ventilated with low a tidal volume.[13] The RMs significantly increased the arterial oxygenation within 3 minutes, however after 30 minutes the oxygenation returned to baseline values. Xi *et al.* in a randomized multicenter study evaluated the effect of a RM delivered every eight hours for five successive days.[14] Except for day one and two, arterial oxygenation was not different between the two groups as well as hospital mortality (42% *vs.* 56%). In patients enrolled in the higher PEEP arm of the Alveoli study, the application of RMs (CPAP up to 35 cmH_2O for 30 seconds) significantly increased the arterial saturation with a highly variability after 60 minutes.[15]

Grasso *et al.* evaluated the physiological effects of sustained inflation RMs. The results were related to partitioned lung and chest wall mechanics.[16] In only the half of twenty two patients enrolled, arterial oxygenation increased after the RM (responders). Chest wall elastance was significantly higher in non-responders and consequently the transpulmonary pressure applied to the lung during the RMs was significantly lower in non-responders than in responders. Meade *et al.* investigated the effects of different inflation pressures and duration of the RMs on arterial oxygenation.[17] They started from standard RMs (CPAP, 35 cmH_2O, for 20 seconds) twice a day. If the response to the standard RMs was sub-optimal, different RMs were tested by either increasing inflation pressure (40-45 cmH_2O) or duration (30-40 seconds). The standard RMs slightly increased the oxygenation only in 14% of the patients; both the increase in RMs duration and inflation pressure did not further improve the oxygenation.

Extended sigh RM

Foti *et al.* investigated the effect of an extend sigh delivered by an intermittent increase in PEEP for two consecutive ventilator cycles.[18] Arterial oxygenation and lung gas volume significantly increased compared to baseline ventilation within 30 minutes. On the contrary in a group of ARDS patients resulting from trauma ventilated with a low tidal volume strategy, the arterial oxygenation was not affected after thirty minutes and two hours of RMs.[19] RMs were performed by increasing PEEP to 30 cmH_2O for 40 seconds and setting the ventilator in pressure control mode with a delta pressure of 10 cmH_2O. To maximize the lung recruitment Borges *et al.* proposed a new maximum recruitment strategy.[20] This strategy consisted of a progressively increase of PEEP from 25 to 45 by maintaining constant the driving pressure at 15 cmH_2O during pressure control ventilation. At the final step (*i.e.* higher airway pressure) the arterial oxygenation and the amount of collapsed lung tissue were significantly higher and lower, respectively, compared to baseline ventilation. By applying a similar aggressive recruitment strategy in the early phase of ALI/ARDS Morán *et al.* found in the average a better oxygenation compared to baseline but with a greater variability with a transitory hypotension; however in forty percent of the patients it was discontinued.[21]

Considering the possible effect of the body mass in altering the chest wall elastance, three different RMs were tested in obese patients.[22] The first RM consisted of a pressure controlled ventilation with an inspiratory pressure of 40 and PEEP of 5 cmH_2O for 1 minute, the second consisted of a CPAP of 45 cmH_2O for 20 seconds and the least 3 consecutive sighs with a tidal volume to reach a plateau pressure of 45 cmH_2O. All the RMs significantly improved the oxygenation however in patients with a body mass index higher than 27 kg/m^2 only the sustained inflation caused a longer improvement in oxygenation compared to the other two up to thirty minutes. Lim *et al.* randomized early ARDS, after applying a PEEP of 15 cmH_2O, to receive a RM or to continue mechanical ventilation.[23] The RMs were performed by an extended sigh with a progressive increase in pressure and time twice with 1 minute interval. After 60 minutes the arterial oxygenation was not higher in the RMs group. The arterial oxygenation was higher in the extrapulmonary ARDS compared to pulmonary ARDS with a mean increase of 130% *vs.* 27% respectively. Constantin *et al.* compared the respiratory effects of two RM a sustained inflation with a CPAP at 40 cmH_2O for 40 seconds and an extended sighs consisting of increasing PEEP 10 cmH_2O above the lower inflection point maintaining a volume controlled ventilation.[24] At 5 minutes both RM significantly increased the arterial oxygenation compared to baseline, however the extended sighs in a greater extension. By comparing the extended sighs and the sustained inflation RM for a similar peak airway pressure (45 cmH_2O) and time (40 seconds), Iannuzzi *et al.* showed that the extended sighs caused a major increase in arterial oxygenation.[25]

In summary, for ARDS patients the effects of RMs in addition to adequate PEEP levels as a component of ventilation strategy may be greater in whom there is a higher potential for lung recruitment. The use of RMs and its positive effects on lung collapse and gas exchange will continue to be guided by individual clinician experience and patient factors as severity of lung disease, amount of edema and the reached airway pressure

Lung open ventilation

Four randomized studies tested in ARDS patients the efficacy of a global lung ventilation strategy (*i.e.*, lung open ventilation) consisting of low tidal volume with high levels of PEEP and RMs compared to conventional strategy.[26–29] The first study compared a tidal volume lower than 6 mL/kg with a PEEP set higher than the inflection point and RMs performed with CPAP mode at 40 cmH_2O for 40 seconds *versus* a tidal volume of 12 mL/kg with the lowest acceptable PEEP.[26] The lung open ventilation significantly reduced the 28 days mortality but not the hospital mortality (38% *vs.* 71%, $P<0.01$; and 45% *vs.* 71%, $P=0.09$). The second study evaluated a lung ventilation with similar tidal volume (*i.e.* 6 mL/kg) with high levels of PEEP and RMs a *versus* low levels of PEEP.[27] RMs were performed by a 40 seconds breath-hold at 40 cmH_2O airway pressure followed each disconnection from the ventilator, up to 4 times daily. Although the lung open ventilation showed a higher arterial oxygenation and PEEP the hospital mortality was not different (36% *vs.* 40%, $P=0.19$). Similarly Huh *et al.* randomized a group of ARDS patients to a ventilation strategy with RMs with PEEP selected at the end of the RM *versus* a control strategy in which PEEP was selected based on a FiO_2/PEEP table.[28] RMs were applied as an extended sigh with incremental PEEP from baseline to 25 cmH_2O and reducing the VT to not overcome an airway pressure of 55 cmH_2O. The oxygenation and the 28 day mortality at were not different (40% *vs.* 33%). Hodgson *et al.* evaluated an open lung ventilation using RMs, high PEEP and permissive hypercapnia compared to a control strategy in ARDS patients.[29] The RMs were delivered in pressure control ventilation with a fixed delta pressure of 15 cmH_2O above different levels of PEEP from 20 to 40 cmH_2O every two minutes. The PEEP and arterial oxygenation were significantly higher in the treatment group compared to control strategy, the hospital survival was not different.

In synthesis, for ARDS patients, since the era of large tidal volume ventilation should be over, the application of protective ventilation settings with small tidal volume and high levels of PEEP and RMs have the most impact on outcome leading to an increase on oxygenation but not in a mortality reduction.

General anesthesia

The role of RMs, although tested in some trials,[15, 27] in clinical practice remains uncertain because of questions about its effect on outcomes and concerns regarding complications (*e.g.*, hemodynamic compromise or pneumothorax).[17] Two trials explored the efficacy of RMs and PEEP in "non-obese patients" during gynecologic laparoscopic surgery: the randomized controlled trial by Park *et al.* demonstrated the effectiveness of "preemptive use" of RMs coupled to 15 cmH_2O of PEEP (applied before insufflation of the peritoneal cavity) by improving oxygenation with the alveolar recruitment.[30] In the same surgical contest, Cinnella *et al.* evaluating an open-lung approach with the combination of RMs and PEEP (5 cmH_2O) after pneumoperitoneum induction showed similar data.[31]

The PROVHILO trial (PROtective Ventilation using HIgh *versus* LOw PEEP) tested the hypothesis that high PEEP levels (12 cmH_2O) associated with RMs could decrease postoperative pulmonary complications during protective ventilation.[32] The trial confirmed the ineffectiveness of high level of PEEP and RMs in reducing the incidence of postoperative pulmonary complications while there was an increased risk of hemodynamic instability, if compared with use of low PEEP without RMs. Futier *et al.* investigated the effectiveness of RMs and high PEEP levels, in a group of obese patients undergoing to laparoscopy, demonstrating the role of RMs associated to PEEP 10 cmH_2O to preserve recruitment of the lungs from the detrimental effects of pneumoperitoneum and Trendelenburg position.[33] Focusing on the protective role of low V_T and PEEP with RMs in patients during general anesthesia for more than 2 hours with open abdominal surgery, Severgnini *et al.* found a significant enhancement of postoperative pulmonary function and confirmed the detrimental effects of large VT during general anesthesia.[34] A similar study design was performed by the IMPROVE Study Group.[35] Authors assigned patients during general anesthesia to receive ventilation according to one of two strategies: a) non protective ventilation with high VT (10-12 mL/kg PBW), without PEEP and no RMs, b) protective ventilation with low VT (6-8 mL/kg PBW) with PEEP (6-8 cmH_2O) and RMs repeated every 30 minutes after tracheal intubation; airway plateau pressure was limited to 30 cmH_2O in each group. The study based on a large number of patients recruited (at risk of pulmonary complications), demonstrated that an intraoperative lung-protective mechanical ventilation improved clinical outcomes and reduced health care utilization after abdominal surgery in patients at high risk of complications. This study addresses the issue of lung protection in patients without pulmonary function abnormalities and match the beneficial effects of low tidal volume with PEEP, but does not support, at least in appearance, the results of the PROVHILO study that instead tests the protective effects (absent) of high PEEP with RM *vs.* non-use of PEEP coupled to the low VT. A more recent meta-analysis including 3365 individual patients showed that postoperative lung injury is associated with increases in in-hospital mortality and durations of stay in intensive care and hospital. Attributable mortality due to postoperative lung injury is higher after thoracic surgery than after abdominal surgery. Lung protective mechanical ventilation strategies reduces incidence of postoperative lung injury but does not improve mortality.[36]

In summary, patients with normal lungs during general anesthesia can improve respiratory function if ventilated with protective ventilation strategy with low VT but associated to RMs and adequate level of PEEP. The only use of high levels of PEEP even if associated to low VT, or high VT without PEEP and RMs do not improve patient outcomes. We point out the effectiveness of high PEEP levels and RMs in obese patients undergoing to laparoscopy, to preserve recruitment of the lungs from the detrimental effects of pneumoperitoneum and Trendelenburg position.

Biological response to RMs in experimental models of acute lung injury

Recruitment maneuvers may induce different biological and morpho-functional response on the pulmonary structure, mainly the epithelium, the endothelium, as well as the extracellular matrix. Specifically, the effects of recruitment maneuvers may depend on the following factors: type of acute lung injury (primary or secondary insult to the lung); the extent of lung injury (predominance of alveolar collapse or alveolar edema); the volemic status (hypervolemia, normovolemia or hypovolemia) and the type of the recruitment maneuvers (sustained inflation, sigh, extended sigh, slow *vs.* fast recruitment maneuvers).

Cause of acute lung injury

Using experimental models of pulmonary and extrapulmonary acute lung injury induced by Escherichia coli lipopolysaccharide admistration intratracheally or intraperitoneally in rats, with similar transpulmonary pressures, Riva *et al.*[37] reported that sustained inflation recruitment maneuver is more effective at opening collapsed alveoli, thus improving lung mechanics and oxygenation with limited damage to alveolar epithelium in extrapulmonary than in pulmonary acute lung injury.

Extent of lung injury (alveolar collapse versus edema)

Santiago *et al.*[38] in an experimental model of acute lung injury induced by different increasing dosage of *Escherichia coli* lipopolysaccharide intraperitoneally in rats reported that recruitment maneuvers promoted a decrease in inflammatory and fibrogenic response, and greater improvement in lung function in the presence of alveolar collapse alone as compared to alveolar collapse associated with alveolar edema.

Effect of volemia

Fluid management plays a relevant role in the management of ARDS. Silva *et al.*[39] investigated the effects of recruitment maneuvers on lung and distal organs in the presence of hypovolemia, normovolemia, and hypervolemia in mice. In hypervolemic animals, recruitment maneuver improved oxygenation but increased lung injury and led to higher inflammatory and fibrogenic responses, suggesting that volemic status should be taken into account during recruitment maneuvers.

Type of RMs: sustained inflation vs. stepwise or slow recruitment

Rzezinski *et al.* investigated the effects of prolonged recruitment maneuver (PRM) compared with sustained inflation (SI) in paraquat-induced mild acute lung injury in rats.[40] Lung static elastance and the amount of alveolar collapse were more reduced with PRM than SI, yielding improved oxygenation. Additionally, tumor necrosis factor-alpha, interleukin-6, interferon-gamma, and type III procollagen mRNA expressions in lung tissue and lung epithelial cell apoptosis decreased more in PRM. In conclusion, PRM improved lung function, with less damage to alveolar epithelium, resulting in reduced pulmonary injury.

Silva *et al.*[41] in experimental model of acute lung injury induced by cecal ligation and puncture in rats found that longer-duration RMs with slower airway pressure increase efficiently improved lung function, while minimizing the biological impact on lungs as compared to sustained inflation or stepwise with reduced duration.

In another study, Silva *et al.*[42] in experimental models of pulmonary and extrapulmonary acute lung injury induced by *Escherichia coli* lipopolysaccharide in rats, found that sustained inflation worsened markers of potential epithelial cell damage in pulmonary acute lung injury, whereas both sustained inflation and stepwise recruitment maneuver yielded endothelial injury in extrapulmonary acute lung injury. In both acute lung injury groups, recruitment maneuvers improved respiratory mechanics, but stepwise recruitment maneuver without sustained airway pressure appeared to associate with less biological impact on lungs.

Conclusions

RMs in ARDS are able to increase in the majority of the patients the oxygenation for a limited period of time, however they seem to not affect the outcome. In healthy subjects during general anesthesia, RMs as a component of an open lung strategy, could improve pulmonary function especially in selected categories of patients with high potential of lung recruitment and without primary pulmonary disease (*i.e.* in presence of impairment of chest wall elastance due to obesity or during laparoscopy surgery).

Future studies will be helpful to determine whether protective lung ventilation strategy with RMs could improve major clinical outcomes thus achieving consensus regarding its appropriate function in clinical practice.

Key messages

— Recruitment maneuvers in acute respiratory distress syndrome improve oxygenation in the majority of the patients.

— The effects of the recruitment maneuvers depend on the transpulmonary pressure generated in the patients.

— Recruitment maneuvers do not improve the outcome in patients with ARDS.

— During general anesthesia, recruitment manures could be used in selected categories of patients.

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