Lung recruitment: who, when and how?

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The role of recruitment in acute lung injury (ALI), usually as part of an "open lung" ventilation strategy, remains controversial. A large randomised controlled trial (RCT), the Lung Open Ventilation Strategy (LOVS) trial,[1] which included a recruitment manoeuvre (RM) of sustained static lung inflation to pressures of 40 cmH_2O for 40 sec (40/40 RM) failed to improve patient survival. Two systematic reviews of multiple studies using similar RMs have shown improved short-term oxygenation, but have failed to show improvement in other clinically relevant variables.[1-3] The study in this issue by Kanoore Edul et al (*page 143*)[4] using a similar RM (40 cmH_2O for 45 sec) has not only shown no improvement in oxygenation but has also shown transient deleterious haemodynamic effects. Does this mean we should abandon RMs?

The motivation for using RMs is based on computed tomography findings in patients with ALI.[5] The lung, which can appear to have relatively uniform injury on plain chest x-ray, has three functionally distinct zones during tidal ventilation:

- The most dependent lung region, which remains collapsed throughout tidal ventilation, despite high positive end-expiratory pressure (PEEP) levels, resulting in chronic collapse injury;[6]
- An intermediate lung region that collapses and re-expands with each breath, resulting in shear stress-induced injury (atelectrauma); and
- The least dependent lung regions, which remain inflated throughout tidal ventilation, receive most of the tidal volume, and can receive overinflation lung injury (volutrauma) by tidal volumes exceeding 6 mL/kg and plateau airway pressure exceeding 30–35 cmH_2O.

All these processes augment the pulmonary elaboration and systemic concentration of injurious cytokines that contribute to the risk of multiple organ failure and mortality in patients with ALI.[7-8]

The "protective" mechanical ventilation strategy, characterised by low tidal volume, limitation of plateau pressure and intermediate PEEP levels, has led to reductions in mortality and is now widely accepted.[9-13] However, this strategy may fail to expand the most dependent lung regions and inadequately reduce cyclic alveolar collapse. These effects may contribute to the progression of lung injury and multiple organ failure. The "open lung" ventilation strategy is based on re-inflating these collapsed lung regions then preventing collapse during the subsequent mechanical ventilation. The aim of this is not simply to improve oxygenation but also to improve lung health, reduce injurious cytokine production, shorten time to recovery and improve patient survival.

Three large RCTs have been performed to address this hypothesis using higher PEEP levels with and without RMs.[1,14,15] One used static RMs (35–40 cmH_2O for 30 sec) in a small subset of patients,[14] one used the 40/40 RM in all patients,[1] and the third did not use RMs.[15] All three studies were potentially disadvantaged by using a similar tidal volume in the treatment and control groups, resulting in a higher plateau pressure level in the treatment group, and all three studies failed to demonstrate a survival advantage compared with control ventilation. However, a meta-analysis of these studies[16] has suggested benefit from higher PEEP in patients with acute respiratory distress syndrome (ARDS) (Pao_2/Fio_2 ratio <200), but not in ALI patients without ARDS (Pao_2/Fio_2 ratio 200–300).

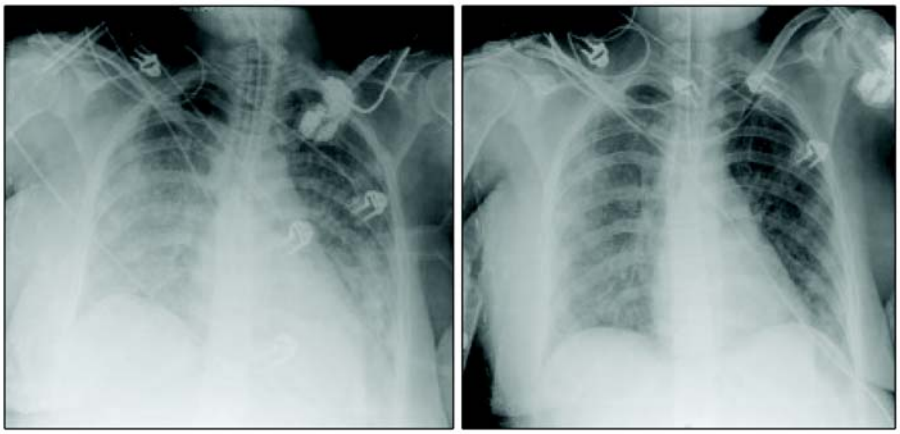
In contradistinction, a meta-analysis of ventilation trials including 40/40 RMs found no significant improvement in length of ventilation, length of ICU or hospital stay, or mortality.[3] Although more data were required to exclude benefit, this did suggest that the 40/40 RM with the associated ventilatory strategies was probably ineffective. Unlike the study by Kanoore Edul et al, two RM meta-analyses did find a significant improvement in oxygenation without significant side effects.[2-3] The reason for this difference may lie in the severity of ALI (Table1).

Table 1. Comparison of the Kanoore Edul et al study with RM meta-analyses for Pao_2/Fio_2 (P/F)

	Hodgson et al (2009)[3]	Fan et al (2008)[2]	Kanoore Edul et al (2010)[4]
Study type	Meta-analysis	Meta-analysis	RCT
Studies included	RCT (2)	RCT & obs (20)	1
No. of patients	490	1185	11
% patients with ARDS	87%	na	30%
Initial PEEP (cmH_2O)	11 ±3	11 ±3	13 ±3
Baseline P/F	144 ±48	139 ±31	215 ±66
Post-RM P/F	185 ±69	251 ±117	212 ±78

ARDS = acute respiratory distress syndrome. na = not available. obs = observational. PEEP = positive end-expiratory pressure. RCT = randomised controlled trial. RM = recruitment manoeuvre.

Figure 1. Changes in chest x-ray appearance following a recruitment manoeuvre



The meta-analyses that reported improved oxygenation with RMs[2,3] had much lower initial Pao_2/Fio_2 values, with 87% of patients having ARDS in one analysis and probably a similarly high proportion of patients with ARDS in the other analysis, based on the lower Pao_2/Fio_2 values. In contrast, the Kanoore Edul study had a high initial Pao_2/Fio_2 value and a lower proportion of patients with ARDS, suggesting a lower severity of lung injury, possibly with less potential to show improvement in oxygenation. This is similar to the high-PEEP meta-analysis, which showed benefit only in the ARDS group.[16] The higher initial PEEP in the Kanoore Edul study also may have reduced the potential for improvement.[17]

The haemodynamic effects of RMs are well documented[18-20] and usually transient. Although transient hypotension has been reported in many studies, most have reported no significant adverse events.[2-3] Kanoore Edul et al reported only a modest reduction in systolic and mean arterial pressure during the RM, but a large and significant reduction (23%) in cardiac index. Although blood pressure and cardiac index had recovered 2 minutes after the RM in their study, it highlights the importance of circulatory depression, which can cause abandonment of an RM, and the importance of not performing RMs in hypovolaemic or hypotensive patients, in whom severe and prolonged circulatory depression may occasionally occur.

Apart from short-term oxygenation improvement, the major RM trials and the RM meta-analyses have failed to show any improvements in outcome. This stimulates consideration of whether the 40/40 RMs themselves are the most effective form of RM and whether any recruitment achieved was adequately maintained after the RM by sufficiently high PEEP levels and by re-recruitment when desaturation, disconnection or suctioning occurred.

When lung recruitment was first proposed,[21] it was suggested that a static lung inflation to 60 cmH_2O for 60 seconds was required maximise recruitment. However, possibly because of poor haemodynamic and ventilatory tolerance, patient discomfort, concerns about barotrauma and physician discomfort, a more conservative version, the 40/40 RM, became much more widely used, but with little clear success.

The search for better RMs led to the use of pressure-control ventilation with incremental PEEP during the RM,[22] with the goal that higher alveolar pressure applied intermittently would enable better lung recruitment with ongoing ventilation and less circulatory depression. Steps up to the maximum PEEP allow assessment of tolerance and steps down in PEEP after the maximum PEEP allow determination of the point at which oxygenation first decreased to determine the PEEP level to use after the RM. The PEEP increments during the RM led to the name "stepwise" or "staircase" RM.

Lim and colleagues have studied the effect of different types of RMs (static, pressure-control with incremental PEEP, and "extended sigh") in porcine lungs with ARDS.[18,23,24] They found the most effective RM to improve oxygenation was pressure-control with incremental PEEP. Borges et al[22] used a stepwise manoeuvre in 26 patients with ARDS to maximum plateau pressure (Pplat) of 60 cmH_2O over a total time for PEEP steps up and down of 20 minutes. This showed a sustained positive response in 24 out of 26 patients (92%), with a mean PEEP of 22 ±4 cmH_2O after PEEP titration. Hodgson et al[25] studied 20 patients with ARDS with a similar staircase RM to a maximum Pplat of 55 ±3 cmH_2O with incremental and decremental PEEP titration over a total time of 15–20 minutes. They found significant improvements in $Pao2/Fio_2$ ratio, shunt fraction, compliance and lung field radiolucency on chest x-ray (Figure 1) that were sustained for an hour after the RM in 90% of patients. The study also found that 40% of patients desaturated at maximum PEEP during the RM but still improved their oxygenation when PEEP was reduced. Hodgson et al suggested that only 45% of the patients would have responded to a 40/40 RM, and Borges et al stated that 54% of patients required a Pplat > 40 cmH_2O for full recruitment (ie, only 46% would have fully responded with a 40/40 RM). Both these studies reported transient haemodynamic changes during the RM, with no significant consequences.[22,25]

A subsequent RCT of 20 patients with ARDS by Hodgson et al[26] compared the staircase RM with an ARDSNet-based

control group. In this study the treatment group, after PEEP titration, received a higher PEEP (15 ± 1 v 10 ± 0.5 cmH_2O) and a lower driving pressure (Pplat-PEEP, 13 ± 1 v 17 ± 1 cmH_2O) than the control group, resulting in the same safe Pplat (28 ± 2 cmH_2O) in both groups. This strategy resulted in improved Pao2/Fio2, compliance and systemic cytokine levels and a non-significant reduction in length of ventilation, ICU stay and hospital stay.[26] While the findings in relation to this method of lung recruitment are positive, they require further investigation in larger RCTs before long-term benefit can be confirmed.

Our group also provides extracorporeal membrane oxygenation (ECMO) for patients with severe ALI (Sa_{O_2} < 90% despite F_{IO_2} 1.0 and PEEP ⩾ 17.5 cmH_2O), and we have found that the staircase RM averts the need for ECMO in over 30% of patients who otherwise would have proceeded to that support.

These findings suggest that ARDS patients (initial Pa_{O_2}/F_{IO_2} ratio < 200) respond better to recruitment and high PEEP than ALI patients without ARDS (Pa_{O_2}/F_{IO_2} ratio 200–300), and that staircase RMs may be effective in a higher proportion of patients with ARDS than 40/40 RMs. Also, many RM studies describe responders and non-responders,[27,28] and there may be benefit in the former subset that is not seen when all patients are included in large study analysis.

In conclusion, studies to date, including the work by Kanoore Edul et al, indicate that sustained lung inflation to a pressure of 40 cmH_2O (40/40 RM) may not be effective in patients with mild ALI and have no established long-term benefit in patients with ARDS. Further trials are needed to establish the role of RMs, particularly with regard to disease severity (ARDS versus ALI) and their effect on clinically relevant outcomes. But in the meantime, this does not mean that RMs should not be used. There is emerging evidence that RMs with incremental PEEP and pressure-controlled ventilation to pressures in excess of 50 cmH_2O (such as the staircase RMs) are safe and well tolerated in patients with ARDS, are more effective than 40/40 RMs, and can be successfully used in patients with significant hypoxaemia.

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