



## LIVES 2017: Lung recruitment and PEEP trial reports results



Results from the Alveolar Recruitment for Acute Respiratory Distress Trial (ART) randomised trial ("ART"), which compared a strategy using a lung recruitment manoeuvre and titrated positive end-expiratory pressure (PEEP) with low PEEP, increased 28-day all-cause mortality of patients with moderate to severe acute respiratory distress syndrome (ARDS). The findings, published in JAMA and presented at the 30th European Society of Intensive Care Medicine in Vienna, do not support the routine use of lung recruitment manoeuvre and PEEP titration in these patients.

Mechanical ventilation is critical for the survival of many patients with ARDS but can also cause ventilator-induced lung injury (VILI). One form of VILI occurs when the lungs exhale to relatively low volumes and airway pressures. This may cause injurious tidal closing and reopening of small bronchioles and alveoli or excessive stress at the margins between aerated and atelectatic airspaces. In animal studies, PEEP reduced or prevented VILI from exhalation to low volumes and pressures.

In some early studies, the levels of PEEP that were applied for lung-protection exceeded the levels that most clinicians use when managing patients with ARDS. This led to recommendations to use higher PEEP in patients with ARDS to minimise low volume and low pressure VILI and hopefully to improve clinical outcomes. The "open lung approach" (OLA) aims to achieve high levels of lung aeration in patients with ARDS by first conducting recruitment manoeuvres (RMs) to reverse atelectasis and then applying high levels of PEEP to keep recruited alveoli open.

The ART study was conducted at 120 intensive care units (ICUs) from nine countries enrolling adults (mean [SD] age, 50.9 [17.4] years) with moderate to severe ARDS. The study compared patients treated with the OLA (n = 501) with those managed with conventional PEEP (n = 509). Patients in the OLA study group received RMs with PEEP as high as 45 cm H<sub>2</sub>O and peak airway pressures as high as 60 cm H<sub>2</sub>O.

The results showed that the OLA was associated with a significantly higher 28-day mortality and 6-month mortality (55.3% vs. 49.3% and 65.3% vs. 59.9%, respectively). A small but statistically significant difference in ventilator-free days favoured the control group (5.3 days in the OLA group vs. 6.4 days in the control group), and there was a higher rate of barotrauma among patients in the OLA group (5.6%) than among those in the control group (1.6%).

The study's corresponding author Alexandre Biasi Cavalcanti, MD, PhD, HCor Research Institute-Hospital do Coração, São Paulo, Brazil, explained the findings in an email to ICU Management & Practice.

"We have found that the strategy with lung recruitment manoeuvre (with stepwise increases in PEEP, achieving a PEEP of 35 cm H<sub>2</sub>O and peak pressure of 50 cm H<sub>2</sub>O), followed by PEEP titrated according to the best static compliance increases the 28-day mortality of moderate-to-severe ARDS patients. It may also increase the risk of barotrauma within 7 days and hypotension or need to start or increase vasopressors within 1 hour. Thus, we believe this strategy should not be used for patients with moderate-to-severe ARDS," Dr. Cavalcanti said.

However, the author doesn't think that this is the end of the Open Lung Approach for ARDS. As the results of ART show us that this strategy may be deleterious when applied to general patients with moderate-to-severe ARDS, the doctor said "we should refrain from doing so in routine practice."

An accompanying editorial in JAMA says the results of the ART trial are not only disappointing but will be unexpected for many intensive care physicians and researchers working on VILI and lung-protective ventilation.

"PEEP has been used during mechanical ventilation since the landmark description of ARDS 50 years ago. However, the best method for setting PEEP levels has still not been established. Perhaps further refinements in the OLA strategy with less aggressive attempts at lung recruitment and a focus on identifying patients who recruit in response to PEEP will lead to more favourable results and leave the door to the OLA cracked open," write Sarina K. Sahetya, MD, and Roy G. Brower, MD, both from the Pulmonary and Critical Care Medicine at Johns Hopkins University School of Medicine (Baltimore, Maryland) in the editorial.

Dr. Cavalcanti agrees with the authors of the editorial that one way forward is to identify patients who respond to PEEP. "I do agree with the position that a way forward is to find in advance patients that respond to increases in PEEP, for example by administering a 'test dose' of PEEP – increasing PEEP from 5 to 15 cm H<sub>2</sub>O, and seeing the response in terms of markers of lung recruitment (imaging or perhaps, improvement in static compliance) (Goligher et al. 2015). Then, enrolling those patients in a randomised controlled trial to test if this subset of PEEP responders actually has benefits on relevant clinical outcomes compared to the conventional low-PEEP strategy," the doctor said.

The ART investigator also cited the need to develop models to predict responsiveness so that we can use several characteristics at baseline to identify patients which are more likely to benefit. "We have begun to work on such predictive models using our database. An excellent example of this strategy is the subgrouping of ARDS into subphenotypes as done by Calfee et al. using statistical techniques (latent class analysis) (Calfee et al. 2014). Subphenotypes are classified using several biomarkers and clinical variables and seem to be useful to predict clinical responsiveness to PEEP," Dr. Cavalcanti explained.

Moreover, the doctor agrees with the editorial authors' suggestion that "allowing part of the lung to stay closed with permissive atelectasis may be more patient-protective than aggressive efforts to keep the lung open.

As Dr. Cavalcanti stated: "I definitely agree with the editorialists that a strategy allowing atelectasis, with low to intermediate PEEP levels, may be more lung-protective than a strategy of aggressive lung recruitment manoeuvres combined with high PEEP. I have specified low to intermediate PEEP because the control group in the ART study actually received PEEP levels that were slightly higher than the PEEP levels applied in the control group of previous PEEP trials."

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Alexandre B. Cavalcanti, will present the results of the trial in the hot topics session, Room Berlin, on Wednesday 27th September, 14.10-17.30.

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