Original Article

Changes in stroke volume during an alveolar recruitment maneuvers through a stepwise increase in positive end expiratory pressure and transient continuous positive airway pressure in anesthetized patients. A prospective observational pilot study

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Abstract

Background and Aims: Recruitment maneuvers may be used during anesthesia as part of perioperative protective ventilation strategy. However, the hemodynamic effect of recruitment maneuvers remain poorly documented in this setting.

Material and Methods: This was a prospective observational study performed in operating theatre including patients scheduled for major vascular surgery. Patients were monitored with invasive arterial pressure and esophageal doppler. After induction of general anesthesia, before surgery began, preload optimization based on stroke volume (SV) variation following fluid challenge was performed. Then, an alveolar recruitment maneuver (ARM) through stepwise increase in positive end expiratory pressure (PEEP) or continuous positive airway pressure (CPAP) was performed. Hemodynamic data were noted before, during, and after the alveolar recruitment maneuver.

Results: ARM through stepwise increase in PEEP and CPAP were applied in 22 and 14 preload independent patients, respectively. Relative changes in SV during ARMs were significantly greater in the ARM_{CPAP} group (-39 ± 20%) as compared to the ARM_{PEEP} group (-15 ± 22%; $P = 0.002$). The difference (95% CI) in relative decrease in SV between ARM_{CPAP} and ARM_{PEEP} groups was -24% (-38 to -9; $P = 0.001$). Changes in arterial pressure, cardiac index, pulse pressure variation, peak velocity, and corrected flow time measures were not different between groups.

Conclusion: During anesthesia, in preload independent patients, ARMs through CPAP resulted in a significantly greater decrease in SV than stepwise increase in PEEP. During anesthesia, ARM should be used cautiously.

Keywords: Alveolar recruitment, anesthesia, esophageal doppler, positive end expiratory pressure, stroke volume, ventilation

Introduction

During general anesthesia, pulmonary atelectasis has been shown to occur in 85--90% of patient.[1,2] Pulmonary atelectasis is associated with postoperative pulmonary complications which have been shown to increase early postoperative mortality.[3,4] Intra and postoperative positive end expiratory pressure (PEEP) and alveolar recruitment maneuvers (ARMs) may be used to limit pulmonary atelectasis, to improve arterial oxygenation and postoperative

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pulmonary function.[5-8] Thus, it has been shown that a lung-protective mechanical ventilation including repeated ARMs [i.e., continuous positive airway pressure (CPAP) of 30 cmH_2O during 30 s] could improve postoperative major clinical outcomes following major abdominal surgery.[9]

However, during CPAP, the positive intrathoracic pressure decreases right ventricular stroke volume (SV) through a decrease in venous return and increase in pulmonary vascular resistance. Because of ventricular interdependence, a subsequent decrease in left ventricular SV occurs.[10] In pigs, a single ARM with CPAP of 40 cm H_2O during 30 s induced a transient but severe (-60% to -90%) decrease in cardiac output depending on the preload dependence status.[11] Following cardiac surgery, an ARM with CPAP of 40 cm H_2O during 20 s induced a -64% decrease in cardiac output and a half decrease in left ventricular end diastolic area.[12] During general anesthesia in patients scheduled for neurosurgery, ARM (CPAP of 30 cm H_2O during 30 s) markedly decreased SV and mean arterial pressure (MAP) in preload dependent patients.[13] In the PROVHILO study, the increased incidence of intraoperative hemodynamic adverse events noted might have been associated with higher PEEP and ARMs.[14] This should be interpreted with the increasingly reported association between intraoperative hypotension and postoperative morbidity.[15]

However, another method for ARMs (stepwise increase and decrease in PEEP) has been studied in acute respiratory distress syndrome but never evaluated in anesthetized patients.

Experimental data suggested that the stepwise increase and decrease in PEEP had less hemodynamic effect than CPAP.[16] At our best knowledge, only one clinical study compared the hemodynamic effect of different ARMs during general anesthesia in patients without acute pulmonary injury.[17] Nevertheless, this study performed in the postoperative period following cardiac surgery cannot be extrapolated to the intraoperative period in non-cardiac surgery.

Consequently, the aim of the present study was to compare the effects of CPAP and stepwise increase in PEEP on SV in anesthetized patients scheduled for vascular surgery. We hypothesized that ARM with stepwise increase in PEEP would have less hemodynamic effect than CPAP. A better understanding of hemodynamic effect of different ARMs during anesthesia may help anesthesiologists to use them.

Material and Methods

This was a single-center prospective observational study conducted from January 2016 to May 2017 in university hospital of Caen. The study was approved by the institutional review board (Comité de Protection des Personnes Caen Nord Ouest III, reference: A15-D27-VOL. 25). Since there was no randomization and only routine care was performed, waiver of written informed consent was authorized by the local medical ethics committee. Nevertheless, oral information and consent was obtained from all patients before surgery. The clinical trial registration number is NCT03215329.

The report of the present study adhered to the STROBE standards for observational studies. Inclusion criteria were adult patients aged 18 years and above, American Society of Anesthesiologists physical status (ASA) II to IV, scheduled for intermediate and high risk surgery (as defined by the European Society of Cardiology (ESC)/European Society of Anesthesiology (ESA) on non-cardiac surgery: assessment and management), and monitored with a radial arterial catheter and transesophageal doppler.

Exclusion criteria were patients less than 18 years old, adults with intellectual disability, pregnant women, atrial fibrillation, history of right ventricular dysfunction, known left ventricular ejection fraction <30%, history of chronic pulmonary obstructive disease, history of asthma.

Study design

After monitoring (IntelliVue MP 70, Philips HealthCare, Amsterdam, The Netherlands) with continuous 5-lead electrocardiography, pulse oximetry, and bispectral index (BIS™ quarto sensor, Covidien, Dublin, Ireland), an intravenous line was placed. A radial intra-arterial catheter (Leader-cath; VYGON, Ecouen, France) was inserted after local anesthesia and connected to a pressure transducer zeroed at the intersection of the mild axillary line and the fifth intercostal space. Arterial pressure and pulse pressure variation (PPV) were continuously displayed on the monitor. After 3--5 min, preoxygenation with 100% FiO_2, anesthesia was induced and maintained using target controlled total intravenous anesthesia with propofol and remifentanil. A neuromuscular blocking agent was administered, and its effect was monitored by accelerometry at the thumb following Train-of-four stimulations of the ulnar nerve repeated every 30 s (Philips IntelliVue NMT, Philips HealthCare, Amsterdam, the Netherlands).

Following orotracheal intubation, patients were ventilated (Aisys, Ge Healthcare, Little Chalfont, UK) with controlled ventilation mode (FiO_2 set to maintain SpO2 >96%, inspired oxygen fraction, tidal volume: 6 to 8 $ml.kg^{-1}$ of ideal body weight, PEEP + 5 cmH_2O, inspiratory to expiratory ratio of ½, respiratory rate between

10 and 16 min^{-1} to maintain an end tidal carbon dioxide partial pressure of 30 to 35 mmHg). An esophageal doppler probe connected to its monitor was inserted after tracheal intubation (CardioQ-ODM, Deltex Medical, UK). Then, a 250 ml fluid challenge with colloid or crystalloid was performed and repeated as long as the SV increased more than 10%.

Then, the ARM was performed after SV optimization. Two pre-set ARMs were available on the anesthesia ventilator sustained airway pressure at + 30 cmH_2O for 30 s (ARM_{CPAP} group) and a stepwise increase and decrease in PEEP from + 5 to + 12 cm H_2O with inspiratory pressure from + 15 to + 20 cm H_2O (ARM_{PEEP} group; Figure 1). The choice of the ARM was left at the discretion of the attending anesthesiologist.

Parameters recorded

Heart rate, arterial pressure, PPV, pulse oximetry, bispectral index, cardiac index, SV, peak velocity, and corrected flow time were recorded by an independent observer before the ARM, during the ARM at the nadir of SV variation, 1 min and 3 min after the end of the ARM.

Definitions of outcomes

The primary outcome was the relative change (delta%) in SV measured before and during the ARM in ARM_{CPAP} and ARM_{PEEP} groups.

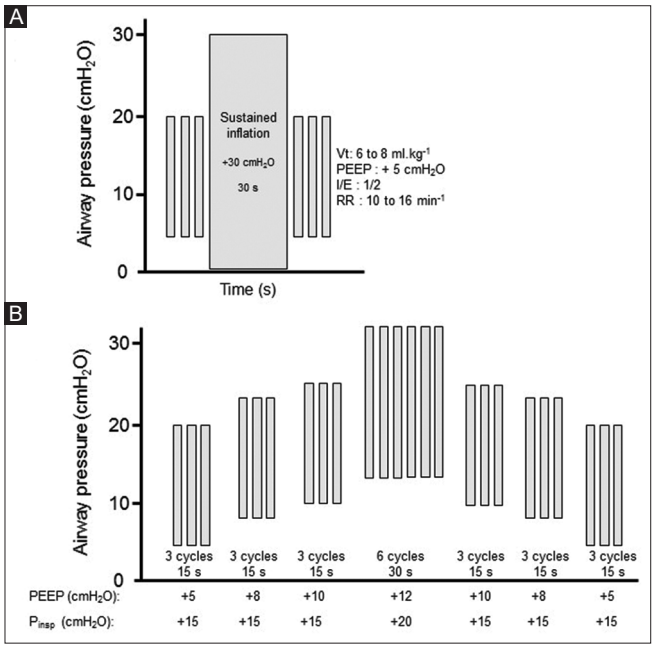

Figure 1: Diagram of the alveolar recruitment maneuver applied in the study. Panel A: the 30 s sustained inflation applied in the ARMCPAP group. Panel B: stepwise increase in positive end expiratory pressure applied in the ARMPEEP group. PEEP: positive end expiratory pressure, Pinsp: inspiratory pressure, Vt: tidal volume, I/E: ratio of inspiratory to expiratory time, RR: respiratory rate

The secondary outcomes were: absolute change in SV (ml) measured before and during the ARM in ARM_{CPAP} and ARM_{PEEP} groups, changes in absolute values of SV, arterial blood pressure (mean, systolic and diastolic), PPV, PV, and corrected flow time according to time and groups.

Statistical analysis

At the time the study started no data were available on the effect of the two methods of ARM on SV in anesthetized patients in operating room. Based on data reported in intensive care units patients we hypothesized that a mean decrease in SV of 40% and 20% would occur in the ARM_{CPAP} and ARM_{PEEP} groups, respectively.[16] Thus, we planned to include 15 patients in each group with an alpha risk = 0.05, a beta risk = 0.10, and assuming a standard deviation (SD) = 15 in both groups.

Data are expressed as mean ± SD or median [1st quartile–3rd quartile] for non-normally distributed continuous variables and numbers (percentages) for categorical variables. The 95% confidence interval (95% CI) were calculated for differences. Normality was tested with the D'Agostino-Pearson test. The Student *t*-test and Mann--Whitney test were used to compare two means and medians, respectively. The comparison of proportions was performed using the Fisher exact test or Chi-square test as appropriate.

The comparison of repeated measures over time was carried out using a linear mixed-effects model with subject as a random effect and time and group as a fixed effect. Multiple post-hoc pairwise comparisons were performed with the Tukey's post-hoc test assuming that population variance were similar.

The statistical analysis was performed using the R software Version 3.4.0 (R: A Language and Environment for Statistical Computing, R Foundation for Statistical Computing, Vienna, Austria; https://www.R-project.org) and packages compare Groups, and nlme.

Results

Patient's characteristics and hemodynamic data

Thirty seven consecutive patients were included (22 in the ARM_{PEEP} group, 14 in ARM_{CPAP} group). One patient was excluded from the ARM_{PEEP} group because SV was not recorded. Table 1 reported the main characteristics of patients.

Hemodynamic and respiratory parameters recorded before the ARM are reported in Table 2.

The median (IQR) volume of crystalloids (ARM_{PEEP}: 250 (250; 500) ml versus ARM_{CPAP}: 375 (250; 500) ml; P = 0.488) and colloids (ARM_{PEEP}: 625 (438; 813) ml

Table 1: Demographic data patient's history and chronic treatments

	ARM_{PEEP} group (n=22)	ARM_{CPAP} group (n=14)	P
Age (year)	64±13	71±12	0.074
Weight (kg)	76±17	75±23	0.917
Height (cm)	171±9	166±7	0.038
Body mass index (kg.m^{-2})	26±6	27±7	0.612
Sex (female/male)	6/16	5/9	0.716
ASA physical status II	8 (36%)	1 (7%)	0.016*
ASA physical status III	8 (36%)	12 (86%)	
ASA physical status IV	6 (27%)	1 (7%)	
History of hypertension	18 (86%)	12 (86%)	1.000
History of ischemic heart disease	6 (29%)	4 (29%)	1.000
History of atrial fibrillation	1 (5%)	2 (14%)	0.551
History of dyslipidaemia	7 (33%)	8 (57%)	1.000
History of peripheral arterial disease	12 (57%)	8 (57%)	0.296
History of diabetes	9 (43%)	10 (71%)	0.188
History of renal dysfunction	3 (14%)	0 (0%)	0.259
Plasma creatinine, micromol.l^{-1}	117±76	74±20	0.063
History of respiratory disease	3 (14%)	1 (7%)	0.635
Active Tobacco	5 (24%)	2 (14%)	0.676
Beta-adrenergic blockers	10 (48%)	4 (29%)	0.439
ACEI and ARA	14 (67%)	5 (36%)	0.146
Calcium channel antagonist	7 (33%)	5 (36%)	1.000
Diuretic	3 (14%)	2 (14%)	1.000
Nitrates	1 (5%)	3 (21%)	0.279
Amiodarone	1 (5%)	0 (0%)	1.000
Antiplatelet treatment	15 (71%)	9 (64%)	0.721
Statin	12 (57%)	9 (64%)	0.944
Insulin	3 (14%)	5 (36%)	0.221

*Value are mean with±SD, or number (%). ASA=American Society of Anesthesiologists, ACEI=Angiotensin-Converting Enzyme Inhibitor, ARA=Angiotensin 2 Receptor Antagonist. *P Chi-2 of heterogeneity for ASA physical status repartition between groups*

Table 2: Hemodynamic and respiratory parameters recorded before the alveolar recruitment maneuver

	ARM_{PEEP} group (n=22)	ARM_{CPAP} group (n=14)	P
Tidal volume (ml.kg^{-1})	7.5±1.2	7.1±1.7	0.497
Respiratory rate (min^{-1})	14±2	14±3	0.427
Systolic arterial pressure (mmHg)	118±20	114±24	0.576
Diastolic arterial pressure (mmHg)	59±11	54±9	0.130
Mean arterial pressure (mmHg)	80±14	75±15	0.259
Heart rate (min^{-1})	66±14	79±19	0.037
Pulse pressure variation (%)	9±3	8±4	0.567
Bispectral index	38±13	45±15	0.196
Peripheral Oxygen saturation (%)	100±1	99±1	0.661
Stroke volume (ml)	64±20	76±22	0.105
Cardiac index (ml.min^{-1}.m^{-2})	3.0±2.3	3.7±1.5	0.294
Stroke volume variation (%)	22±13	20±12	0.670

Data are mean with±SD

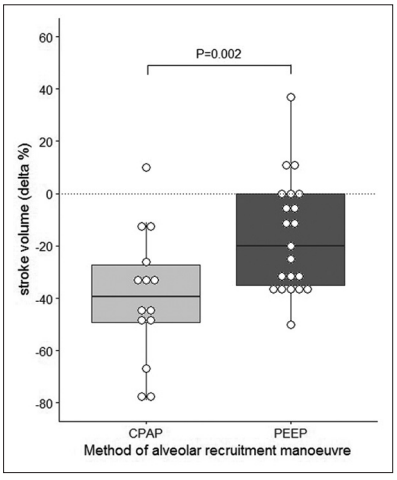

Figure 2: Relative change in stroke volume measured during alveolar recruitment maneuver. CPAP: Continuous + 30 cmH2O positive airway pressure applied for 30 s applied in the ARMCPAP group. PEEP: stepwise increase in positive end expiratory pressure applied in the ARMPEEP group

versus ARM_{CPAP} group: 750 (625; 875) ml; P = 0.683) administered before the ARM were not different between groups.

Primary outcome

As depicted in Figure 2, the relative changes in SV during ARMs were significantly greater in the ARM_{CPAP} group (-39 ± 20%) as compared to the ARM_{PEEP} group (-15 ± 22%; P = 0.002). The difference (95% CI) in relative decrease in SV between ARM_{CPAP} and ARM_{PEEP} groups was -24% (-38 to -9; P = 0.001).

Secondary outcomes

The absolute decreases in SV during the ARM were significant in the ARM_{CPAP} group (-29 ± 18 ml; P = 0.002) but

not in the ARM_{PEEP} group (-9 ± 14 ml; $P = 0.889$). The difference (95% CI) in absolute decrease in SV between ARM_{CPAP} and ARM_{PEEP} groups was -20 ml (-32 to -8; $P = 0.001$). The linear mixed effects model for repeated SV measures showed a significant effect of time ($P < 0.001$) but not of group ($P = 0.712$). Absolute values of SV, arterial pressure, heart rate, cardiac index, PPV, peak velocity, and corrected flow time according to time and groups are summarized in Table 3.

The linear mixed effects model for repeated arterial pressure, cardiac index, PPV, peak velocity, and corrected flow time measures showed a significant effect of time but not of group.

The linear mixed effects model for repeated heart rate measures showed a significant effect of time ($P < 0.001$) and group ($P = 0.03$).

Discussion

This is the first study which compares two methods for alveolar recruitment in patients scheduled for general surgery and in whom preload dependence was corrected. This pilot study strongly suggest that the decrease in SV was more pronounced during ARM using brief CPAP than during ARM using stepwise increase and decrease in PEEP.

Atelectasis is frequent in anesthetized patients, could persist in the postoperative period, and could result in postoperative pulmonary complications.[1-4,18] This may justify the use of a lung-protective ventilation strategy including repeated ARMs during general anesthesia.[19] The most commonly used ARM consists of a transient sustained lung inflation (CPAP of 30--40 cmH_2O during 30--40 s).[9,11-14] In acute lung injury, a stepwise increase and decrease in PEEP has been proposed with the advantage of a better hemodynamic tolerance.[16,17]

Few clinical studies examined the hemodynamic effects of ARM in anesthetized patients with a normal respiratory system.[12,13,17] Following cardiac surgery, sustained lung inflation decreased by half cardiac output and left ventricular end diastolic area, and MAP by 20%.[12] In 28 patients scheduled for neurosurgery, Biais *et al*. reported a 20--43% mean decrease in SV and a 24--28% decrease in MAP in fluid non-responders and responders patients, respectively. Importantly, among the 16 fluid responders patients, 5 (31%) had a decrease in SV by more than 50%. Our results, in fluid non-responders patients showed a moderate decrease in MAP. In contrast, there was a 39% decrease in SV in the AMR_{CPAP} group which is greater than the 20% reported by Biais *et al*. in 12 fluid non-responders patients.[13] However, the data reported by Biais *et al*. cannot be compared to the present study because of a different study design and goal.

Table 3: Absolute value of hemodynamic parameters according to the time of measurements and groups

	ARM_{PEEP} (n=22)	ARM_{CPAP} (n=14)
Stroke volume (ml)		
Before	64±20	76±22*
During	55±24	47±20
1 min after ARM	64±22	75±28*
3 min after ARM	65±22	69±24
Systolic arterial pressure (mmHg)		
Before	118±20	114±24
During	102±19	97±23
1 min after ARM	114±23	110±28
3 min after ARM	119±21	113±23
Diastolic arterial pressure (mmHg)		
Before	59±11	54±9
During	55±10	50±12
1 min after ARM	59±14	53±11
3 min after ARM	61±14	53±8
Mean arterial pressure (mmHg)		
Before	80±13	75±15
During	70±13	66±18
1 min after ARM	79±17	72±15
3 min after ARM	81±15	74±13
Heart rate (bpm)		
Before	66±14	79±19
During	67±23	77±20
1 min after ARM	69±17	80±18
3 min after ARM	67±16	75±13
Cardiac index ($l.min^{-1}.m^{-2}$)		
Before	3.0±2.3	3.7±1.5
During	2.1±1.0	2.4±1.7
1 min after ARM	2.3±0.9	3.5±2.0
3 min after ARM	2.4±0.9	3.1±1.3
Pulse pressure variation		
Before	9±3	8±4
During	14±6*	12±6*
1 min after ARM	10±5	8±4
3 min after ARM	10±4	8±6
Peak velocity ($cm.s^{-1}$)		
Before	61±13	60±17
During	60±16	54±17
1 min after ARM	61±14	62±20
3 min after ARM	61±14	61±20
Corrected flow time (s)		
Before	281±62	337±74*
During	241±68	229±88
1 min after ARM	282±77	323±87*
3 min after ARM	289±67	301±86

*Differences according to the adjusted P value from Tukey's post hoc multiple comparisons test. *P<0.05 vs. During value within the same group. ARM=Alveolar recruitment maneuver*

The present results suggested that ARM using stepwise increase in PEEP may induce less adverse hemodynamic events than sustained inflation. The decrease in SV was significantly lower in the ARM_{PEEP} group than in the ARM_{CPAP} group. The concomitant increase in PPV and decrease in corrected flow time observed in the present study are in accordance with the known decrease in right and subsequent left ventricle preload that occur during the increase in intrathoracic pressure.[10] In anesthetized elderly patients scheduled for major surgery, two studies suggested that ARM using stepwise increase in PEEP has a good hemodynamic tolerance.[5,8] To the best of our knowledge, only one clinical study compared two methods of ARM in anesthetized patients following coronary artery bypass surgery.[17] However, the authors only reported changes in MAP and central venous pressure and the ARM used did not used stepwise increase in PEEP. Nevertheless, the decrease in MAP and increase in CVP were more pronounced during sustained inflation than during increase in PEEP.[17,20] In experimental models of acute lung injury, Lim *et al*. showed that the hemodynamic effects of ARMs depended both on lung properties, applied level of alveolar pressure, and on the ARM method.[16] In an acute pneumonia lung injury model with preserved respiratory system compliance, the sustained lung inflation (45 cm H_2O for 40 s) induced a significantly greater decrease in cardiac output (-67%) than the stepwise PEEP method (-54%). In contrast, in an acute respiratory distress syndrome model with low respiratory system compliance, the hemodynamic effects of ARM were identical and less pronounced.[16]

Our study presents several limitations primarily related to its observational nature and small sample size. Because of its observational nature, the two ARMs method evaluated were not randomized resulting in unbalanced sample size and heterogeneity of the ASA physical status distribution between groups [Table 1]. Although history of diseases and chronic treatments were comparable, we cannot rule out that the reported hemodynamic effect of ARM might depend also on unknown patient's characteristics. In our center, the two ARMs methods may be used and it can be hypothesized that anesthesiologists may have favor stepwise PEEP ARM in high risk patients because of their own clinical experience. Furthermore, ARM using stepwise increase in PEEP were used more often in our center. Although the sample size is small because it was estimated on the relative SV change, the results reported were in accordance with our initial hypothesis for sample size calculation.

Although we did not measure the respiratory system compliance, patients had no acute or chronic pulmonary disease and we can assume that static compliance was normal or slightly decrease by general anesthesia.[21]

Finally, we do not measure echocardiographic parameters which do not enable us to determine the effects of ARMs on right and left ventricular function. However, echocardiographic examination was not planned during the intraoperative care of these patients. Furthermore, echocardiographic measurements could be difficult to obtain during a 30 s CPAP maneuver.

Definitely, large sample size studies are mandatory to better examine the hemodynamic effects of ARM during general anesthesia and to determine the effect on clinical outcomes including postoperative pulmonary complications.

Conclusion

The results of our pilot study provides additional knowledge on the hemodynamic adverse effects of two methods of alveolar recruitment during general anesthesia in fluid non-responders. The hemodynamic response to ARM might be less pronounced during a stepwise increase and decrease in PEEP than during transient sustained lung inflation. Future randomized studies must be performed to examine the hemodynamic effects of different intraoperative ARMs.

Ethics considerations

The study was approved by the "Comité de Protection des Personnes Caen Nord Ouest III" (reference number: A15-D27-VOL. 25 on june 10, 2015), Chaiperson Mme charlotte Gourio, CHU de Caen, 14033 Caen cedex, France, email: cppnordouest3@orange.fr.

Because there was no randomization and only routine care was performed, waived written informed consent was authorized by the local medical ethics committee. Nevertheless, oral information and consent was obtained from all patients before surgery.

The Clinical trial registration number is NCT03215329.

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Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Hedenstierna G, Edmark L. Mechanisms of atelectasis in the perioperative period. Best Pract Res Clin Anaesthesiol 2010;24:157-69.
2. Rothen HU, Sporre B, Engberg G, Wegenius G, Reber A, Hedenstierna G. Prevention of atelectasis during general anaesthesia. Lancet 1995;345:1387-91.
3. van Kaam AH, Lachmann RA, Herting E, De Jaegere A,

van Iwaarden F, Noorduyn LA, *et al*. Reducing atelectasis attenuates bacterial growth and translocation in experimental pneumonia. Am J Respir Crit Care Med 2004;169:1046-53.
4. Fernandez-Bustamante A, Frendl G, Sprung J, Kor DJ, Subramaniam B, Martinez Ruiz R, *et al*. Postoperative pulmonary complications, early mortality, and hospital stay following noncardiothoracic surgery. A multicenter study by the perioperative research network investigators. JAMA Surg 2016;152:157-66.
5. Weingarten TN, Whalen FX, Warner DO, Gajic O, Schears GJ, Snyder MR, *et al*. Comparison of two ventilatory strategies in elderly patients undergoing major abdominal surgery. Br J Anaesth 2010;104:16-22.
6. Coppola S, Froio S, Chiumello D. Protective lung ventilation during general anesthesia: Is there any evidence. Crit Care 2014;18:210.
7. Severgnini P, Selmo G, Lanza C, Chiesa A, Frigerio A, Bacuzzi A, *et al*. Protective mechanical ventilation during general anesthesia for open abdominal surgery improves postoperative pulmonary function. Anesthesiology 2013;118:1307-21.
8. Tusman G, Böhm SH, Vazquez de Anda GF, Do Campo JL, Lachmann B. 'Alveolar recruitment strategy' improves arterial oxygenation during general anaesthesia. Br J Anaesth 1999;88:8-13.
9. Futier E, Constantin J-M, Paugam-Burtz C, Pascal J, Eurin M, Neuschwander A, *et al*. A trial of intraoperative low-tidal-volume ventilation in abdominal surgery. N Engl J Med 2013;369:428-37.
10. Verhoeff K, Mitchell JR. Cardiopulmonary physiology: Why the heart and lungs are inextricably linked. Adv Physiol Educ 2017;41:348-55.
11. Nielsen J, Nilsson M, Freden F, Hultman J, Alström U, Kjaergaard J, *et al*. Central hemodynamics during lung recruitment maneuvers at hypovolemia, normovolemia and hypervolemia. A study by echocardiography and continuous pulmonary artery flow measurements in lung injured pigs. Intensive Care Med 2006;32:585-94.
12. Nielsen J, Ostergaard M, Kjaergaard J, Tingleff J, Berthelsen PG, Nygard E, *et al*. Lung recruitment maneuver depresses central hemodynamics in patients following cardiac surgery. Intensive Care Med 2005;31:1189-94.
13. Biais M, Lanchon R, Sesay M, Le Gall L, Pereira B, Futier E, *et al*. Changes in stroke volume induced by lung recruitment maneuver predict fluid responsiveness in mechanically ventilated patients in the operating room. Anesthesiology 2016;126:260-7.
14. Network Investigators for the Clinical Trial Network of the European Society of Anaesthesiology, Hemmes SN, Gama de Abreu M, Pelosi P, Schultz MJ. High versus low positive end-expiratory pressure during general anaesthesia for open abdominal surgery (PROVHILO trial): A multicentrerandomised controlled trial. Lancet 2014;384:495-503.
15. Sessler DI, Meyhoff CS, Zimmerman NM, Mao G, Leslie K, Vasquez SM, *et al*. Period-dependent associations between hypotension during and for four days after noncardiac Surgery and a composite of myocardial infarction and death. A substudy of the POISE-2 trial. Anesthesiology 2018;128:317-27.
16. Lim SC, Adams AB, Simonson DA, Dries DJ, Broccard AF, Hotchkiss JR, *et al*. Transient hemodynamic effects of recruitment maneuvers in three experimental models of acute lung injury. Crit Care Med 2004;32:2378-84.
17. Celebi S, Köner Ö, Menda F, Korkut K, Suzer K, Cakar N. The pulmonary and hemodynamic effects of two different recruitment maneuvers after cardiac surgery. Anesth Analg 2007;104:384-90.
18. Di Marco F, Bonacina D, Vassena E, Arisi E, Apostolo A, Banfi C, *et al*. The effects of anesthesia, muscle paralysis, and ventilation on the lung evaluated by lung diffusion for carbon monoxide and pulmonary surfactant protein B. Anesth Analg 2015;120:373-80.
19. Futier E, Maret E, Jaber S. Perioperative positive pressure ventilation. An integrated approach to improve pulmonary care. Anesthesiology 2014;121:400-8.
20. Marini JJ. Recruitment by sustained inflation: Time for a change. Intensive Care Med 2011;37:1572-4.
21. Hedenstierna G, Edmark L. Effects of anesthesia on the respiratory system. Best Pract Res Clin Anaesthesiol 2015;29:273-84.