Compliance and Dead Space Fraction Indicate an Optimal Level of Positive End-Expiratory Pressure After Recruitment in Anesthetized Patients

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BACKGROUND: "Optimal" positive end-expiratory pressure (PEEP) can be defined as the PEEP that prevents recollapse after a recruitment maneuver, avoids over-distension, and, consequently, leads to optimal lung mechanics at minimal dead space ventilation. In this study, we analyzed the effects of PEEP and recruitment on functional residual capacity (FRC), compliance, arterial oxygen partial pressure (Pao_2) and dead space fraction, and we determined the most suitable variables indicating optimal PEEP.

METHODS: We studied 20 anesthetized patients with healthy lungs undergoing faciomaxillary surgery. After a stepwise increase of PEEP/inspiratory pressures (0/10, 5/15, 10/20, 15/25 cm H_2O, each level lasting for 20 min) using a pressure-controlled ventilation mode, a recruitment maneuver (at 20/45 cm H_2O for a maximum of 20 min) was performed, followed by a stepwise pressure reduction (15/25, 10/20, 5/15, 0/10 cm H_2O, with 20 min at each level). At each pressure level, FRC, compliance, Pao_2, and dead space fraction were measured.

RESULTS: When comparing the values before and after recruitment at identical PEEP levels, all variables showed significant changes at 10/20 cm H_2O; compliance was also significantly higher at the pressure step 15/25 cm H_2O. In addition, FRC values showed significant differences at 5/15 cm H_2O and 15/25 cm H_2O.

CONCLUSIONS: All variables showed the positive effects of PEEP in conjunction with a recruitment maneuver. Optimal PEEP was 10 cm H_2O because at this pressure level the highest compliance value in conjunction with the lowest dead space fraction indicated a maximum amount of effectively expanded alveoli. FRC and Pao_2 were insensitive to alveolar over-distension.

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General anesthesia affects ventilation and gas exchange by causing atelectasis.[1–4] Various studies in patients with healthy lungs undergoing general anesthesia have demonstrated that recruitment maneuvers remove atelectasis, improve lung mechanics and gas exchange, and reduce dead space fraction.[5–10] If positive end-expiratory pressure (PEEP) was applied after recruitment, it could prevent recollapse of alveoli.[9,11,12] However, PEEP levels should not be too high, to avoid over-distending the lung. The PEEP, which prevents re-collapse, but avoids over-distension while optimizing lung mechanics at minimal dead space ventilation, can be defined as optimal PEEP. However, the question of which variables reliably determine this optimal PEEP remains unanswered.

We hypothesized that functional residual capacity (FRC), compliance, arterial oxygenation, and dead space fraction should show the positive effects of PEEP after a recruitment maneuver, and compliance and dead space fraction are the two most suitable variables for determining optimal PEEP.

Therefore, the aims of this study were 1) to evaluate the effects of PEEP on FRC, compliance, arterial oxygenation, and dead space fraction before and after a recruitment maneuver in healthy patients undergoing general anesthesia, 2) to decide which of the above variables indicates optimal PEEP, and 3) to determine optimal PEEP for this group of patients.

METHODS

The study was conducted at the University Hospital of Hamburg, Germany, after approval was obtained from the local ethics committee and written informed consent from each patient. Twenty patients were studied: 12 men and 8 women with an age of

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41 ± 16 yr (mean ± SD) and a body mass index of 24 ± 4 kg/m^2. Nine of the patients were smokers. The patients had no relevant cardiopulmonary disease and were classified as ASA I (5) or II (15). They were studied during general anesthesia for elective faciomaxillary surgery. Surgery in the supine position had to have an expected duration of general anesthesia of at least 3.5 h. During these operations, the surgeon did not influence the thorax or position of the diaphragm.

Anesthesia, Ventilation, and Monitoring

After 5 min of administration of pure O_2, general anesthesia was induced as a target-controlled infusion. Remifentanil was started at 0.6 $\mu g \cdot kg^{-1} \cdot min^{-1}$ and propofol was begun with a calculated target plasma drug concentration of 4 μg/mL. Neuromuscular block was achieved by rocuronium 0.6 mg/kg. After tracheal intubation, anesthesia was maintained with a propofol target plasma drug concentration of 3–4 μg/mL and remifentanil 0.2–0.4 $\mu g \cdot kg^{-1} \cdot min^{-1}$. Neuromuscular block was monitored continuously with a nerve stimulator ("Innervator", Fisher & Paykel Healthcare, Auckland, New Zealand). We gave 25% of the initial dose of rocuronium if train-of-four stimulation showed the third response.

Lungs were ventilated with an EVITA 4 (Drägerwerk AG, Lübeck, Germany) in a pressure-controlled ventilation mode (bilevel positive airway pressure) and with an inspired oxygen fraction (FIO_2) of 0.3. Ventilation started with a PEEP of 5 cm H_2O and an inspiratory pressure (IP) of 15 cm H_2O. Respiratory rate was set between 10 and 14 breaths/min, inspiratory time was set at 2.0 s, and expiratory time was maintained between 2.3 and 4.0 s. The respiratory rate was regulated according to arterial carbon dioxide partial pressure ($PaCO_2$), which was kept between 36 and 42 mm Hg.

For an initial period of 30 min after start of surgery, lungs were ventilated using the ventilator settings described above. Before starting PEEP titration, arterial blood gases were measured. Each pressure level was maintained for approximately 20 min, except for the recruitment phase, during which the highest pressures (PEEP/IP = 20/45 cm H_2O) were applied for 20 min or shorter if any of the hemodynamic variables deviated from baseline by more than 15%. Alveolar recruitment and PEEP titration were applied as follows: Pressures were increased stepwise from a PEEP of 0 cm H_2O and an IP of 10 cm H_2O (further reported as PEEP/IP = 0/10 cm H_2O) to 5/15 cm H_2O, 10/20 cm H_2O, and 15/25 cm H_2O. For recruiting collapsed alveoli, a PEEP of 20 cm H_2O combined with an IP of 45 cm H_2O was used. Afterwards, pressures were reduced to a PEEP of 0 cm H_2O and an IP of 10 cm H_2O in a manner that mirrored the previous pressure increase. Figure 1 shows the phases of incremental PEEP, recruitment maneuver, and decremental PEEP. Every patient received 500 mL of Ringer's solution and 500 mL of 6% hydroxyethyl starch 130/0.5 (Voluven®; Fresenius Kabi, Bad Homburg, Germany) during induction of anesthesia. Another 500 mL of Ringer's solution was infused into every patient before the start of the recruitment maneuver.

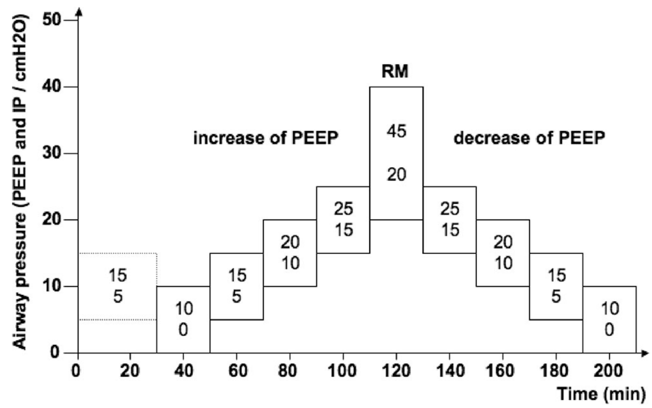

Figure 1. Schematic representation of different protocol phases. Increase of positive end-expiratory pressure (PEEP), recruitment maneuver (RM), and decrease of PEEP (IP = inspiratory pressure).

Heart rate, invasive systolic, diastolic, and mean arterial blood pressure, and peripheral oxygen saturation by pulse oximetry were measured by the Datex Ohmeda S/5 monitor (Datex-Ohmeda Division, Instrumentarium Corp., Helsinki, Finland) during the entire study period. From the readings of the EVITA 4, the variables end-tidal carbon dioxide concentration ($PETCO_2$), PEEP, IP, tidal volume, and minute ventilation were recorded. All patients had a chest radiograph within 6 h after surgery to exclude a pneumothorax or other potential complications.

Measurements

The determination of FRC was performed by a novel FRC measurement procedure called LUFU ("*lu*ng *fu*nction," Drägerwerk AG, Lübeck, Germany). LUFU is based on the quantitative recording of the amounts of oxygen, which are washed in and washed out during corresponding changes of FIO_2.[13,14] The equipment for LUFU consists of a ventilator, a paramagnetic side stream O_2 sensor, and a dedicated personal computer. Values of $PETCO_2$, PEEP, IP, tidal volume, and minute ventilation were transferred in real-time via serial bus to a personal computer, recorded digitally and analyzed off-line. The method can be done with relatively minor additional effort and uses a respirator, which has not been changed. All these factors make LUFU potentially suitable for clinical use. Approximately 10 min was required for one FRC measurement. In our study, oxygen washin was performed by a FIO_2 increase from 0.3 to 0.6 and oxygen washout by a FIO_2 reduction from 0.6 to 0.3 on each pressure step. From the results of these two corresponding measurements, a mean FRC value for each step was calculated automatically.

On every PEEP level, 2 end-inspiratory holds ("inspiration holds") and 2 end-expiratory holds ("expiration holds") were performed (each lasting for at least 5 s). Intrinsic PEEP, i.e., a remaining positive alveolar pressure as a result of dynamic hyperinflation with a FRC exceeding the relaxation volume of the respiratory system,[15] was determined automatically by the EVITA 4. Static compliance of the respiratory system was calculated by dividing the expiratory tidal volume by the pressure difference between end-inspiratory plateau pressure and total end-expiratory pressure.[16] Dynamic compliance was determined automatically by the EVITA 4.

Arterial blood samples were drawn at the end of each protocol step and analyzed for arterial oxygen partial pressure (Pa_{O_2}), Pa_{CO_2}, arterial oxygen saturation (Sa_{O_2}), and the pHa. These values were determined using the blood-gas analyzer ABL 700 (Radiometer, Copenhagen, Denmark). Samples were processed within 5 min.

For analyzing dead space fraction, the average alveolar expired P_{CO_2} ($PAECO_2$) was determined offline by using the mean value of slope III of the capnogram recorded by the EVITA 4. Using a time-based capnogram for determining $PAECO_2$ is a modification of the well-known method, which obtains $PAECO_2$ from a volume-based capnogram.[17–20] Dead space fraction is defined as the ratio of physiological dead space to tidal volume (V_{D/V_T}), and was calculated by Enghoff's modification of Bohr's equation.[21]

$$V_D/V_T = (Pa_{CO2} - PAECO_{CO2}) / Pa_{CO2}$$

Statistical Analysis

All data were analyzed using the statistics program SPSS 11.5 (SPSS Inc., Chicago, IL). Changes of FRC, compliance, Pa_{O_2}, and dead space fraction were evaluated a posteriori by Bonferroni correction of the Wilcoxon test. P values <0.05 were considered significant.

RESULTS

Twenty patients were included in and completed the study. We could not evaluate $PAECO_2$ in two patients because of defective recordings of expired P_{CO_2}. Results of FRC, static compliance of the respiratory system, Pa_{O_2} dead space fraction, and Pa_{CO_2} are listed in Figures 2–4.

Comparing the same pressure level before and after recruitment, FRC values and compliance values were significantly higher on all pressure steps, except for the pressure level PEEP/IP 0/10 cm H_2O. Significant changes of Pa_{O_2} values and dead space fraction after the recruitment maneuver were found only at the corresponding pressure levels of 10/20 cm H_2O.

Static compliance of the respiratory system and the dynamic compliance determined by the EVITA 4 were highly correlated (with $r = 0.98$). Intrinsic PEEP remained below 2 cm H_2O in all patients.

The optimal PEEP was found to be 10 cm H_2O after the recruitment maneuver. At this pressure level, all four variables showed significant changes when compared with the corresponding pressure steps before the intervention.

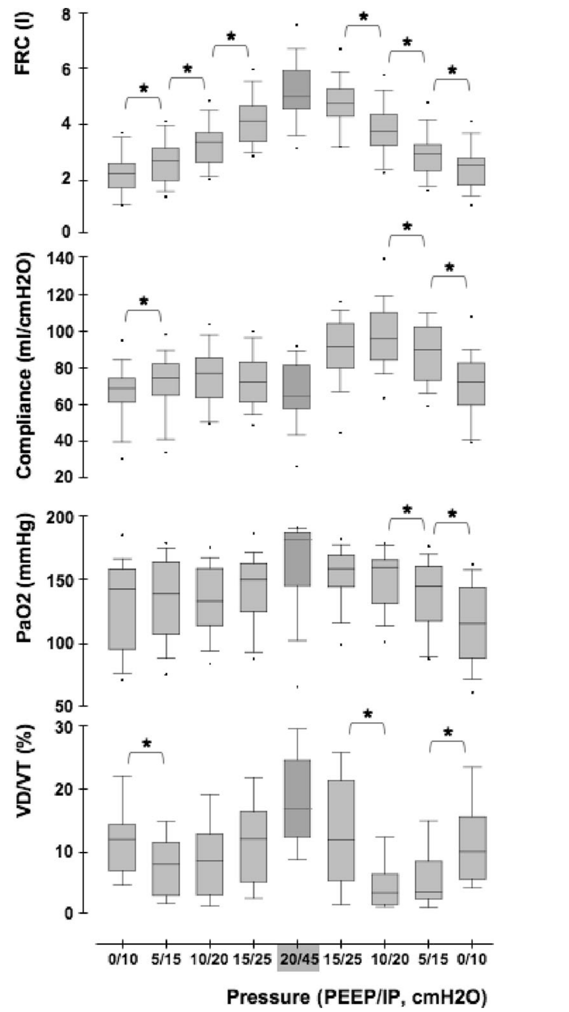

Figure 2. Functional residual capacity (FRC, $n = 20$), static compliance of the respiratory system ($n = 20$), arterial oxygen partial pressure (Pa_{O_2}, $n = 20$), and dead space fraction (V_D/V_T, $n = 18$) values are shown as median (line in the box), 75% and 25% percentiles (upper and lower edge of the box), 90% and 10% percentiles (horizontal line of the "t" and reversed "t," respectively), 95% and 5% percentiles (dot above and below 90% and 10% percentiles) (95% and 5% percentiles are not shown for V_D/V_T). $^*P < 0.05$ was considered significant comparing adjacent positive end-expiratory pressure levels (except for recruitment).

Sa_{O_2}, arterial blood pressure, and heart rate did not differ between test periods. End-tidal CO_2 concentrations were not significantly different, except for a diminution of P_{ETCO_2} during the recruitment maneuver. With respect to the recruitment maneuver, there were no clinically relevant hemodynamic alterations, ventilatory side effects, or any other complications. However, arterial blood pressure decreased by more than 15% from baseline in two patients, leading to early termination of the recruitment procedure after 15 and 11 min, respectively. The maximum tidal volume per kilogram body weight during the recruitment maneuver showed a mean value of 11.4 ± 3.3

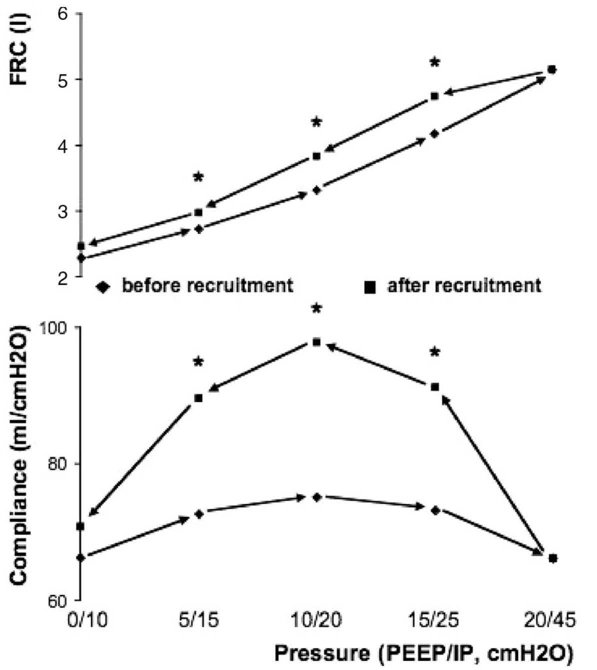

Figure 3. Typical hysteresis curves for variables of lung mechanics: functional residual capacity (FRC) and static compliance of the respiratory system characterized by significant (*$P < 0.05$) differences before and after recruitment at identical positive end-expiratory pressure levels. The graph represents median.

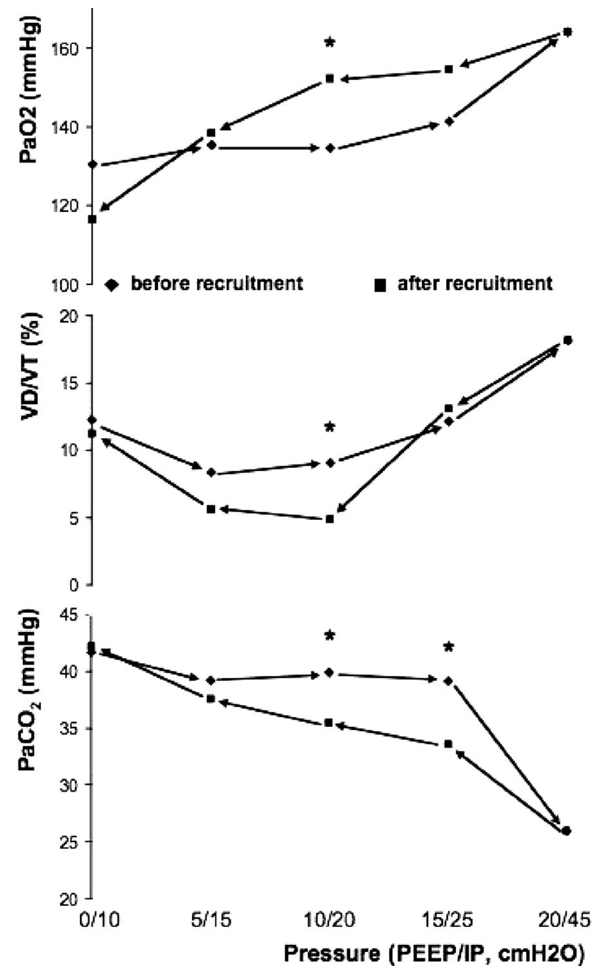

Figure 4. Typical hysteresis curves for variables of efficiency of gas exchange: arterial oxygen partial pressure (Pa_{O_2}), dead space fraction (V_D/V_T), and arterial partial carbon dioxide pressure (Pa_{CO_2}) characterized by significant (*$P <$ 0.05) differences before and after recruitment at identical positive end-expiratory pressure levels. The graph represents median.

mL/kg for all patients and a maximum value of 16.3 mL/kg in one patient. As a result of this hyperventilation, P_{ETCO_2} during the recruitment period temporarily decreased to values between 20 and 32 mm Hg (mean ± SD was 24.3 ± 3.6 mm Hg).

DISCUSSION

The first main finding of our study was that a recruitment maneuver in conjunction with PEEP caused a significant increase in FRC, compliance, and Pa_{O_2} in concert with a significant decrease in dead space fraction when compared with the same levels of PEEP before the maneuver. These findings imply that patients with healthy lungs undergoing general anesthesia during operations without the surgical procedure influencing the lung, thorax, or position of the diaphragm might benefit from a recruitment maneuver in conjunction with a PEEP of 10 cm H_2O.

The second main finding was that compliance and dead space fraction can identify an optimal PEEP level because the highest compliance value in conjunction with the lowest dead space fraction indicates a maximum amount of effectively expanded alveoli. This gain in the efficiency of ventilation implies an increase in the number of functional lung units and not a mere expansion of previously open alveoli, thereby eliminating any significant over-distension. In our study, optimal PEEP after the recruitment maneuver was 10 cm H_2O. Although both Pa_{O_2} and FRC showed a recruitment effect, they could not differentiate between an increase in the number of functional alveolar units and an increase in lung volume due to distension.

Although both compliance and dead space fraction suggested an identical value for optimal PEEP, this result may have been coincidental. Therefore, we prefer using both variables together to determine optimal PEEP until further studies can clarify whether compliance or dead space fraction is superior in determining optimal PEEP. Compliance could be easier to measure in the clinical setting, but may have some limitations. A study by Rothen et al.[22] showed that the changes over time of static compliance and in the amount of atelectasis estimated by computed tomography (CT) were not in parallel. On the other hand, data from a recent animal study support the use of compliance as a marker of optimal PEEP. The point of maximum compliance indicated the PEEP level at which lung collapse started to occur, as confirmed by the appearance of atelectasis on the CT scan.[23] Although dead space fraction might be more difficult to analyze, it provides information about the matching of ventilation and perfusion and is, therefore, particularly suited for establishing an optimal PEEP that is linked to an efficient gas exchange.[24,25]

The positive effects of recruitment on static compliance of the respiratory system are obvious (Figs. 2 and 3). The distinct differences seen in compliance at identical pressure levels before and after recruitment support the idea of a gain in the number of open alveoli by the recruitment maneuver itself. The marked decrease in compliance at high pressures can be explained by a distension of open alveoli. Because static compliance of the respiratory system and the dynamic compliance automatically determined by the EVITA 4 were very comparable and showed similar behavior over the course of the entire protocol, the latter can easily be used in clinical routine requiring no intervention by the user.[23]

Dead space fraction expressed as the relation of physiological V_D/V_T represents over-distension of alveoli. Therefore, a gain in ventilated alveoli due to a recruitment maneuver should decrease dead space fraction, and its minimum value should correspond to optimal PEEP.[25] According to Breen et al.,[21] it is important to calculate dead spaces using $PAECO_2$ instead of P_{ETCO_2} to obtain correct dead space fraction values. A well-known method for calculating the dead space is $V_{D/V_T} = (P_{ACO_2} - PAECO_2)/Pa_{CO_2}$, in which the values for $PAECO_2$ were obtained from a volumetric capnogram.[16–19] We used a slight modification of the original method, in which $PAECO_2$ was obtained by plotting exhaled P_{CO_2} against time. Comparison of the time-based and the volume-based capnograms shows no major difference in the $PAECO_2$ values, since both reflect the mean value of the alveolar part of the CO_2 curve. Even if there were small differences between these methods, they would not have influenced our results, since we compared different ventilatory conditions within each patient while using identical apparatuses and methods. Determining the effects of PEEP after recruitment by using dead space fraction values is somewhat cumbersome because arterial blood samples and $PAECO_2$ values from the recorded capnogram are required. In an attempt to simplify dead space determination, other noninvasive indicators of dead space should be evaluated for their usefulness in determining optimal PEEP.[25]

For detecting FRC, we used a new device which was validated recently *in vitro* and *in vivo*.[14,26] The FRC results of this study revealed a plausible physiologic picture of the effects of PEEP and PEEP in conjunction with a recruitment maneuver. At identical pressure levels, a larger FRC can be found after the recruitment when compared with the corresponding value before it (Figs. 2 and 3). However, FRC seems to be insensitive for detecting lung over-distension. A gain in absolute lung volume (FRC) after the recruitment, when compared with the same PEEP before it, cannot result from a pure distension of aerated alveoli or airways but must be the result of an increase in the number of functional alveolar units. Thus, this is proof for the intended "opening effect" of an alveolar recruitment.

Determination of the effects of PEEP after recruitment is often done by analyzing Pa_{O_2}, assuming that the extent of lung collapse can be derived from arterial oxygenation. According to different authors, a Pa_{O_2} of more than 400 or 450 mm Hg at pure oxygen breathing is characteristic for a nonatelectatic lung.[11,27,28] Arterial oxygenation, however, is nonspecific for judging recruitment effect, since Pa_{O_2} depends on the hemodynamic and metabolic state as well. Moreover, Pa_{O_2} determination is insensitive to the over-distension of alveoli. Even in grossly over-distended lungs, verified by reduced compliance and increased dead space fraction, Pa_{O_2} increases until capillary and vascular compression occurs. This fact was also confirmed in our study. As can be seen in Figure 2, the highest Pa_{O_2} was reached at recruitment pressures of 20/45 cm H_2O. It can be argued that even at these relatively high airway pressures, either no relevant compression of lung vessels or a parallel decline in both ventilation and perfusion in over-distended lung regions was present. Another disadvantage of using Pa_{O_2} to determine the effects of PEEP after recruitment is the trouble and expense of drawing and analyzing a series of arterial blood samples in a timely manner.

The deterioration of gas exchange as a result of lung collapse is caused mainly by the following pathomechanisms: first, intrapulmonary shunting, and second, a reduced lung volume with a concomitant diminution of compliance.[2–4,29–31]

Studies have shown that atelectatic lung areas can be opened actively by increased end-IPs and then kept open by sufficient PEEP.[5,9,32] One method to overcome atelectasis during general anesthesia is the "Alveolar Recruitment Strategy " introduced by Tusman et al.,[10,20,33] in which PEEP is increased from 0 to 20 cm H_2O whereas IPs of around 40 cm H_2O are used to actively recruit the lungs. In our study, this procedure was once again slightly modified by choosing an IP of 45 cm H_2O for the recruitment maneuver to reach a complete recruitment in all patients.[7]

The effects of a recruitment maneuver on Pa_{O_2},[7,9] on compliance,[9,22,23,34] on the relation of ventilation to perfusion,[22] on dead space fraction[10,20,25] and on FRC[7,22] have been investigated in various studies. However, in the context of recruitment and PEEP, FRC has only been assessed by indirect CT methods, not direct measurements.[2,35]

There are limitations to our study. When searching for the optimal PEEP for an individual patient we suggest performing a titration. In our study, however, this titration was done in PEEP steps of 5 cm H_2O because of overall operating time restrictions in relation to the time needed for performing each FRC measurement. Therefore, our results suffer from a poor resolution for detecting the truly optimal PEEP.

In future studies, PEEP and IP should be decreased in smaller steps (i.e., 2 cm H_2O) for a more exact identification of optimal PEEP.

In this investigation, study periods were long because we determined both FRC in duplicate and blood gas values at the end of each protocol step. To merely recruit collapsed lung tissue, it would have been sufficient to perform a short recruitment maneuver lasting only for a few breaths and a quicker PEEP titration, thereby minimizing the side effects of the recruitment maneuver and PEEP in the clinical setting.

In our study, we did not provide outcome data but physiological surrogates for a better patient condition. There is some evidence that adverse effects of atelectasis persist in the postoperative period and can affect patient recovery.[29] Since use of recruitment maneuvers in conjunction with sufficient PEEP can overcome atelectasis, it seems to be consequential that lung recruitment might also improve outcome. However, to date it has only been demonstrated that lung recruitment improves physiologic variables such as oxygenation and work of breathing,[29] and it remains to be shown the extent to which lung recruitment may affect hospital stay and other variables of outcome.[36] Further limitations of this study are the lack of data on oxygen transport, the simplified method for determining dead space fraction, and the small number of patients studied.

In conclusion, significant increases in FRC, compliance, and Pao_2 and a significant reduction of the dead space fraction could be induced by recruitment in conjunction with sufficient PEEP in patients with healthy lungs. PEEP applied without recruitment did not show the same effects. Compliance and dead space fraction were indicators for efficient ventilation at an optimal PEEP. Although both FRC and Pao_2 changed with recruitment and PEEP, these variables proved insensitive to alveolar distension.

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