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Respiration and the Airway

Effect of positive end-expiratory pressure on pulmonary shunt and dynamic compliance during abdominal surgery

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Abstract

Background: General anaesthesia decreases pulmonary compliance and increases pulmonary shunt due to the development of atelectasis. The presence of capnoperitoneum during laparoscopic surgery may further decrease functional residual capacity, promoting an increased amount of atelectasis compared with laparotomy. The aim of this study was to evaluate the effects of different levels of positive end-expiratory pressure (PEEP) in both types of surgery and to investigate whether higher levels of PEEP should be used during laparoscopic surgery.
Methods: This prospective observational study included 52 patients undergoing either laparotomy or laparoscopic surgery. Three levels of PEEP were applied in random order: (1) zero (ZEEP), (2) 5 cmH_2O and (3) 10 cmH_2O. Pulmonary shunt and ventilation/perfusion mismatch were assessed by the automatic lung parameter estimator system.
Results: Pulmonary shunt was similar in both groups. However, in laparotomy, a PEEP of 5 cmH_2O significantly decreased shunt when compared with ZEEP (12 *vs* 6%; P=0.001), with additional PEEP having no further effect. In laparoscopic surgery, a significant reduction in shunt (13 *vs* 6%; P=0.001) was obtained only at a PEEP of 10 cmH_2O. Although laparoscopic surgery was associated with a lower pulmonary compliance, increasing levels of PEEP were able to ameliorate it in both groups.
Conclusion: Both surgeries have similar negative effects on pulmonary shunt, while the presence of capnoperitoneum reduced only the pulmonary compliance. It appears that a more aggressive PEEP level is required to reduce shunt and to maximize compliance in case of laparoscopic surgery.

Key words: end-expiratory pressure, positive; laparoscopic surgery; laparotomy; pulmonary compliance; shunt

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Editor's Key Points

- Atelectasis during laparoscopic surgery may be attenuated by positive end-expiratory pressure (PEEP) but the optimum PEEP is uncertain.
- Using an automated system, this study assessed the effects of different PEEP values on calculated shunt and other respiratory variables.
- Major laparotomy and laparoscopy had similar effects in pulmonary shunt and compliance.
- Shunt during laparoscopy was more resistant to increasing PEEP compared with patients undergoing laparotomy.
- However, the absolute differences were small and more data are required.

General anaesthesia causes impairment in pulmonary gas exchange and respiratory mechanics, even in patients with healthy lungs.[1] Such effects primarily result from the development of atelectasis[2] with subsequent shunting of pulmonary blood flow and impairment of gas exchange.[3] Atelectasis has been described both during laparotomy and laparoscopic surgery.[4] The latter is becoming increasingly prevalent, being associated with a lower incidence of respiratory complication,[5] a reduction in inflammatory and metabolic responses,[5] and a reduction in postoperative pain and analgesic consumption.[5–7] However, laparoscopic surgery is not without potential complications, having been associated with increased intra-abdominal pressure (IAP) due to the presence of capnoperitoneum, which causes further cranial shift of the diaphragm, favouring lung collapse, and decreasing both chest wall compliance and functional residual capacity (FRC).[4] Andersson and colleagues demonstrated that capnoperitoneum results in an increased amount of atelectasis (66%) and a 16% reduction in FRC.[8] The decrease in FRC can lead to ventilation at low lung volume, which in turn can lead to peripheral airway collapse, when the airways closing volume exceeds the end-expiratory lung volume (EELV).[8–10] Positive end-expiratory pressure (PEEP) can counterbalance the decrease in EELV, thereby preventing atelectasis during the intraoperative period,[11–13] improving pulmonary mechanics and decreasing pulmonary shunt.[1] The physiological effects of PEEP may lead the clinician to question whether an increased PEEP level might be beneficial during laparoscopic surgery, providing compensatory alveolar pressure against the collapsing alveolar pressure. To address this question, this study investigated the effects of PEEP on pulmonary mechanics and gas exchange during both laparotomy and laparoscopic surgery. Therefore, the primary endpoint of the present study was to investigate whether different levels of PEEP should be used during major abdominal laparoscopic surgery or laparotomy in order to optimise intraoperative pulmonary shunt, as assessed by the automatic lung parameter estimator (ALPE) system. The secondary endpoints were the variations of both respiratory system compliance ($C_{dyn,rs}$) and low V/Q at different levels of PEEP.

Methods

After obtaining approval from the ethics committee of our institution (Arcispedale Sant′Anna, Ferrara, Italy), informed consents were obtained from each patient. The study was performed in consecutive patients undergoing elective abdominal surgery from June 2014 to January 2015. We enrolled patients >18 yr of age, with an American Society of Anesthesiologists Physical Status Classification score of 1–3, scheduled for either laparoscopic surgery or laparotomy.

Patients with haemodynamic instability, severe chronic respiratory failure, non-elective surgery, or preoperative anaemia (haemoglobin <10 g 100 ml^{-1}) were excluded from the study.

All patients were breathing a fraction of inspired oxygen (F_{IO_2}) of 1.0 during the induction of general anaesthesia. The latter was induced with propofol (1.5–2 mg kg^{-1}) and fentanyl (3 μg kg^{-1}). Muscle paralysis was obtained with rocuronium (0.6 mg kg^{-1}) to facilitate tracheal intubation. Patients were intubated via an endotracheal low-pressure cuffed tube with an internal diameter ranging between 7.5 and 8.0 mm (Rushelit Rush AG Lab, Waiblingen, Germany). Anaesthesia was maintained with an infusion of propofol (150–200 μg kg^{-1} min^{-1}), remifentanil (0.1–0.2 μg kg^{-1} min^{-1}), and cisatracurium (1.5 μg kg^{-1} min^{-1}). The lungs were ventilated through a Dräger Primus ventilator (Drägerwerk AG & Co. KGaA, Lübeck, Germany) with a square flow waveform with a tidal volume (TV) of 6–8 ml kg^{-1} ideal body weight, inspiratory time of 33%, and an inspiratory pause of 20%. The respiratory rate was varied to ensure eucapnia [end-tidal carbon dioxide partial pressure ($EtCO_2$) 3.9–5.3 kPa]. Patients were ventilated using oxygen and air with an F_{IO_2} set at ≥40%, to maintain the peripheral oxygen saturation (SpO_2) at ≥95%. At the start of the study, PEEP was set to zero. Patients were given 8 ml kg^{-1} of Ringer's lactate intravenously before the induction of anaesthesia and were then maintained with 5 ml kg^{-1} h^{-1} Ringer's lactate. During laparoscopic procedures, capnoperitoneum was established with CO_2 insufflation and the intra-abdominal pressure was maintained automatically at 12–13 mmHg.

Patients were monitored by ECG, pulse oximetry, $EtCO_2$, and invasive arterial pressure using a Datex Ohmeda S/5 monitor (Datex-Ohmeda Division, Instrumentarium Corp., Helsinki, Finland). The radial artery was cannulated before induction of anaesthesia, in line with the standard practice of our institution, for invasive blood pressure and blood gas monitoring. Analysis of arterial blood gases was performed within 3 min from sampling using an ABL 330 blood gas analyser (Radiometer, Copenhagen, Denmark). The depth of anaesthesia was monitored through bispectral index monitoring (Aspect A-2000; Aspect Medical System, Newton, MA, USA).

Study protocol

To analyse the effects of PEEP, patients in each group were subjected to different values of PEEP: (1) 0 cmH_2O (ZEEP), (2) 5 cmH_2O, and (3) 10 cmH_2O. About 15 min after incision (for laparotomy) or capnoperitoneum (for laparoscopy), if the patients were haemodynamically stable, that is, mean blood pressure ≥80 mmHg and heart rate ≥60 beats min^{-1}, the protocol started.

Although patients were not randomized to laparoscopic surgery or laparotomy, the level of PEEP applied was randomized by using a computer-generated number. After the onset of the protocol study at PEEP 0 cmH_2O, each patient was ventilated with PEEP levels of 0, 5, or 10 cmH_2O in random order. Once haemodynamic stability was achieved, the level of PEEP was maintained for a period of 15 min. A 15 min period was chosen to allow the effects of PEEP to reach equilibrium. Apart from the variations in PEEP described here, basal ventilator settings were maintained for each patient throughout the experiment.

At each PEEP level, and following the 15 min period, pulmonary shunt and V/Q mismatch were assessed by the ALPE system (ALPE Integrated, Mermaid Care A/S, Nr. Sundby, Denmark). The ALPE system includes pulse oximetry, capnography, and indirect calorimetry and mathematical models, which describe the patient's V/Q matching. ALPE measures SpO_2, oxygen consumption (VO_2), respiratory frequency and tidal volume, and inspiratory and expiratory partial pressure of oxygen. These measurements are taken automatically by inserting a sampling tube in the respiratory circuit for measurement of flow, oxygen and CO_2 and by placing the pulse oximeter on a finger. The dead space of the ALPE system sampling tube is 6.9 ml. In order to calibrate the oxygen dissociation curve included in the mathematical models, a blood gas sample was taken and blood gas values were input to the ALPE.

To estimate the degree of pulmonary shunt and low V/Q, ALPE requires measures of respiratory gas, volume and SpO_2 at three to four levels of F_{IO_2}. These values are used by the ALPE to automatically calculate pulmonary shunt and oxygen loss (O_2 loss), the latter being descriptive of low V/Q mismatch. The principle behind this technique is that, in the case of pulmonary shunt, SpO_2 values change little on varying F_{IO_2}. This is in contrast to regions of the lung with low V/Q where the SpO_2 of blood passing through these regions changes greatly with F_{IO_2}. Changes in F_{IO_2} therefore provide an appropriate signal to distinguish between pulmonary shunt and low V/Q mismatch. Low V/Q mismatch (O_2 loss) is represented as the difference in oxygen partial pressure between end-expired gas and blood leaving lung capillaries prior to mixing with shunted venous blood.[14] An O_2 loss of 10 kPa can be interpreted as a need for an increase in F_{IO_2} of ~10% so as to normalize SpO_2 in the non-shunted blood flow.

The mathematical models used by the ALPE system to estimate pulmonary shunt and low V/Q mismatch are based on continuous ventilation and perfusion and mass conservation. The ALPE technique of using oxygen as a tracer gas assumes there is a steady state and that variation in F_{IO_2} does not affect lung physiology. The ALPE technique and the validity of its assumptions have been described in detail previously,[14 15] and studies have been performed evaluating and applying ALPE. These include evaluation against the reference technique, the Multiple Inert Gas Elimination Technique,[16–18] investigation in postoperative patients, and investigation in intensive care patients.[19–22]

Data analysis

Age, sex, American Society of Anesthesiologists classification, height, weight, and body mass index were recorded for all patients. Physiological variables were recorded continuously throughout the study, including haemodynamics (heart rate, mean blood pressure), gas exchange and ventilation (total volume, respiratory rate and minute volume ventilation). The magnitude of airway pressure measured at the point of zero flow (P_1) at the end of inspiration was obtained directly from the ventilator. Total respiratory dynamic compliance ($C_{dyn,rs}$) was calculated with the following equation: $C_{dyn,rs}$=TV/(P_1−PEEP).

Statistical analysis

Power analysis was performed with G*Power 3.1. We assumed that changes in intrapulmonary shunt with PEEP and the difference between induction or no induction of capnoperitoneum would reflect previous studies.[23 24] Power analysis was performed expecting a standard deviation in shunt of 4%, as observed previously,[21 23] and a moderate correlation (0.7) among repeated measures within subjects. A total of 50 patients were required for repeated measures analysis of variance (ANOVA) to detect an interaction between surgery type and PEEP of at least 1.5% additional change in shunt per step in PEEP in one surgery type compared with the other, with a power of 0.8 and significance level of 0.05.

Data are reported as mean and standard deviation (SD) or median and interquartile range for continuous variables and as absolute or relative frequencies (%) for categorical variables. Normal distribution of data was tested by the Shapiro–Wilk Normality Test.

Unpaired Student's *t*-tests or Mann–Whitney *U*-tests for data with normal or not normal distribution, respectively, were used to compare continuous variables in the laparoscopic and laparotomy groups as appropriate.

Differences between measurements at different PEEP levels were analysed using repeated measures ANOVA or Friedman's rank analysis for data with normal or not normal distribution, respectively. When multiple comparison were made, *P*-values were adjusted by the Bonferroni post hoc procedure. Two-way repeated measures ANOVA was employed to test for group effects evaluating the effects of PEEP levels, surgery type, and their interaction. Furthermore, the influence of the order of PEEP levels was assessed by a two-way ANOVA taking into account PEEP level and order.

A multiple linear regression model was used to examine the effect of independent ventilatory variables ($C_{dyn,rs}$ and PEEP) and physical characteristics (age and BMI) on shunt reduction.

In all statistical analyses, a two-tailed test was performed and a *P*-value ≤0.05 was considered statistically significant.

Statistical analysis was performed with using SPSS Statistics for Windows, Version 20.0 (IBM, Armonk, NY, USA).

Results

Among the 84 screened patients, 52 were finally recruited (Fig. 1). The clinical characteristics of the enrolled patients are shown in Table 1, while ventilation settings and main physiological parameters are shown in Table 2.

For all patients, pulmonary shunt was significantly decreased (P<0.001) and dynamic compliance was significantly increased (P<0.001) on increasing values of PEEP. A significant difference in values of $C_{dyn,rs}$ between surgery types was seen at all PEEP levels. Patients undergoing laparotomy showed statistically higher $C_{dyn,rs}$ compared with those undergoing laparoscopic surgery at ZEEP and at PEEPs of 5 and 10 cmH_2O. For both laparoscopic surgery and laparotomy, $C_{dyn,rs}$ increased significantly with each increase in PEEP (P<0.05; Table 2).

Although no statistical significance was found for differences between surgical groups in relation to values of shunt (P=0.40), differences could be seen if changes in shunt with PEEP were analysed for each surgical group. During laparotomy, pulmonary shunt statistically decreased when a PEEP value of 5 cmH_2O was used compared with ZEEP (12 *vs* 7%; P=0.001) (Table 2). An additional increase in the PEEP value from 5 cmH_2O to 10 cmH_2O did not result in further, statistically significant reduction in pulmonary shunt. No significant changes were observed in the low V/Q ratio (i.e. O_2 loss) between PEEP levels.

During laparoscopic surgery, shunt showed a slight, but not significant, decrease when a PEEP of 5 cmH_2O was used compared with ZEEP (13 *vs* 10%; P=0.14). The reduction of pulmonary shunt became significant when a PEEP of 10 cmH_2O was used (10 *vs* 6%; P<0.05) Table 2). No statistically relevant variations were observed for lung areas with low V/Q (O_2 loss). A decrease of shunt was associated with increased oxygenation in both groups (Table 2). For all results, the two-way ANOVA for repeated measures showed no carryover effect with the order of PEEP changes (P=0.65). Considering a multiple linear regression model that takes into account compliance, age, BMI, and level of PEEP, the

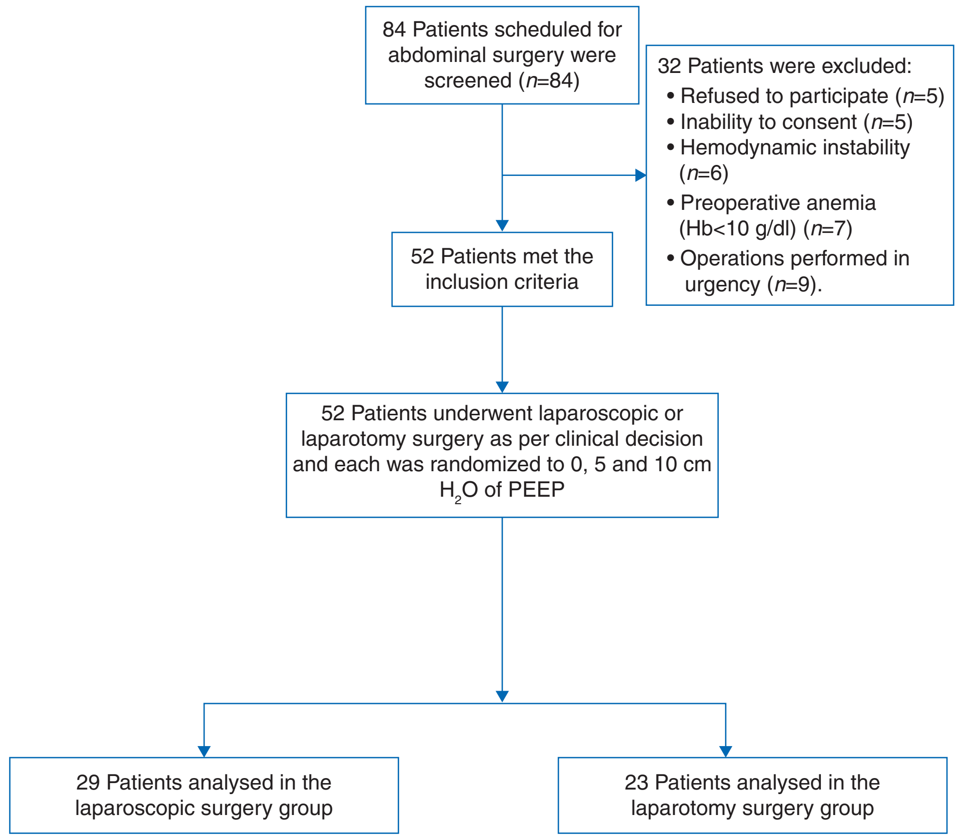

Fig 1 Study flowchart.

Table 1 Perioperative characteristics of patients undergoing laparoscopic or laparotomy abdominal surgery. Normally distributed variables are reported as mean (SD) and non-normally distributed variables as median (interquartile range). BMI, body mass index; ASA, American Society of Anesthesiologists; Hb, haemoglobin

	Laparotomy (*n*=23)	**Laparoscopic (*n*=29)**
Age (yr)	69 (63–75)	71 (56–78)
Height (cm)	168 (7)	172 (9)
BMI (kg m^{-2})	25 (19–34)	25 (19–43)
Male, *n* (%)	15 (65)	17 (59)
ASA physical status I/II/III, *n*	1/10/12	1/16/12
Current smokers, *n* (%)	3 (13)	6 (20)
Pack per years, *n* (%)	26 (12)	28 (10)
Preoperative Hb (g dl^{-1})	13 (2.2)	13 (1.5)
Preoperative creatinine (mg dl^{-1})	0.92 (0.1)	0.94 (0.4)
Surgical procedures, *n*		
Lower intestinal resection	18	21
Cholecystectomy	1	5
Pancreaticoduodenectomy	2	—
Splenectomy	2	3
Duration of anaesthesia (min)	252 (78)	211 (80)
Intraoperative urine output (ml)	200 (100–375)	200 (100–400)

only variable associated with the variation of shunt was the level of PEEP. Although ANOVA showed that PEEP reduced pulmonary shunt (P<0.001), the latter was not influenced by the type of surgery (P=0.40). There was no significant interaction between PEEP and surgery type, indicating that the pulmonary shunt reduction was consistent only with PEEP level.

Table 2 Comparison between laparoscopy and laparotomy patients at different levels of PEEP. Values are presented as mean (SD) or median (interquartile range). ‡: comparison between laparoscopy and laparotomy group at each level of PEEP (unpaired Student's t-tests or Mann–Whitney U-test; $P<0.05$); †: comparison between PEEP 0 and PEEP 5; #: comparison between PEEP 5 and PEEP 10; *: comparison between PEEP 0 and PEEP 10 in the same group (repeated measure ANOVA with multiple pairwise comparisons and Bonferroni correction or Friedman's rank analysis; $P<0.05$). PEEP, positive end-expiratory pressure; $C_{dyn,rs}$, total respiratory system dynamic compliance; TV, tidal volume; RR, respiratory rate; Pa_{O2}, arterial partial pressure of oxygen; Pa_{CO2}, arterial partial pressure of carbon dioxide; FI_{O_2}, fraction of inspired oxygen

	PEEP 5		PEEP 0		PEEP 10	
	Laparoscopy	Laparotomy	Laparoscopy	Laparotomy	Laparoscopy	Laparotomy
$C_{dyn,rs}$ (ml cm^{-1} H_2O)	27 (7)‡,†,*	35 (9)†,*	31 (8)$^{‡,\#}$	39 (11)$^{\#}$	35 (9)‡	42 (13)
Shunt (%)	13 (7)*	12 (7)†,*	10 (6)	7 (5)	6 (7)	6 (4)
O_2 loss (kPa)	2.3 (0.9–3.9)	2.6 (0.6–4.0)	4.5 (0.3–6.2)	2.8 (1.3–4.7)	3.9 (1.5–6.4)	3.0 (1.7–5.4)
TV (ml kg^{-1})	7.0 (1.4)	6.7 (0.7)	6.9 (1.3)	6.7 (0.9)	6.9 (1.4)	6.5 (0.8)
RR (cycles min^{1})	13 (1.5)	13 (1.2)	14 (2.0)	13 (1.3)	14 (1.8)	13 (1.0)
Arterial pH	7.39 (0.03)	7.38 (0.05)	7.38 (0.02)	7.39 (0.02)	7.39 (0.03)	7.37 (0.01)
Pa_{O_2}, (kPa)	18 (5)†	16 (4)†,*	17 (4)$^{\#}$	17 (4)	19 (4)	17 (3)
Pa_{CO_2}, (kPa)	5.6 (0.6)†,*	5.6 (0.9)†,*	5.7 (0.4)$^{‡,\#}$	5.2 (0.5)	5.9 (0.3)‡	5.2 (0.5)
Pa_{O_2}/FI_{O_2} ratio (kPa)	45 (32–55)*	32 (24–48)†,*	46 (32–56)$^{\#}$	37 (31–49)	49 (33–62)	37 (31–49)

Discussion

The main finding of the present study is that setting PEEP is important during laparotomy and laparoscopic surgery. Increased PEEP levels statistically improved both pulmonary shunt and dynamic compliance regardless of surgical type. The results are perhaps less conclusive as to whether an increased PEEP is required to compensate for the effects of capnoperitoneum. Values of shunt were not statistically different between groups, suggesting that capnoperitoneum appears not to cause very much shunt, despite the fact that values of dynamic compliance were different in the two surgical groups. This is probably due to the use of CO_2 for capnoperitoneum. Recently Strang and colleagues[25] demonstrated in pigs that the reabsorption of CO_2 is able to ameliorate V/Q mismatch by decreasing perfusion. The authors explained their results by the attractive hypothesis that CO can potentiate hypoxic vasoconstriction, in this way decreasing the shunt fraction.[25] In our study, however, increasing PEEP improved dynamic compliance in both groups but appeared to have different effects in relation to shunt. While a PEEP of 5 cmH_2O was able to produce a significant reduction in shunt in patients undergoing laparotomy, a PEEP of 10 cmH_2O seemed necessary to achieve the same result during laparoscopy. It may therefore be the case that for patients with pulmonary shunt, a more aggressive PEEP strategy is required in laparoscopic surgery. The prevalent hypothesis for changes in pulmonary mechanics and gas exchange after induction of anaesthesia is the development of atelectasis due to low lung volume ventilation and reabsorption of oxygen when used at high inspiratory fractions.[26] Indeed, the magnitude of pulmonary shunt has been shown to correlate with the degree of atelectasis.[27] It has been shown previously that pulmonary shunt increases during anaesthesia and muscle paralysis.[28–30] A mean shunt of ~8% (range 0–23%)[29] has been demonstrated in young patients, with more severe impairment of lung function seen in older patients resulting in higher values [~15% (range 0–30%)].[1] In addition, there are some data suggesting lower values of shunt with intravenous anaesthesia, possibly because of more moderate reductions in FRC[31] or a more preserved hypoxic pulmonary vasoconstriction.[32]

Anaesthetists can counterbalance the development of atelectasis and the negative effect of low lung volume ventilation by using PEEP.[12 13 33] However, the correct value of PEEP during anaesthesia remains a matter of debate, perhaps due to the differences in preoperative clinical characteristics of patients or different surgical procedures performed. Laparoscopic surgery is associated with capnoperitoneum that can cause a cranial shift of the diaphragm by 1–3 cm and a decrease of lung volume[10] that results in a greater reduction of FRC when compared with laparotomy. This can result in the closing volume (CV) becoming greater than the EELV, promoting closure of the small airways, increasing atelectasis, and therefore requiring higher values of PEEP to compensate for these mechanisms.[34] To understand whether an increased PEEP would be beneficial during laparoscopic surgery, providing compensatory alveolar pressure against the collapsing alveolar pressure, we applied different levels of PEEP in patients undergoing laparotomy and laparoscopic surgery. The level of PEEP necessary to achieve similar levels of pulmonary compliance, and possibly to maximise the reduction of shunt, was different between the two groups, being higher in the laparoscopic group. Presently we do not have an explanation. However, we can hypothesize that this higher level of PEEP is needed to keep open the small airways when CV is greater than EELV. Only by stabilizing the small airways is it possible to reduce atelectasis, achieve higher compliance and ameliorate shunt.

Furthermore, as pointed out by other authors in patients with acute respiratory distress syndrome (ARDS), a role should be played by the superimposed pressure (i.e. the hydrostatic pressure at the dependent portion of the lung resulting from the weight of the tissue above, which is the main reason for lung collapse).[35] It can be hypothesized that a PEEP of 5 cmH_2O during laparoscopic surgery is not high enough to act against a superimposed pressure, a result achieved by a PEEP 10 cmH_2O. This level of PEEP should also be able to counterbalance part of the intra-abdominal pressure (IAP) created by capnoperitoneum and its negative effects on respiratory mechanics and gas exchange. It has been previously proposed to use a value of PEEP ranging between half of the IAP and the IAP, particularly in the presence of injured lungs.[36 37] Hence a PEEP of 10 cmH_2O might act as a positive pressure that is able to counterbalance the effects of IAP on respiratory mechanics, as previously pointed out by Kundra and colleagues.[38]

Finally, a role can be played by the higher alveolar pressure obtained when a given tidal volume is delivered in the presence of high PEEP, allowing better recruitment of collapsed lung regions. The application of 10 cmH_2O of PEEP has been shown to reopen collapsed lung tissue.[12 34] Loeckinger and colleagues[39] demonstrated that a PEEP of 15 cmH_2O resulted in significantly less blood flow to lung areas with shunt and significantly more blood flow to lung areas with normal V/Q. We cannot confirm these data since we avoided such high values of PEEP because of concern for possible haemodynamic side effects. Moreover, the study of Loeckinger and colleagues was done in pigs, and hence these results might not easily be applied to humans. It is true, for example, that pigs should have stronger hypoxic pulmonary vasoconstriction than humans. Moreover, the pig's abdomen, which relative to its thorax is larger than in humans, is possibly more distensible, suggesting that chest wall compliance is different.

This study has some important limitations. Our results are applicable in patients in which the induction of anaesthesia has been made with a high $F_{I_{O_2}}$. Indeed, avoidance of the preoxygenation procedure eliminates atelectasis formation during the induction and subsequent anaesthesia.[4] It can then be hypothesized that induction with an $F_{I_{O_2}}$ <60% would have created less atelectasis and hence more moderate changes in mechanics and gas exchange, rendering the effects of PEEP less predictable. Further, a slight Trendelenburg position was used during laparoscopy. Although it has been previously demonstrated that changing position from supine to Trendelenburg or reverse Trendelenburg does not significantly affect the compliance of the respiratory system in either normal weight or obese patients,[40] our results were different when using a more pronounced Trendelenburg position.

Another limitation is the lack of randomization of the surgical procedures, as we were able to randomize only the PEEP level. Finally, one can hypothesize that factors modifying shunt fraction measurements can represent a limitation for the present study. However, many of the variables one might consider as modifying the estimation of shunt are taken into account by the ALPE system. The models are adjusted to account for acid–base status and haemoglobin concentration. Oxygen consumption is measured, as is arterial oxygen concentration, meaning that the only assumed value in the calculation of mixed venous oxygen concentration is the cardiac output. Indeed, cardiac output is the only factor that has been estimated and which may have a direct effect on the estimate of shunt. A sensitivity analysis was performed previously looking at how a large error in the measurement of cardiac output of ±2 litre min^{-1} would affect the ALPE estimate of shunt. It was found that shunt varies by ~2% $litre^{-1}$ min^{-1} of error in the cardiac output estimate.[28] Hence the effect of cardiac output estimation is irrelevant for pulmonary shunt determination.

In conclusion, we demonstrated that although laparoscopy is associated with acceptable respiratory gas exchange, setting PEEP is important during both laparoscopic surgery and laparotomy, with PEEP having a significant effect on pulmonary shunt and dynamic compliance. Despite similar levels of shunt at ZEEP, it appears that a more aggressive PEEP level is required to reduce shunt and to normalize respiratory compliance in the case of laparoscopic surgery.

Authors' contribution

All authors are responsible for the work described in this article.
S.S., C.A.V., and M.V. conceived the study design, analysed the data and wrote the manuscript.
T.M., S.E.R., and D.S.K. helped design the study and reviewed and constructively criticized the manuscript.
F.M., R.R., and E.M. contributed to data analysis and manuscript revision for important intellectual content.
C.C. and G.V. helped conduct the study and analyse the data.

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Declaration of interests

None of the authors received compensation to perform this study. S.E.R is a board member and minor shareholder of Mermaid Care A/S, who commercially produces the ALPE system. D.S.K. has performed consultancy work for Mermaid Care A/S. Respiratory tubes and loan of the ALPE machine were provided free of charge by Medigas, Italy, a distributor for Mermaid Care.

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