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Respiration and the Airway

RESPIRATION AND THE AIRWAY

Individualised positive end-expiratory pressure guided by electrical impedance tomography for robot-assisted laparoscopic radical prostatectomy: a prospective, randomised controlled clinical trial

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Abstract

Background: Robot-assisted laparoscopic radical prostatectomy requires general anaesthesia, extreme Trendelenburg positioning and capnoperitoneum. Together these promote impaired pulmonary gas exchange caused by atelectasis and may contribute to postoperative pulmonary complications. In morbidly obese patients, a recruitment manoeuvre (RM) followed by individualised PEEP improves intraoperative oxygenation and end-expiratory lung volume (EELV). We hypothesised that individualised PEEP with initial RM similarly improves intraoperative oxygenation and EELV in non-obese individuals undergoing robot-assisted prostatectomy.

Methods: Forty males (age, 49–76 yr; BMI <30 kg m^{-2}) undergoing prostatectomy received volume-controlled ventilation (tidal volume 8 ml kg^{-1} predicted body weight). Participants were randomised to either (1) RM followed by individualised PEEP (RM/PEEP$_{IND}$) optimised using electrical impedance tomography or (2) no RM with 5 cm H_2O PEEP. The primary outcome was the ratio of arterial oxygen partial pressure to fractional inspired oxygen ($Pa_{O_2}/F_{I_{O_2}}$) before the last RM before extubation. Secondary outcomes included regional ventilation distribution and EELV which were measured before, during, and after anaesthesia. The cardiovascular effects of RM/PEEP$_{IND}$ were also assessed.

Results: In 20 males randomised to RM/PEEP$_{IND}$, the median PEEP$_{IND}$ was 14 cm H_2O [inter-quartile range, 8–20]. The $Pa_{O_2}/F_{I_{O_2}}$ was 10.0 kPa higher with RM/PEEP$_{IND}$ before extubation (95% confidence interval [CI], 2.6–17.3 kPa; $P=0.001$). RM/PEEP$_{IND}$ increased end-expiratory lung volume by 1.49 L (95% CI, 1.09–1.89 L; $P<0.001$). RM/PEEP$_{IND}$ also improved the regional ventilation of dependent lung regions. Vasopressor and fluid therapy was similar between groups, although 13 patients randomised to RM/PEEP$_{IND}$ required pharmacological therapy for bradycardia.

Conclusion: In non-obese males, an individualised ventilation strategy improved intraoperative oxygenation, which was associated with higher end-expiratory lung volumes during robot-assisted laparoscopic prostatectomy.

Clinical trial registration: DRKS00004199 (German clinical trials registry)

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Keywords: electrical impedance tomography; minimally invasive surgery; positive pressure ventilation; pulmonary gas exchange; radical prostatectomy

Editor's key points

- Steep Trendelenburg positioning and capnoperitoneum promote pulmonary collapse, impaired gas exchange, and pulmonary complications after surgery in non-obese individuals.
- Individualised positive end-expiratory pressure, titrated by electrical impedance tomography, improves intraoperative oxygenation and end-expiratory lung volumes in obese patients.
- In this randomised study, individualised PEEP settings were quite variable, suggesting that one-size-fits-all ventilatory strategies are suboptimal.
- Individualised PEEP improved oxygenation during robot-assisted laparoscopic radical prostatectomy in non-obese individuals.

Robot-assisted laparoscopic radical prostatectomy[1] has become an increasingly popular procedure used by surgeons to minimise surgical trauma and blood loss, preserve of nerve structures, and hasten recovery after surgery.[2,3] However, robot-assisted laparoscopic radical prostatectomy adversely affects respiratory mechanics during general anaesthesia because of high intra-abdominal pressures generated by the combination of capnoperitoneum and the extreme Trendelenburg position required for optimal surgical access.[1] Taken together, these factors promote the development of pulmonary atelectasis,[4] which leads to reduced end-expiratory lung volume (EELV) and impaired oxygenation, and may contribute to postoperative pulmonary complications (PPCs).[5,6] Levels of PEEP that are often used during mechanical ventilation to counteract these effects[7,8] do not typically exceed 5 cm H_2O,[9] which may be too low to prevent atelectasis. Thus, patients' individual constitution, BMI, positioning, and intra-abdominal pressure may warrant a more individual approach to set PEEP.

One method to determine the lowest PEEP level that minimises atelectasis while optimising tidal volume is the use of electrical impedance tomography (EIT) imaging.[10] In a previous study, recruitment manoeuvres (RMs) in combination with individualised determination of the optimal PEEP level by EIT in morbidly obese patients undergoing laparoscopic bariatric surgery improved intraoperative oxygenation, by increasing EELV and improving lung mechanics, compared with standard ventilation with a PEEP of 5 cm H_2O.[11]

Here, we tested the hypothesis that an initial RM and individualised PEEP would improve intraoperative oxygenation and EELV in patients with a BMI <30 kg m^{-2} at risk of PPCs after robot-assisted laparoscopic radical prostatectomy.

Methods

A detailed description of the methods used in this prospective, parallel-arm, randomised single-centre study was presented in a previous publication in obese patients.[11] The study reported here is the second part of a larger project with a total of 113 planned patients (a run-in feasibility part with 5, a randomised part with 54 obese and a randomised part with 54 non-obese patients) and was approved by the local ethics committee (University of Leipzig, No. 196-11-ff-8042011) and registered in the WHO-listed German trials registry (DRKS00004199). The first part with obese patients has already been published (appendix A).[11] All non-obese patients were recruited at the University of Leipzig Medical Centre between February 2016 and December 2017. Informed consent of all patients was obtained before inclusion.

Inclusion criteria

Males $\geq$18 yr of age, with a BMI <30 and >18.5 kg m^{-2} and intermediate to high risk of postoperative pulmonary complications (ARISCAT score [Assess Respiratory Risk in Surgical Patients in Catalonia Score] $\geq$31)[12] undergoing robot-assisted laparoscopic radical prostatectomy were eligible for inclusion.

Exclusion criteria

The presence of implanted cardiac devices, chronic pulmonary disease, congestive heart failure New York Heart Association III/IV, and severe haemodynamic instability after induction of anaesthesia were defined as exclusion criteria.

Anaesthesia

After induction of anaesthesia with standard doses of remifentanil, propofol, and rocuronium, general anaesthesia was maintained as TIVA by continuous infusion of propofol and remifentanil. Intravenous crystalloids and noradrenaline were provided as necessary and at the discretion of the treating anaesthetist, who was not part of the study team.

Intraoperative ventilation

All patients were ventilated in a constant-flow, volume-controlled mode using a standard mechanical respirator (EVITA-XL; Draeger Medical, Lübeck, Germany). Initial settings after intubation were a tidal volume of 8 ml kg^{-1} predicted body weight (PBW) and a ventilatory frequency of 12 breaths min^{-1} in all patients. PEEP was adjusted according to the experimental protocol (see below). The responsible anaesthetist was instructed to adapt ventilatory rate before a change of tidal volume in the event of substantial hypercapnia (Pa_{CO_2} >6 kPa). Inspiratory flow was set to achieve an inspiratory pause >0.2 s with an I/E ratio of 1:2. F_{IO_2} was 0.4 and was increased if necessary to maintain a peripheral oxygen saturation of $>92\%$.

Measurements

EELV was determined with the multiple breath nitrogen washout method using respiratory mass spectrometry (RMS, AMIS 2000; Innovision, Odense, Denmark) using the Consensus technique.[13]

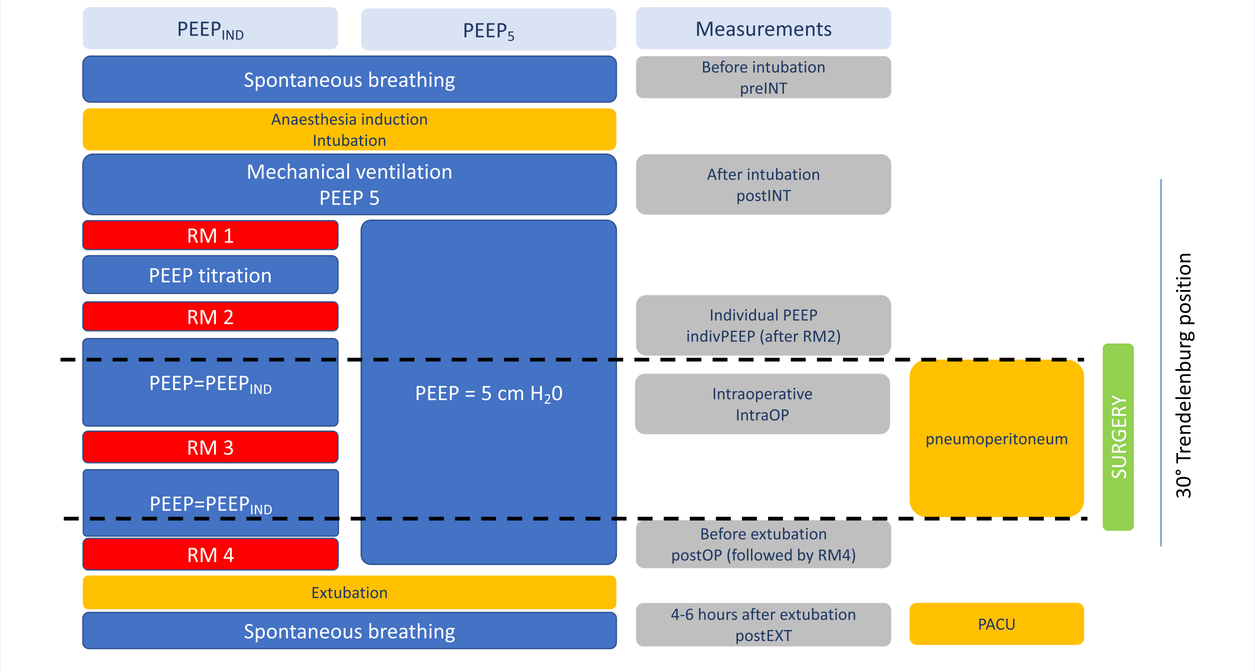

Fig 1. Experimental protocol timeline and interventions for both groups. PEEP$_{IND}$, individual PEEP group; PEEP$_5$, control group; RM, recruitment manoeuvre.

Arterial blood gas samples were analysed with a standard co-oximeter (ABL 800; Radiometer, Copenhagen, Denmark).

Ventilation parameters and standard parameters of the respiratory system (static and dynamic compliance, resistance) were derived from the mechanical ventilator (EVITA-XL; Draeger Medical). All variables were averaged for 20 ventilatory cycles.

EIT data were acquired with a commercially available EIT system (PulmoVista500; Dräger Medical, Lübeck, Germany). In addition to the regional ventilation delay index (RVDI), parameters quantified by EIT were regional ventilation distribution, the global inhomogeneity index (GI), and tidal ventilatory distribution between dependent and non-dependent lung zones, which were calculated offline using the Dräger EIT analysis tool®, Version 6.1 (Draeger Medical).

Protocol

The study protocol is summarised in Figure 1. Randomisation was performed after obtaining patient informed consent the day before surgery with using a minimisation algorithm with a stochastic component, stratified by age (<45 *vs* ≥45 yr) and ARISCAT score (<45 *vs* ≥45 points). Measurements of EELV, arterial blood gas analyses with an $F_{I_{O_2}}$ of 1.0 and EIT were performed before induction of anaesthesia and 4–6 h after extubation in the spontaneously breathing patient using a special mouthpiece and a nose clamp. A first baseline measurement was performed 10 min after induction of anaesthesia at a PEEP of 5 cm H_2O in both groups, followed by another two measurements at defined time points during general anaesthesia, either at a PEEP of 5 cm H_2O (control group) or individual PEEP (intervention group). PEEP remained at 5 cm H_2O in the control group throughout the entire period of mechanical ventilation without any RM. Subsequent to a first RM followed by PEEP titration, an additional RM and setting of the individual PEEP followed in the intervention arm. All RMs were performed in pressure-controlled mode and consisted of 10 respiratory cycles with a PEEP of 20 cm H_2O, a peak inspiratory pressure of 40 cm H_2O, and a ventilatory frequency of 6 breaths min^{-1} with an I/E of 1:2. Patient positioning was supine before induction of anaesthesia. All measurements in the intubated patient were performed in the 30° Trendelenburg position, except the last measurement 4–6 h after extubation, which was performed in 30° reverse Trendelenburg position.

Individualised ventilatory strategy: PEEP titration

After baseline measurements at a PEEP of 5 cm H_2O (see above), a first RM was performed. Subsequently, the decremental PEEP trial was initiated by setting PEEP to 20 cm H_2O and decreasing it stepwise by 2 cm H_2O until a PEEP of 4 cm H_2O was reached (volume controlled mode, tidal volume 8 ml kg^{-1} PBW, ventilatory frequency 12 breaths min^{-1}, I/E 1:2, $F_{I_{O_2}}$ 0.4), with a low flow manoeuvre (LFM) at each PEEP step (single breath, inspiratory flow: 4 L min^{-1}; tidal volume: 12 ml kg^{-1} PBW). As reported in our previous work, RVDI for each of the 11 LFM was calculated offline using customised software. In brief, the regional ventilation delay during the LFM for each pixel in the EIT image was determined, and the RVDI was then defined as the standard deviation (SD) for all pixels' regional ventilatory delay. The PEEP corresponding to the lowest RVDI was set as

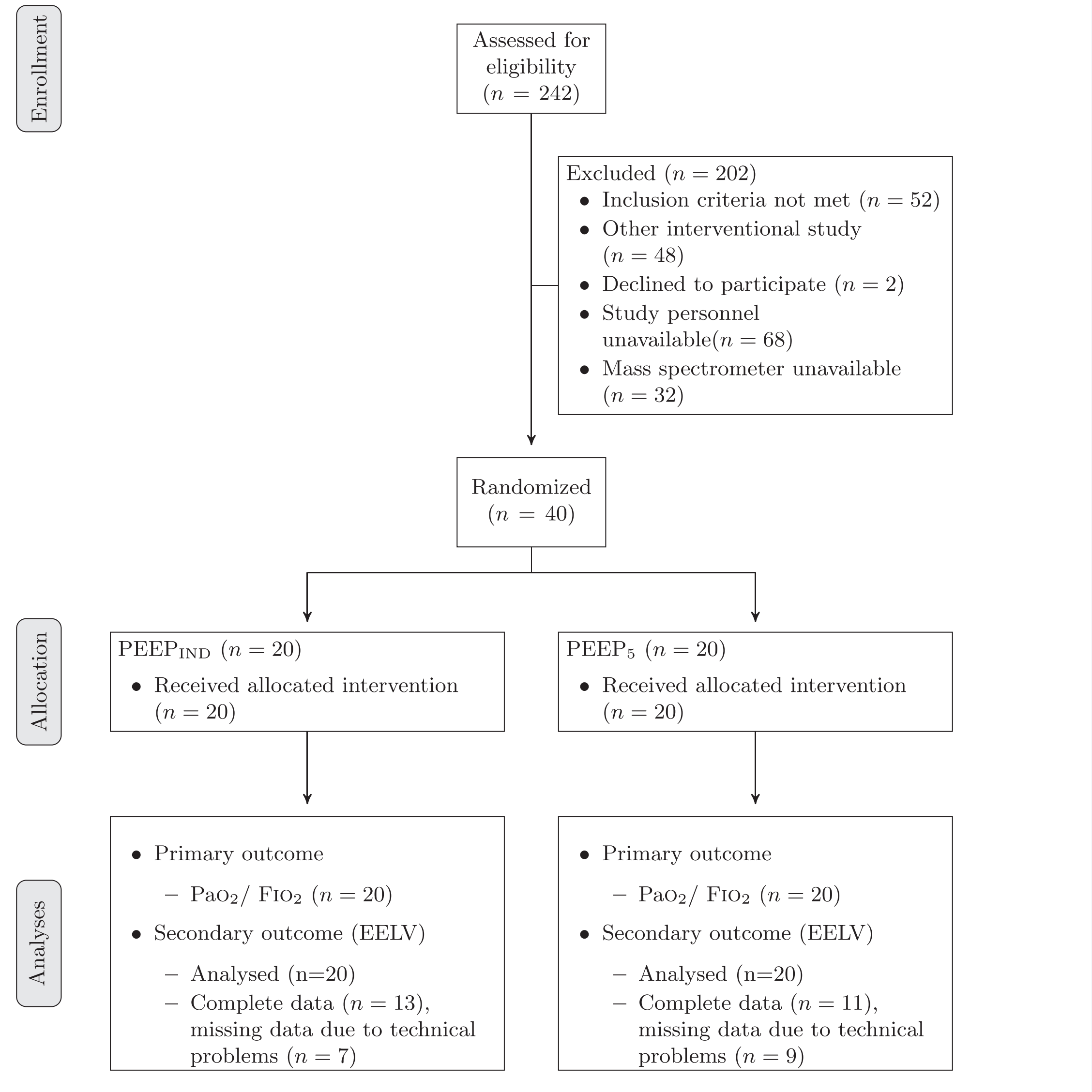

Fig 2. Flowchart of enrolment and outcomes. EELV = end-expiratory lung volume; $\text{F}_{\text{I}}\text{O}_2$ = fraction of inspired oxygen; PaO_2 = partial pressure of oxygen in arterial blood; PEEP = positive end-expiratory pressure.

PEEP_{IND}. After another RM, PEEP_{IND} was maintained throughout the entire period of mechanical ventilation. After resolution of the capnoperitoneum at the end of the operation, a last (fourth) RM was performed immediately before extubation (see also Fig. 1). Patients were postoperatively monitored in the PACU for at least 6 h and received standard postoperative care.

Primary outcome

The primary outcome was the $\text{Pa}\text{O}_2/\text{F}_{\text{I}}\text{O}_2$ ratio before the last RM before extubation.

Secondary outcomes

We measured the following secondary outcomes:

1. EELV before last RM.
2. $\text{Pa}\text{O}_2/\text{F}_{\text{I}}\text{O}_2$ ratio and EELV at different points in time during and after ventilation.
3. Vasopressor, fluid, and heart rate-related pharmacological interventions were recorded to determine whether the ventilation strategies explored had any cardiovascular effects.

Sample size calculation

The sample size calculation was based on detecting differences in $\text{Pa}\text{O}_2/\text{F}_{\text{I}}\text{O}_2$ of 13.3 kPa (100 mm Hg) between the two ventilation strategies, with an SD of 90 mm Hg in each arm. Accounting for drop-outs, 27 subjects were planned for each ventilation strategy so as to have 22 subjects with complete data, to achieve a power of 90%. Because of the low drop-out

Table 1 Baseline characteristics of the study population. Entries are mean (standard deviation, SD), mean (range) or numbers (%). ARISCAT score, Assess Respiratory Risk in Surgical Patients in Catalonia score; ASA, American Society of Anesthesiologists; EIT, electrical impedance tomography; $PEEP_{IND}$, designation for the intervention arm, in which an individual PEEP was determined with EIT titration; $PEEP_5$, designation for the control arm, where a standard PEEP of 5 cm H_2O was used; NA, not available.

	$PEEP_{IND}$ (n=20)	$PEEP_5$ (n=20)
Number of males	20 (100%)	20 (100%)
Age (yr)	62.6 (49–76)	64.2 (50–76)
BMI (kg m^{-2})	25.3 (2.3)	25.6 (2.5)
ARISCAT score	36.1 (5.3)	35.0 (4.0)
>44	2 (10%)	1 (5%)
ASA physical status		
1	7 (35%)	2 (10%)
2	12 (60%)	16 (80%)
3	1 (5%)	2 (10%)
Smoking		
Never	10 (53%)	8 (42%)
Former	3 (16%)	4 (21%)
Current	6 (32%)	7 (37%)
Alcohol use		
None	2 (11%)	1 (6%)
Rarely	8 (42%)	7 (39%)
Regularly	9 (47%)	10 (56%)
Heart failure	0 (0%)	1 (5%)
Coronary heart disease	1 (5%)	3 (16%)
Bronchitis within past month	1 (5%)	1 (5%)
Sleep apnoea	1 (5%)	0 (0%)
Diabetes mellitus	0 (0%)	2 (10%)

rates in the obese part of the trial along with large effect sizes,[11] we were able to reduce the sample size from 44 to 40 analysed subjects.

Statistical analysis

The Pa_{O_2}/F_{iO_2} and EELV were analysed using analysis of covariance, with the value before extubation as the dependent variable, the value after intubation as a covariate, and the assigned arm as a factor. A linear mixed model with interaction between the randomisation group and the point in time was used to compare Pa_{O_2}/F_{iO_2} and EELV data at multiple time points between both ventilation strategies, with prespecified multiple comparisons performed using the ‘multcomp’ package and the Westfall adjustment for *P*-values. Patients with at least one measurement provide information that enters into the estimates of the coefficients. Missing data for EELV were treated with multiple imputation with 50 iterations using the ‘mice’ R-package.[14] Because purely technical issues unrelated to lung volume led to missing data, they were treated as ‘missing completely at random’; an analysis of the existing data provides a non-biased estimate as a sensitivity analysis.[15] Finally, a robustness analysis was conducted to determine the magnitude of the effect needed before a different conclusion would be drawn from the data. Comparisons for count data were made using Fisher’s exact test. Statistical analyses were performed using R Version 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria; www.R-project.org). *P*-values <0.05 denote statistical significance.

Results

Subject characteristics

All 40 subjects completed the study (Fig. 2). The mean BMI, 25.3 (2.4) kg m^{-2}, was similar between each group (Table 1). No subjects required mechanical ventilation after the operation. Complete Pa_{O_2}/F_{iO_2} data were available for all subjects, but complete EELV data as a secondary endpoint could only be computed for 24 subjects. In the other subjects, technical issues with mass spectrometry such as vacuum pump failure, calibration issues, and leakage with nitrogen inflow during spontaneous breathing because of patients’ inability to maintain a closed loop system with the mouthpiece resulted in incomplete data. At least one EELV data point was available for 35 patients, and all of these subjects were included in the mixed model.

Individualised ventilation strategy

The median PEEP in the intervention group was 14 cm H_2O [inter-quartile range, 8–20].

Primary outcome: Pa_{O_2}/F_{iO_2} before extubation

Before extubation, Pa_{O_2}/F_{iO_2} was 10.0 kPa higher in the $PEEP_{IND}$ during capnoperitoneum (95% confidence interval [CI], 2.6–17.3 kPa; P=0.0094) compared with the $PEEP_5$ group (Fig. 3a).

Secondary outcomes: end-expiratory lung volume

EELV declined in both groups after induction of general anaesthesia and intubation (Fig. 3b). In the $PEEP_{IND}$ group, EELV increased after initial RM and application of $PEEP_{IND}$, but remained unchanged in the $PEEP_5$ group until after extubation. Before extubation, EELV was 1.01 L higher in the $PEEP_{IND}$ compared with the $PEEP_5$ group (95% CI, 0.79–1.27 L; P<0.001). In the corresponding sensitivity analysis with complete data, the estimate was 1.49 L higher in the $PEEP_{IND}$ compared with the $PEEP_5$ group (95% CI, 1.09–1.89 L; P<0.001). From the robustness analysis, we found similar results, unless mean EELV among the missing data were 1.4 L lower in the $PEEP_{IND}$ group.

Lung mechanics

Intubation and ventilation with a PEEP of 5 cm H_2O led to a shift of ventilation distribution to non-dependent lung areas in both groups. This effect was partly counterbalanced by RM and individualised PEEP in the $PEEP_{IND}$ group during capnoperitoneum. After release of capnoperitoneum, ventilation distribution reached preoperative values measured during spontaneous breathing. In contrast, ventilation remained primarily in the non-dependent lung areas during mechanical ventilation in the $PEEP_5$ group until the patients returned to spontaneous ventilation (Fig. 3c). Postoperatively, ventilation distribution did not differ from preoperative values. Ventilation inhomogeneity as calculated by the GI also increased in

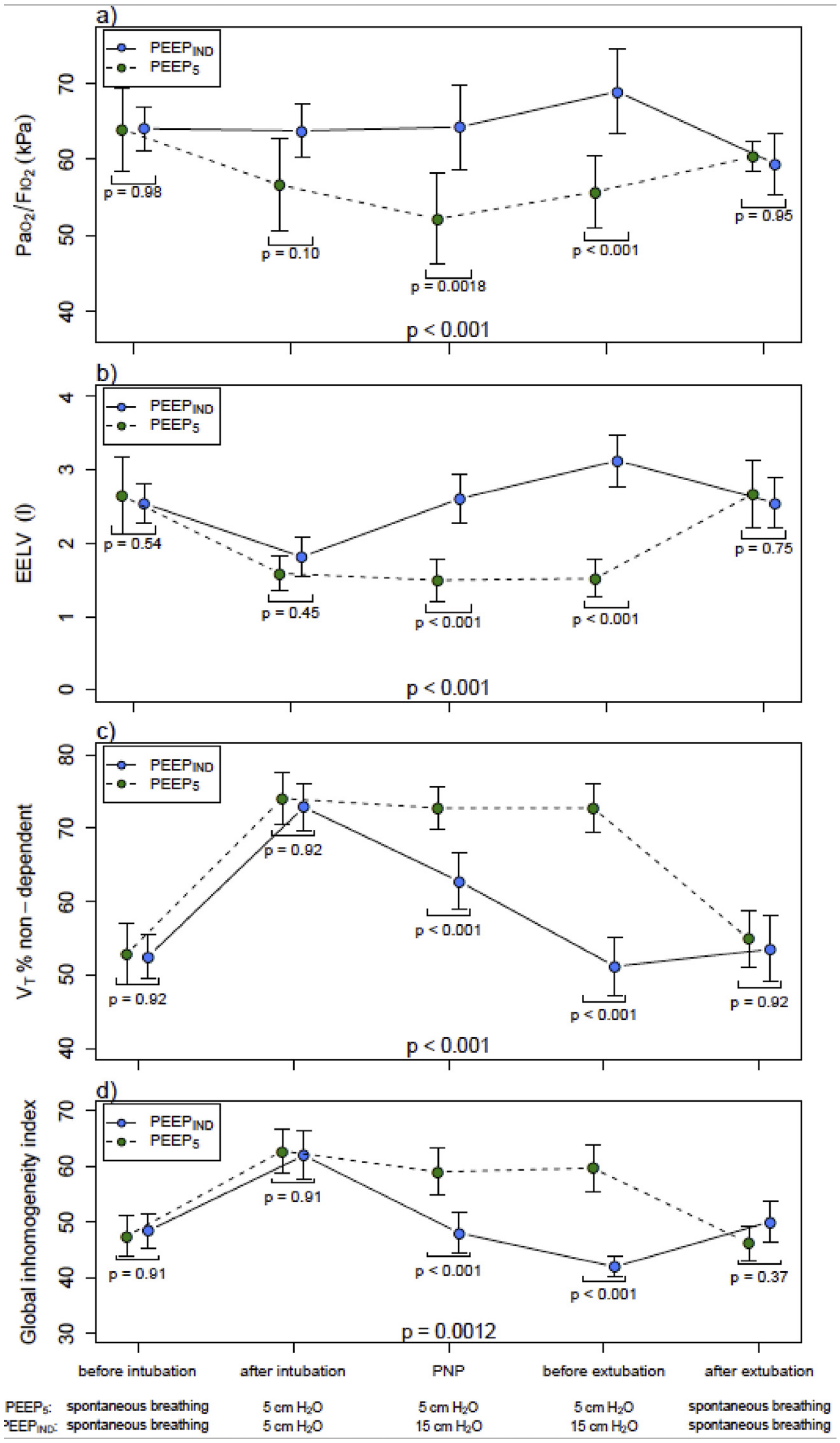

Fig 3. Time course of Pao$_2$/Fio$_2$ (a), EELV calculated from multiple breath nitrogen washout (b), global inhomogeneity index (c) and distribution of regional ventilation of tidal volume (VT) distributed to the non-dependent lung (d), with the last two both calculated from electrical impedance tomography. Points represent means and whiskers 95% confidence intervals from the data at that given time point (i.e. not from the repeated-measures analysis of variance). For the points in time from left to right, EELV was available for *n*=22, 29, 28, 26, and 19 patients, respectively. EELV, end-expiratory lung volume; Fio$_2$, fraction of inspired oxygen; PNP, capnoperitoneum; PEEP$_{IND}$, electrical impedance tomography-based individualised PEEP arm; PEEP$_5$, standard PEEP of 5 cm H$_2$O arm.

both groups after intubation. Mechanical ventilation with individualised PEEP led to a significant improvement in ventilation homogeneity in the $PEEP_{IND}$ group. However, we observed a return to pre-intubation levels in the $PEEP_{IND}$ group resulting in comparable GI in the $PEEP_{IND}$ and $PEEP_5$ group postoperatively (Fig. 3d). Peak and plateau pressures were higher in the $PEEP_{IND}$ group, but this resulted in significantly lower driving pressures (12(3) *vs* 17(3) cm H_2O, $P<0.001$; see also Table 2).

Cardiovascular effects of PEEPIND

Doses of vasopressor and fluid infusions during mechanical ventilation were similar between groups (Table 3). Thirteen patients showed relevant bradycardia during RM or PEEP titration phases requiring pharmacological intervention.

Discussion

In the present study, EIT-guided $PEEP_{IND}$ with RM resulted in better oxygenation and greater EELV, compared with a standard PEEP of 5 cm H_2O without RM. Our findings confirm our previous study in obese patients,[11] in which ventilation with $PEEP_{IND}$ and RM also resulted in better intraoperative oxygenation, higher EELV, higher ventilation homogeneity, and improved respiratory system mechanics. The current study shows that this holds in non-obese patients undergoing invasive prostatectomy requiring capnoperitoneum and extreme Trendelenburg positioning, although mean PEEP was 3.5 cm H_2O lower than for obese patients.

The differences between the study groups concerning oxygenation and EELV resolved quickly after extubation. However, EELV was comparable with the values measured preoperatively and oxygenation worsened only slightly, which is in contrast to our findings in morbidly adipose patients where differences were substantial.[11] We observed that atelectasis caused by mechanical ventilation, extreme Trendelenburg positioning and capnoperitoneum resolved after extubation in the control group. Ventilation with $PEEP_{IND}$ with RM in normal weighted patients therefore exerts its effects mainly on intraoperative lung function. In our study group consisting of non-obese patients with healthy lungs, atelectasis did not have detrimental effects on oxygenation, despite an observed average reduction of EELV of about 1 L after intubation compared with preoperative values in the control group. Even if we did not observe any hypoxic events in our study group, the improvement in oxygenation in the intervention group could be crucial in patients with impaired lung function. $PEEP_{IND}$ also resulted in better respiratory mechanics indicated by lower driving pressures, which may be a surrogate for ventilator-induced lung injury.[16,17]

The majority of patients required vasopressor support during anaesthesia. However, the mean vasopressor doses were low and were similar between groups. Furthermore, most cardiovascular complications such as bradycardia and hypotension occurred during the application of RM in the intervention group and were only transient with quick resolution after termination of the RM. Cardiocirculatory depression is one of the main reasons why anaesthesiologists hesitate to perform RM, and their relevance in context with other elements of a lung protective ventilation strategy has been questioned.

The decrease in EELV with shift of ventilation to non-dependent lung areas indicates rapid development of atelectasis in dependent lung areas only 10 min after intubation and Trendelenburg positioning. In a comparable clinical scenario, Futier and colleagues[18] showed that the addition of RM to PEEP led to significant improvement in oxygenation compared with PEEP alone in non-obese and obese patients. Therefore, we still consider RM followed by adequate PEEP to be a cornerstone of a lung protective ventilation strategy. RMs were thus included in the $PEEP_{IND}$ arm in line with other recent PEEP studies.[11,19]

Our study was a proof-of-concept study and not designed to detect whether the RM/$PEEP_{IND}$ strategy resulted in differences in postoperative pulmonary complications (PPCs). The recent Intraoperative Ventilation with Higher *vs* Lower Levels of Positive End-Expiratory Pressure in Obese Patients (PROBESE) study) did not detect differences in PPC in obese patients when comparing a PEEP of 12 cm H_2O with RM to PEEP of 4 cm H_2O. However, given that individual PEEP values were substantially higher in a physiological study in obese patients,[11] a PEEP value of 12 cm H_2O might have been ineffective for entire prevention of atelectasis in the PROBESE study. In non-obese patients with abdominal surgery, the large Ventilation Using High *vs* Low Positive End-Expiratory Pressure (PROVHILO) study compared PEEP values of 12 cm H_2O with RM with PEEP ≤ 2 cm H_2O without RM and did not observe differences in PPC.[20] Apart from the lack of PEEP individualisation, however, PROVHILO did not include patients with laparoscopic surgery.[20] In a recent meta-analysis including 12 trials, Cui and colleagues[21] suggested that a lung protective ventilation strategy with RM is associated with a lower incidence of PPC in non-obese patients.

Our study has several limitations. In contrast to Andersson and colleagues,[4] we did not measure the real extent of atelectasis and alveolar recruitment by RM and $PEEP_{IND}$. However, EELV measured by the nitrogen washout method shows a good correlation with EELV measured by CT,[22] although in this particular study the method was fraught with technical challenges leading to missing data for some interventions. We performed sensitivity and robustness analyses, which clearly showed that effects were so large that missing data was unlikely to affect our conclusions. For practical reasons, PEEP titration and determination of $PEEP_{IND}$ was done in 30° Trendelenburg position, but before initiation of capnoperitoneum. Furthermore, the capnoperitoneum measurement was undertaken without readjustment of $PEEP_{IND}$. Few clinical data are available concerning the additional effects of capnoperitoneum on respiratory mechanics and lung volumes in extreme Trendelenburg positioning. In a small study including 30 obese and 30 normal weight patients, capnoperitoneum led to a decrease in respiratory system compliance, but patients were not positioned in the Trendelenburg position.[18] In our study, EELV did not decrease further in the $PEEP_5$ group after initiation of capnoperitoneum compared with the levels measured after intubation and Trendelenburg positioning of the patient, indicating that capnoperitoneum might not have relevant effects on EELV in addition to that caused already by the Trendelenburg position. Accordingly, Loring and colleagues[23] did not detect a significant decrease of EELV after initiation of capnoperitoneum in a small study including mainly obese patients. However, clinical experience and the

Table 2 Respiratory and blood parameters at three time points during mechanical ventilation. Gas volumes are given in body temperature and pressure saturated (BTPS) conditions. Entries are mean (standard deviation) and P-values compare the two arms from a repeated-measures analysis of variance. BE, acid–base excess; $F_{I}O_2$, fraction of inspired oxygen; $Pe_{T}CO_2$, end-tidal partial pressure of carbon dioxide; PBW, predicted body weight; $PEEP_{IND}$, designation for the intervention arm, where an individual PEEP was determined with titration; $PEEP_5$, designation for the control arm where a standard PEEP of 5 cm H_2O was used; PNP, pneumoperitonium.

	$PEEP_{IND}$ (n=20)			$PEEP_5$ (n=20)			P
	After intubation	PNP	Before extubation	After intubation	PNP	Before extubation	
Tidal volume (ml)	643 (91)	652 (97)	641 (90)	603 (58)	606 (62)	611 (69)	–
Tidal volume/PBW (ml kg^{-1})	8.33 (0.78)	8.45 (0.70)	8.30 (0.69)	8.46 (0.48)	8.50 (0.54)	8.55 (0.57)	–
PEEP (cm H_2O)	5.0 (0.0)	14.7 (3.3)	14.7 (3.3)	5.0 (0.0)	5.0 (0.0)	5.0 (0.0)	<0.001
Peak pressure (cm H_2O)	23.4 (5.3)	34.9 (3.9)	29.9 (3.7)	24.2 (4.3)	30.4 (4.6)	25.5 (4.0)	0.025
Plateau pressure (cm H_2O)	15.8 (2.2)	26.4 (4.4)	22.2 (3.8)	16.6 (3.0)	22.3 (3.3)	17.2 (2.7)	0.012
Driving pressure (cm H_2O)	10.8 (2.2)	11.7 (2.9)	7.7 (1.8)	11.6 (3.0)	17.3 (3.3)	12.2 (2.7)	<0.001
Resistance (cm H_2O)	7.7 (5.4)	8.4 (2.3)	7.5 (2.7)	7.8 (2.9)	7.9 (1.9)	8.1 (1.9)	0.89
$Pe_{T}CO_2$ (kPa)	6.26 (0.54)	6.40 (0.83)	6.64 (1.09)	6.53 (0.63)	5.93 (0.44)	5.87 (0.43)	0.080
Ventilatory frequency (breaths min^{-1})	12 (0.9)	15 (2.7)	15 (2.9)	12 (1.1)	17 (3.6)	17 (3.8)	0.059
Minute ventilation (L min^{-1})	7.9 (1.3)	9.8 (2.2)	9.6 (2.0)	7.5 (0.9)	10.1 (2.2)	10.3 (2.3)	0.66
$Pa_{O_2}/F_{I}O_2$ (kPa)	63.8 (7.9)	64.3 (12.7)	69.0 (12.9)	56.6 (14.0)	52.2 (13.7)	55.7 (10.8)	<0.001
Pa_{CO_2} arterial (kPa)	4.62 (0.41)	4.82 (0.85)	4.78 (0.91)	4.76 (0.53)	4.55 (0.55)	4.49 (0.60)	0.40
pH	7.461 (0.028)	7.429 (0.060)	7.426 (0.066)	7.445 (0.040)	7.444 (0.038)	7.431 (0.089)	0.90
Haemoglobin (mmol L^{-1})	8.6 (0.8)	8.4 (0.7)	8.2 (0.6)	8.6 (0.6)	8.4 (0.7)	8.3 (0.8)	0.83
BE (mmol L^{-1})	0.9 (1.5)	−0.5 (1.4)	−0.6 (1.4)	0.5 (1.5)	−0.3 (1.3)	−0.1 (1.0)	0.84
HCO_3^- (mmol L^1)	24.8 (1.4)	23.6 (1.4)	23.4 (1.5)	24.8 (1.3)	24.0 (1.3)	24.2 (1.1)	0.40
Temperature (°C)	35.7 (0.4)	36.5 (0.5)	36.5 (0.5)	35.7 (0.3)	36.2 (0.4)	36.3 (0.4)	0.13

study by Andersson and colleagues[4] suggest that both Trendelenburg positioning and capnoperitoneum contribute to atelectasis-induced loss of FRC. Another explanation for the apparent absence of further reductions in EELV after initiation of capnoperitoneum in the $PEEP_5$ group could be that significant airway closure has already occurred after Trendelenburg positioning of the patient. This would limit the further loss of EELV.

In summary, the results of the current work combined with our previous study in obese patients[11] show that individualised PEEP improves intraoperative oxygenation and lung mechanics compared with a lower standard PEEP in both normal weight and obese patients undergoing laparoscopic surgery. To date, the main shortcoming of an individualised PEEP strategy using EIT is that it extends the duration of anaesthesia, which may limit clinical utility.

Table 3 Vital parameters, vasoactive medication and complications during and after surgery. Entries are means (standard deviations) or numbers (%), where means for vasoactive medication refer only to those who received it. Bolus equivalents are measured in units of single ampoules of 1+20 mg for theodrenaline + cafedrine or 5 μg of norepinephrine. Amounts of vasoactive injected medication is compared for the 14 individualised and 19 standardised patients, who received such medication, but did not receive norepinephrine infusions. Blood pressure complications are defined by <90 mm Hg (systolic) or <60 mm Hg (diastolic) for 10 min. The particular pulmonary and extra-pulmonary complications are explained in the text. Fluid infusion was entirely crystalloid, no colloids were used: $Pe_{T}CO_2$, partial pressure of end-tidal carbon dioxide; PEEP, positive end-expiratory pressure; $PEEP_{IND}$, designation for the intervention arm, in which an individual PEEP was used; $PEEP_5$, designation for the control arm, where a standard PEEP of 5 cm H_2O was used; Sp_{O_2}, peripheral capillary oxygen saturation.

	$PEEP_{IND}$ (n=20)	PEEP5 (n=20)	P
During surgery			
Heart rate (beats min^{-1})	60 (10)	58 (9)	0.64
Mean arterial blood pressure (mm Hg)	77 (9)	78 (9)	0.66
Total fluid infusion rate (ml h^{-1} kg^{-1})	7.03 (3.24)	8.46 (3.08)	0.16
Vasoactive injections			
Received medication	18 (90%)	14 (70%)	0.24
Amount (bolus equivalents)	2.0 (8.9)	0.0 (0.2)	0.34
Norepinephrine infusion			
Received medication	18 (90%)	15 (75%)	0.41
Maximal rate (μg^{-1} min^{-1})	0.089 (0.124)	0.043 (0.021)	0.14
Blood pressure complications	8 (40%)	5 (25%)	0.50
After operation (day of OP)			
Sp_{O_2} <90%	0 (0%)	0 (0%)	–
$Pe_{T}CO_2$ >6.7 kPa	0 (0%)	0 (0%)	–
Blood pressure complications	0 (0%)	1 (5%)	1.00
Vasoactive medication administered	0 (0%)	2 (10%)	0.49

Further physiological studies are required to develop individualised PEEP measurements in a more time-efficient manner.

Authors' contributions

Conception of study design: PS, AWR, HW
Study design: PS, AWR, HW
Patient recruitment: FG, GH, PS
Data collection: FG, SuS, CK, StS, ML, PS
Data analysis: FG, DP, PS, AGn, AB, ACJN, HW
Drafting of the manuscript: FG, DP, PS, HW
All authors participated in critical revision of the manuscript for important intellectual content.

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Declarations of interest

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Appendix A.

The study was conceived to contain two randomised populations: the obese and non-obese. The decision to recruit, analyse and publish them separately was taken because of fundamental differences between them: (1) evaluating the main research question did not necessarily need a control group of a different patient population (obese *vs* non-obese), and (2) the obese patient group was expected to contain predominantly females with all patients undergoing bariatric upper abdominal surgery performed in reverse Trendelenburg position. In contrast, the non-obese group were exclusively male patients undergoing robot-assisted laparoscopic radical prostatectomy. This operation, however, is performed in extreme Trendelenburg position.

Whereas the trial protocol is explicit about analysing the groups separately, the registered information on the trial unfortunately does not make it clear that there exist two groups, nor that they were recruited consecutively.

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