© 2017 EDIZIONI MINERVA MEDICA
Online version at http://www.minervamedica.it

Minerva Anestesiologica 2018 February;84(2):159-67
DOI: 10.23736/S0375-9393.17.12042-0

ORIGINAL ARTICLE

Physiological effects of the open lung approach during laparoscopic cholecystectomy: focus on driving pressure

Davide D'ANTINI [1] *, Michela RAUSEO [1], Salvatore GRASSO [2],
Lucia MIRABELLA [1], Luigi CAMPOROTA [3, 4], Antonella COTOIA [5],
Savino SPADARO [5], Alberto FERSINI [6], Rocco PETTA [1], Rosaria MENGA [1],
Alberto SCIUSCO [7], Michele DAMBROSIO [1], Gilda CINNELLA [1]

[1]Department of Anesthesia and Intensive Care, University of Foggia, Foggia, Italy; [2]Department of Anesthesia and Intensive Care, University of Bari, Bari, Italy; [3]Asthma, Allergy and Lung Biology Division, King's College London, London, UK; [4]Department of Adult Critical Care, Guy's and St Thomas' NHS Foundation Trust, King's Health Partners, London, UK; [5]Department of Morphology, Surgery and Experimental Medicine, University of Ferrara, Ferrara, Italy; [6]Department of General Surgery, University of Foggia, Foggia, Italy; [7]Department of Intensive Care and Anesthesia, North Bristol NHS Trust, Bristol, UK

*Corresponding author: Davide D'Antini, Department of Anesthesia and Intensive Care, University of Foggia, Viale Pinto 1, 71100 Foggia, Italy. E-mail: davide.dantini@unifg.it

ABSTRACT

BACKGROUND: During laparoscopy, respiratory mechanics and gas exchange are impaired because of pneumoperitoneum and atelectasis formation. We applied an open lung approach (OLA) consisting in lung recruitment followed by a decremental positive-end expiratory pressure (PEEP) trial to identify the level of PEEP corresponding to the highest compliance of the respiratory system (best PEEP). Our hypothesis was that this approach would improve both lung mechanics and oxygenation without hemodynamic impairment.
METHODS: We studied twenty patients undergoing laparoscopic cholecystectomy. We continuously recorded respiratory mechanics parameters throughout a decremental PEEP trial in order to identify the best PEEP level. Furthermore, lung and chest wall mechanics, respiratory and transpulmonary driving pressures (ΔP), gas exchange and hemodynamics were recorded at three time-points: 1) after pneumoperitoneum induction (T_{preOLA}); 2) after the application of the OLA ($T_{postOLA}$); 3) at the end of surgery, after abdominal deflation (T_{end}).
RESULTS: The "best PEEP" level was 8.1±1.3 cmH_2O (range 6 to 10 cmH_2O), corresponding to the highest compliance of the respiratory system (C_{RS}). This "best PEEP" level corresponded with lowest ΔP_L. OLA increased the compliance of the lung and of the chest wall, and decreased ΔP_{RS} and ΔP_L. PaO_2/FiO_2 increased from 299±125 mmHg to 406±101 mmHg ($P=0.04$). Changes in respiratory mechanics, driving pressures and oxygenation were maintained until T_{end}. Hemodynamic parameters remained stable throughout the study period.
CONCLUSIONS: In patients undergoing laparoscopic cholecystectomy, the OLA was suitable for bedside PEEP setting, improved lung mechanics and gas exchange without significant adverse hemodynamic effects.

(*Cite this article as:* D'Antini D, Rauseo M, Grasso S, Mirabella L, Camporota L, Cotoia A, *et al*. Physiological effects of the open lung approach during laparoscopic cholecystectomy: focus on driving pressure. Minerva Anestesiol 2018;84:159-67. DOI: 10.23736/S0375-9393.17.12042-0)

Key words: Respiratory mechanics - Pneumoperitoneum - Laparoscopic cholecystectomy.

Laparoscopy is the preferred surgical approach in several abdominal and pelvic procedures.[1] However, the resultant pneumoperitoneum impairs the respiratory mechanics [2] and worsens gas exchange by increasing the intra-abdominal pressure and favoring the formation of atelectasis.[3]

Comment in p. 147.

During positive pressure mechanical ventilation, the transpulmonary pressure (P_L) represents the amount of pressure that is directly applied to the lung parenchyma and determines lung inflation.[4] At any given level of airway opening pressure (P_{RS}), P_L is determined by the interplay of lung and chest wall elastance (E_L and E_{CW}, respectively). In healthy subjects, E_L and E_{CW} are approximately equal, hence P_L is approximately half the P_{RS}.[5, 6] During laparoscopic surgery P_L significantly decreases due to the pneumoperitoneum-induced increase in E_{CW}.[7] The reduced lung-distending pressure is responsible for worsening of gas exchange and lung mechanics through the generation of atelectasis in the dependent lung regions. A recruitment maneuver (RM) followed by the application of a standard positive end-expiratory pressure (PEEP) level of 5 cmH_2O is commonly suggested to restore P_L.[7] However, physiological data suggest that immediately after the RM, PEEP should be individualized to maximize alveolar recruitment while minimizing alveolar hyperinflation.[4] Despite these physiological considerations, little is known about how to set the optimal PEEP level during laparoscopic surgery.

In this study we investigated the physiological effects of the open lung approach (OLA) in patients undergoing abdominal laparoscopic surgery. We reproduced the same physiological approach applied in patients with ARDS [8] consisting in a RM immediately followed by a standardized stepwise decremental PEEP trial, to find the "best PEEP," *i.e.* the PEEP corresponding to the highest respiratory system compliance (C_{RS}).[9-11] We tested the hypothesis that, in patients undergoing laparoscopy in reverse Trendelenburg position, the PEEP level that allows to obtain the highest C_{RS} during the decremental PEEP trial would increase end-inspiratory P_L and that, consequently, this approach would both improve both lung mechanics and gas exchange without inducing significant hemodynamic impairment.

Our secondary aim was to evaluate the impact of the OLA on the driving pressure applied on the respiratory system and to the lung (ΔP_{RS} and ΔP_L, respectively).

Materials and methods

After obtaining approval from the Ethics Committee of the Ospedali Riuniti Hospital of Foggia, Italy (protocol no. 17/CE/2012, obtained on 27/02/2012) and written informed consent from each patient, the study was performed in consecutive patients scheduled to undergo elective laparoscopic cholecystectomy from January to July 2013.

Inclusion criteria were ages 18 years or older, ASA (American Society of Anesthesiology) physical status I and II. Patients with preexisting respiratory or cardiac diseases, and obesity (body mass index [BMI] ≥30 kg/m^2) were excluded.

Upon their arrival in the operating room, patients were pre-medicated with midazolam 0.03-0.04 mg/kg. After applying standard monitoring device (electrocardiogram and pulse oximeter [Intellivue MP40 monitor, Philips, Boeblingen, Germany]), the radial artery was cannulated (Radial Artery Catheterization Set, Arrow International, Reading, PA, USA) for continuous monitoring of blood pressure (BP). The arterial line was connected to the FloTrac™ sensor and the Vigileo™ monitor (Edwards Life Sciences LLC, Irwine, CA, USA, software version 03.10), which allows cardiac output (CO) and stroke volume (SV) estimation from the arterial pressure waveform and computes cardiac index (CI) and the stroke volume variation (SVV) as an index of fluid responsiveness.[12]

Patients were given 7 mL/kg of 0.9% NaCl IV before the induction of anesthesia and were then maintained with 5 mL/kg/h of 0.9% NaCl solution. Anesthesia was induced with propofol 2 mg/kg, fentanyl 3 µg/kg and succinylcholine 1 mg/kg. After induction the trachea was intubated with an endotracheal tube of appropriate size (Rushelit Rush AG Lab, Waibling, Germany). Anesthesia was maintained with an infusion of propofol 150-200 µg/kg/min, remifentanil 0.1-0.2 µg/kg/min and cisatracurium 1.5 µg/kg/min. The level of anesthesia was assessed through bi-spectral index (BIS) monitoring (Aspect A-2000®, Aspect Medical System, Newton, MA, USA). The infusion rate of propofol was varied in order to target a BIS value between 50 and 60. Patients were mechanically ventilated with a Servo Ventilator 900C (Siemens-Elema AB, Berlin, Germany) with a square flow waveform with a tidal volume (Vt) of 8 mL/kg ideal body weight (IBW), respiratory rate (RR) of 12 breath/min, inspiratory time (Ti) of 33% and an inspiratory pause of 20%. Patients were ventilated using an inspiratory oxygen fraction (FiO_2) of 0.40 as needed to maintain the $SaO_2 \geq 95\%$. External PEEP was set at 4-5 cmH_2O as per our standard clinical practice.

A thin latex balloon-tipped esophageal catheter (Compliance catheter, Microtek Medical B.V. Zutphen- NL) was inserted through the mouth, advanced deflated into the esophagus and connected by means of a polyethylene catheter to a pressure transducer (Digima Clic), to measure esophageal pressure (P_{ES}). The esophageal balloon was filled with 1-1.5 mL of air and its correct positioning in the lower third of the esophagus was checked by assessing heart artifacts and verifying that the appropriate P_{ES} increase in response to a moderate transient manual on the abdomen [13-15] were quantitatively equivalent to the increase in P_{AO}.

A standardized protocol for hemodynamic management was applied in order to assure fluid volume optimization. Briefly, if SVV was <13%, no additional fluids were given whereas if SVV was higher 13%, additional boluses of 250 ml of crystalloids were infused over 15-20 minutes. After each bolus SVV was re-evaluated, and a further bolus was administered if SV increased by more than 10%, until reaching a SVV<13%.[12]

Study protocol

After the induction of pneumoperitoneum (abdominal CO_2 inflation to obtain an intra-abdominal pressure of 10-12 mmHg) and hemodynamic stabilization, a recruiting maneuver (RM) was applied,[11] consisting in pressure controlled ventilation with a driving pressure of 20 cmH_2O and PEEP applied in steps of 5, 10, 15, and 20 cmH_2O every five respiratory breaths; subsequently, after setting a driving pressure of 15 cmH_2O and keeping it constant throughout the decremental PEEP trial, PEEP was stepwise reduced by 2 cmH_2O every 2 minutes.[11] Static compliance of the respiratory system (C_{RS}) was measured at every step. The PEEP level corresponding to the highest C_{RS} during the decremental trial was identified as the "best PEEP." Subsequently, the lungs were recruited again and the "best" PEEP was applied. Afterwards, the ventilator was switched to the volume-control ventilation maintaining the baseline settings, except than for the "best PEEP level. These settings were maintained until the end of surgery. Respiratory mechanics, hemodynamics and gas exchange were measured with the patient in reverse Trendelenburg position (20° legs down) at three time points: 1) after the pneumoperitoneum induction (T_{preOLA}); 2) after the application of the open lung strategy ($T_{postOLA}$); and 3) at the end of surgery, after abdominal deflation (T_{end}). Hemodynamic recordings were also performed continuously during the RM.

Respiratory mechanics and hemodynamic measurements

Hemodynamic and respiratory mechanics parameters were recorded, digitized and collected on a personal computer through a 12-bit analog-to digital converter board (DAQCard 700, National Instrument, Austin, TX, USA) at a sample rate of 200 Hz (ICU Lab, KleisTEK Engineering, Bari, Italy). Intravascular pressure measurements were adjusted to zero at atmospheric pressure and leveled to the mid-axillary line. Analysis of arterial blood gases was performed (ABL 330, Radiometer, Copenhagen, Denmark).

Airflow was measured with a heated pneumotachograph (Fleisch no.2, Fleisch, Lausanne, Switzerland) linear over the experimental range of flow, connected to a differential pressure transducer (Diff-Cap, ±1 cmH_2O; Special Instruments, Nordlingen, Germany) inserted between the Y-piece of the ventilator circuit and the endotracheal tube. Airway opening pressure (P_{RS}) was measured proximal to the endotracheal tube with a pressure transducer (Special Instruments Digima-Clic ±100 cmH_2O; Nordlingen, Germany). Volume was obtained by numerical integration of the flow signal over time.

Peak and plateau P_{RS} ($P_{RS,PEAK}$ and $P_{RS,PLAT}$ respectively), and total and static intrinsic PEEP of the respiratory system ($PEEP_{TOT,RS}$ and $PEEPi_{RS}$, respectively), inspiratory and expiratory plateau esophageal pressures ($P_{ES,PLAT}$ and P_{ES,END_EXP}), were measured according to standard methods.[16]

Static compliance of the respiratory system (C_{RS}) and chest wall (C_{CW}) were calculated as $V_T/(P_{RS,PLAT} - PEEP_{TOT,RS})$ and $V_T/(P_{ES,PLAT} - P_{ES,END\_EXP})$, respectively. Lung compliance (C_L) was calculated as the difference between C_{RS} and C_{CW} ($C_L^{-1} = C_{RS}^{-1} - C_{CW}^{-1}$). End-inspiratory and end-expiratory transpulmonary pressure ($P_{L,PLAT}$ and P_{L,END_EXP}, respectively), were measured as already described.[5, 8, 17] Respiratory system and transpulmonary driving pressure (ΔP_{RS} and ΔP_L) were calculated as ($P_{RS,PLAT} - PEEP_{TOT,RS}$) and ($P_{L,PLAT} - P_{L,END\_EXP}$), respectively.[8]

Total airways resistances (Raw) were calculated as the difference between $P_{AO,PEAK}$ and $P_{AO,PLAT}$ divided the inspiratory airflow.[18]

Statistical analysis

A sample size calculation was performed using data from our previous study [7] on the effects of recruiting maneuvers in patients undergoing gynecological laparoscopic surgery. Based on these data, a 16 mL/cmH_2O increase in C_{RS} with a SD of 4 was considered significant. By using a one-sample, one-sided test the sample size calculated was of 15 patients; this number was increased to 20 to allow for an expected drop-out of around one-third of patients and was used for patient enrolment. The α and β errors for the sample size were chosen as 0.05 and 95%, respectively.

Statistical comparison of demographic, respiratory mechanics, hemodynamic and gas exchange data was performed between the three study steps: 1) T_{preOLA}; 2) $T_{postOLA}$; and 3) T_{end}. Non-continuous data are expressed as numbers and percentages. Continuous data were tested for normal distribution by the Kolmogorov-Smirnov goodness- of -fit test and are presented as means and standard deviations.

Data analysis was performed by means of repeated measure ANOVA. If significant, the Fischer exact test was applied for post-hoc comparison between the different study steps. P value less than 0.05 was considered statistically significant. Statistical analysis was performed using Statistica v. 10.0 (Statsoft Italia srl ©2011; www.statsoft.com).

Results

The enrolment flow diagram is reported in Figure 1. Twenty out of 26 eligible patients were included in the study. Demographic characteristics of the population studied are presented in Table I.

Respiratory mechanics during the decremental PEEP trial

The decremental PEEP trial targeting the highest C_{RS} (71.2±8.3 mL/cmH_2O) identified a PEEP level ranging from 6 to 10 cmH_2O (mean: 8.9±1.3 cmH_2O) as the "best PEEP" (Table II, Figure 2). This "best PEEP" level correspond-

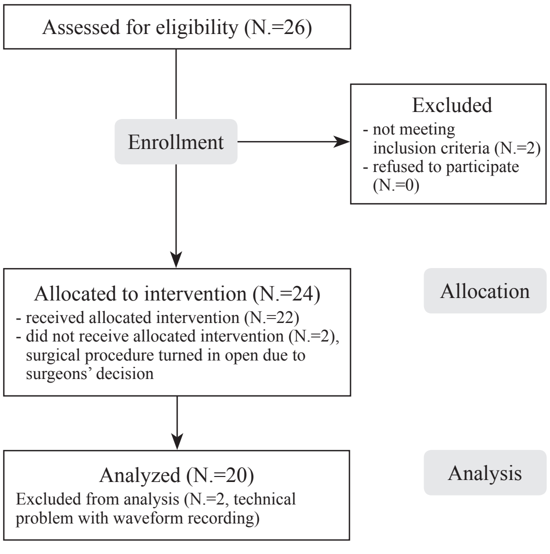

Figure 1.—Flow-diagram of the progress through the phases of the trial.

TABLE I.—*Patients demographic characteristics.*

Characteristics	Value
N. patients	20
Age, years	47±15
Sex, N. (%)	
Male	13 (65%)
Female	7 (35%)
ASA, N. (%)	
I	7 (35%)
II	13 (65%)
BMI, kg/m^2	24±1.8
Coexisting condition, N. (%)	
Current smoking	9 (45%)
Any alcohol intake	5 (25%)
Chronic obstructive pulmonary disease	4 (20%)
Chronic arterial hypertension	6 (30%)
Diabetes mellitus	2 (10%)
Duration of surgery, min	50±10

Data are shown as number (percentage) or as mean±SD.
ASA: American Society of Anesthesiology; BMI: Body Mass Index.

ed to the lowest transpulmonary driving pressure (ΔP_L = 5.1 ± 0.26 cmH$_2$O) (Figure 2).

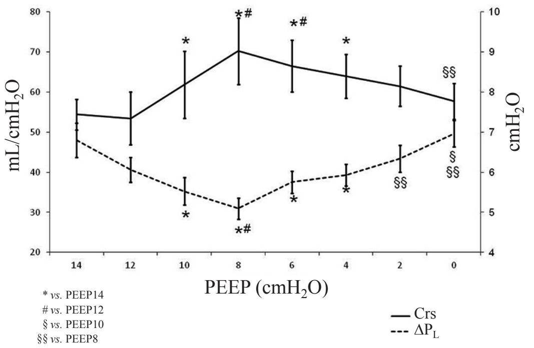

Figure 2.—Respiratory system compliance (Crs) and transpulmonary driving pressure (ΔP_L) during decremental PEEP trial.
Crs: PEEP12 *vs.* PEEP14, P=0.99; PEEP10 *vs.* PEEP14, P=0.013; PEEP8 *vs.* PEEP14, P=0.00003; PEEP6 *vs.* PEEP14, P=0.003; PEEP4 *vs.* PEEP14, P=0.022; PEEP8 *vs.* PEEP12, P=0.00014; PEE6 *vs.* PEEP12, P=0.003; PEEP0 *vs.* PEEP8, P=0.05.
ΔP_L: PEEP12 *vs.* PEEP14, P=0.078; PEEP10 *vs.* PEEP14, P=0.036; PEEP8 *vs.* PEEP14, P=0.005; PEEP6 *vs.* PEEP14, P=0.038; PEEP4 *vs.* PEEP14, P=0.049; PEEP8 *vs.* PEEP12, P=0.041; PEEP0 *vs.* PEEP10, P=0.0068.

Effect of the OLA on the partitioned respiratory mechanics, gas exchange and hemodynamics

Table II shows that $C_{RS,}$ C_L and C_{CW} increased significantly following OLA and remained stable until T_{end}. R_{AW} decreased significantly (P=0.002) and remained stable thereafter. The PaO$_2$/FiO$_2$, that was 299±125 mmHg at T_{preOLA}, increased to 406±101 mmHg at $T_{postOLA}$ (P=0.04), remaining stable until the end of surgery. PaCO$_2$ and pH remained stable

TABLE II.—*Breathing pattern and gas exchange parameters during the different experimental conditions.*

Parameters	T_{preOLA}	$T_{postOLA}$	T_{end}	P value
V_T, mL/Kg IBW	6.4±0.3	6.7±0.4	6.7±0.3	0.47
RR, breaths/min	12±1	12±1	12±1	0.77
$P_{AO,PLAT}$, cmH$_2$O	13.4±0.8	15.6±1.4*	15.1±1.4*	0.003
PEEPi,$_{RS}$, cmH$_2$O	0.8±0.9	0.8±0.7	0.7±0.7	0.81
$PEEP_{TOT,RS}$, cmH$_2$O	4.8±0.9	8.9±1.3*	8.7±1.4*	0.0001
DP_{RS}, cmH$_2$O	8.7±0.7	6.7±0.7*	6.3±0.6*	0.0001
$P_{L,PLAT}$, cmH$_2$O	7.6±0.8	9.0±1.2*	8.9±1.3*	0.007
$P_{L,END\text{-}EXP,}$ cmH$_2$O	1.5±0.6	4.2±0.4*	4.1±0.5*	0.0003
DP_L, cmH$_2$O	6.2±0.5	4.8±0.6*	4.7±0.5*	0.0015
Raw, cmH$_2$O/L/s	13.9±3.4	7.2±1.8*	8.8±1.4*	0.002
C_{RS}, mL/cmH$_2$O	55.4±4.7	71±8.2*	70.1±9.2*	0.0005
C_L, mL/cmH$_2$O	67.7±6.4	84.5±8.7*	82.9±8.3*	0.0013
C_{CW}, mL/cmH$_2$O	275±50.2	372±43.5*	358±47*	0.0007
PaO$_2$/FiO$_2$, mmHg	299±125	406±101*	424±104*	0.004
PaCO$_2$, mmHg	35±3.7	30±5	33±4.1	0.17
pH	7.36±0.5	7.38±0.4	7.36±0.4	0.25

*Statistically significant difference *vs.* T_{preOLA}.
Data are expressed as mean±SD. Repeated measure ANOVA was used for the comparison of continuous variables. Fischer Test for *post-hoc* comparison.
C_{RS}: respiratory system compliance; C_L: lung compliance; C_{CW}: chest wall compliance; ΔP_{RS}: respiratory system driving pressure; ΔP_L: transpulmonary driving pressure; FiO$_2$: inspiratory oxygen fraction; PaO$_2$: partial pressure arterial oxygen; PEEP: positive end expiratory pressure; PEEPi,$_{RS}$: respiratory system static intrinsic PEEP; $PEEP_{TOT,RS}$: respiratory system total PEEP; $P_{AO,PLAT}$: respiratory system plateau airways pressure; RR: respiratory rate; V_T: tidal volume; Raw: total airways resistance; PaCO$_2$: partial pressure arterial carbon dioxide; $P_{L,PLAT}$: end-inspiratory transpulmonary pressure; $P_{L,END\text{-}EXP}$: end-expiratory transpulmonary pressure.

TABLE III.—*Hemodynamics during the different experimental conditions.*

	T_{preOLA}	$T_{postOLA}$	T_{end}	P value
HR, bpm	69±10	73±10	70±10	0.78
MAP, mmHg	94±19	103±23	86±14	0.07
CI, L/min/m²	2.8±0.5	2.9±0.7	2.8±0.7	0.58
SVV, %	13.2±4.8	12.8±3.5	11.5±3	0.34

Data are expressed as mean±SD. Repeated measure ANOVA was used for the comparison of continuous variables. Fischer Test for *post-hoc* comparison.
RM: recruitment maneuver; HR: heart rate; MAP: mean arterial pressure; CI: cardiac index; SVV: stroke volume variation.

throughout all the study steps. Hemodynamics (SVV, mean arterial pressure and HR) remained stable throughout the observation period (Table III).

Discussion

In patients undergoing laparoscopic cholecystectomy in reverse Trendelenburg position: 1) during the decremental PEEP trial the lowest transpulmonary driving pressure (ΔP_L) was found at a level of external PEEP corresponding to the highest C_{RS}; 2) the "best PEEP" identified through a recruiting maneuver immediately followed by a decremental PEEP trial targeting the highest respiratory system compliance improved lung and chest wall mechanics and oxygenation and did not worsen hemodynamics; 3) those effects were maintained until the end of surgery.

Laparoscopy is the preferred surgical approach for several abdominal or pelvic procedures, because of pain reduction [19, 20] faster postoperative recovery and shorter hospital stay.[21] However, the increase in intra-abdominal pressure due to pneumoperitoneum, pushes the diaphragm towards the thoracic cavity and stiffens the chest wall, and induces atelectasis in the dependent lung regions, as shown in computed tomographic studies.[3] Atelectasis are associated with perioperative complications, particularly in predisposed patients.[22] Patient's positioning also plays a role: there is wide agreement in literature that Trendelenburg posture (head down) further impairs respiratory system mechanical properties through gravitational effects. We recently demonstrated that C_{RS} and C_L decreases in patients undergoing gynecological laparoscopic surgery in Trendelenburg position.[7] The effects of the reverse Trendelenburg position (head up, *i.e.* the one applied in the present study) on respiratory mechanics are less known [2, 23] though some studies suggest a worsening in respiratory mechanics in obese patients [1, 21] Although the present study was not specifically designed to assess position-related changes in respiratory mechanics, our data indirectly suggest that the combined effects of reverse Trendelenburg and pneumoperitoneum induce a worsening in lung mechanics that responds to the OLA strategy (Table II).

Ventilator-induced lung injury (VILI) is widely recognized as one of the risks of mechanical ventilation, and can occur in both already injured and healthy lung.[22] Lung protective protocols aim to minimize tidal alveolar hyperinflation and opening/collapse (atelectrauma) through the use of low V_T, low lung distending pressures and adequate PEEP levels.[23] In surgical patients this strategy has been shown to improve lung aeration while reducing atelectrauma [24] and seems to improve clinical outcomes and to reduce health care utilization.[25, 26] However, the approach to PEEP setting and, overall, to lung recruitment is not standardized. The OLA tested in the present study was proposed for ARDS patients [27] and for preventing anesthesia-induced alveolar collapse.[11, 28] The physiological premise is that, owing to the hysteresis between the inspiratory and expiratory volume-pressure curve, the PEEP level needed to keep the lung open once it has been fully recruited is lower than the pressure required to recruit the lung.[29] Accordingly, PEEP titration along the expiratory limb of the pressure-volume curve would allow to find the "best PEEP" that represents the optimal compromise between recruitment and hyperinflation.[28, 30, 31] The two proposed physiological targets to identify the "best PEEP" are SpO_2 and C_{RS}.[28] Both are easy to monitor at the bedside but, of note, oxygenation is influenced also by cardiac output and other confounding factors. In the present study we targeted the decremental PEEP trial to the highest C_{RS} and obtained remarkable results in terms of lung mechanics and gas exchange (Table II).

Nevertheless, the C_{RS} depends from the interplay between chest wall and lung mechanical properties.[4] Accordingly, the best method would be partitioning between lung and chest wall mechanics and target to the higher C_L rather than to the higher C_{RS}. In the present study we partitioned respiratory system mechanics into its lung and chest wall components by measuring P_{ES}.[32] Interestingly, our results suggest that, at least in the cohort of patients undergoing laparoscopic cholecystectomy in reverse Trendelemburg position, the C_{RS} behavior mirrors the one of C_L (Table II).

To our knowledge, the present study is the first that assesses simultaneously C_{RS} and P_L during a decremental PEEP trial, demonstrating a specular behavior of these parameters. Furthermore, during the decremental PEEP trial, when C_{RS} reached its *zenith* (identifying the "best PEEP"), ΔP_L reached its *nadir*. These data, although needing further validation, provide a further important physiological rationale for titrating PEEP on C_{RS}, at least in this cohort. Overall, it seems that the OLA, while improving respiratory mechanics and oxygenation minimizes the mechanical stress imposed by positive pressure tidal inflation by minimizing ΔP_{RS} and ΔP_L, although we must point out that both these values were already in the "safe" range before OLA implementation.[33]

Recently, the role of the ΔP_{RS} has been recognized as one of the main ventilation outcome parameters in ARDS patients [33] and a meta-analysis has suggested a correlation between ΔP_{RS} and postoperative pulmonary complications in surgical patients.[34] Moreover, increase in PEEP was found to be effective in reducing post-operative mechanical complications only when associated with a decrease in the overall ΔP_{RS}.[34] Our data show a significant OLA-Induced decrease in ΔP_{RS} ($P=0.0001$) (Table II). This seems to suggest that the OLA decreased the overall mechanical stress posed on lung parenchyma. However, we must point out that the thresholds for "injurious" ΔP_{RS} in patients with healthy lungs undergoing general anesthesia are not known.[34] Of note, despite ΔP_{RS} seems to be a key variable in ARDS and anesthesia and has the advantage of a straightforward calculation, several authors sustain that the real driving pressure responsible for the dynamic mechanical lung stress is the transpulmonary driving pressure (ΔP_L).[35] Since in the present study we partitioned lung and chest wall mechanics,[5, 36] we were able to calculate simultaneously the ΔP_{RS} and the ΔP_L. We found that, at least in this setting, ΔP_{RS} mirrored the ΔP_L (Table II).

Accordingly, our data suggest that ΔP_{RS} could be taken as a surrogate for ΔP_L. Overall, our findings that in C_{RS} and ΔP_{RS} in this context are suitable surrogates for C_L and ΔP_L has important practical implications, considering that measuring P_{ES} to obtain partitioned respiratory system mechanics is time consuming and requires dedicated monitoring tools and considerable expertise.

Limitations of the study

We must acknowledge some limitations of our study: 1) we studied a relatively small number of low risk patients, undergoing a relatively simple surgical procedure; 2) we could not include, for practical reasons, a step of respiratory mechanics measurements before pneumoperitoneum in our study design; 3) since our focus was a physiological one, we did not assess the clinical effects of the OLA in the postoperative period. On the other hand, a multicenter, randomized controlled trial is at present enrolling patients to investigate whether a perioperative OLA including a decremental PEEP trial is able to affect postoperative pulmonary complications in high risk patients undergoing surgery [37] and we think that our physiological findings could be useful to interpret its results; lastly, 4) the values of chest wall compliance in our patients were relatively higher compared with our previous studies. We ascribe this result to the reverse Trendelenburg position, which reduces the shift of the diaphragm toward the thorax, in comparison with the Trendelenburg position. Furthermore we studied healthy patients with BMI≤30 kg/m^2: obese patients would probably have shown different values of chest wall compliance.

In conclusion, we tested the effects of the OLA protocol in patients undergoing abdominal laparoscopic surgical procedure and found that it increased the compliance of the lung and chest wall and decreased the total (respiratory system) and transpulmonary driving pressure while improving oxygenation, without inducing significant adverse hemodynamic effects. Further studies are needed to assess the impact of the OLA on postoperative respiratory complications.

Key messages

— Laparoscopic cholecystectomy necessitates a pneumoperitoneum, which affects respiratory mechanics and gas exchange by promoting atelectasis in dependent lung regions.

— This paper shows that the OLA, *i.e.* the application of a PEEP level titrated to achieve the best respiratory system compliance immediately after a lung recruiting maneuver, is able to reverse several detrimental effects of pneumoperitoneum on lung mechanics and gas exchange.

— Driving Pressure is recognized as a key parameter associated with postoperative pulmonary complications in surgical patients. This study shows that the OLA decreases the respiratory system and transpulmonary driving pressures.

References

1. Oti C, Mahendran M, Sabir N. Anaesthesia for laparoscopic surgery. Br J Hosp Med 2016;77:24-8.
2. Fahy BG, Barnas GM, Nagle SE, Flowers JL, Njoku MJ, Agarwal M. Effects of Trendelenburg and reverse Trendelenburg postures on lung and chest wall mechanics. J Clin Anesth 1996;8:236-44.
3. Andersson LE, Baath M, Thorne A, Aspelin P, Odeberg-Wernerman S. Effect of carbon dioxide pneumoperitoneum on development of atelectasis during anesthesia, examined by spiral computed tomography. Anesthesiology 2005;102:293-9.
4. Mietto C, Malbrain ML, Chiumello D. Transpulmonary pressure monitoring during mechanical ventilation: a bench-to-bedside review. Anaesthesiol Intensive Ther 2015;47 Spec No:27-37.
5. Gattinoni L, Chiumello D, Carlesso E, Valenza F. Bench-to-bedside review: chest wall elastance in acute lung injury/acute respiratory distress syndrome patients. Crit Care 2004;8:350-5.
6. Talmor D, Sarge T, O'Donnell CR, Ritz R, Malhotra A, Lisbon A, *et al.* Esophageal and transpulmonary pressures in acute respiratory failure. Crit Care Med 2006;34:1389-94.
7. Cinnella G, Grasso S, Spadaro S, Rauseo M, Mirabella L, Salatto P, *et al.* Effects of recruitment maneuver and positive end-expiratory pressure on respiratory mechanics and transpulmonary pressure during laparoscopic surgery. Anesthesiology 2013;118:114-22.
8. Cinnella G, Grasso S, Raimondo P, D'Antini D, Mirabella L, Rauseo M, *et al.* Physiological Effects of the Open Lung Approach in Patients with Early, Mild, Diffuse Acute Respiratory Distress Syndrome: An Electrical Impedance Tomography Study. Anesthesiology 2015;123:1113-21.
9. Hickling KG. Best compliance during a decremental, but not incremental, positive end-expiratory pressure trial is related to open-lung positive end-expiratory pressure: a mathematical model of acute respiratory distress syndrome lungs. Am J Respir Crit Care Med 2001;163:69-78.
10. Girgis K, Hamed H, Khater Y, Kacmarek RM. A decremental PEEP trial identifies the PEEP level that maintains oxygenation after lung recruitment. Respir Care 2006;51:1132-9.
11. Tusman G, Belda JF. Treatment of anesthesia-induced lung collapse with lung recruitment maneuvers. Curr Anaesth Crit Care 2010;21:244-9.
12. Benes J, Chytra I, Altmann P, Hlucky M, Kasal E, Svitak R, *et al.* Intraoperative fluid optimization using stroke volume variation in high risk surgical patients: results of prospective randomized study. Crit Care 2010;14:R118.
13. Benditt JO. Esophageal and gastric pressure measurements. Respir Care 2005;50:68-77.
14. Talmor D, Sarge T, Malhotra A, O'Donnell CR, Ritz R, Lisbon A, *et al.* Mechanical ventilation guided by esophageal pressure in acute lung injury. N Engl J Med 2008;359:2095-104.
15. Hedenstierna G. Esophageal pressure: benefit and limitations. Minerva Anestesiol 2012;78:959-66.
16. Cinnella G, Grasso S, Natale C, Sollitto F, Cacciapaglia M, Angiolillo M, *et al.* Physiological effects of a lung-recruiting strategy applied during one-lung ventilation. Acta Anaesthesiol Scand 2008;52:766-75.
17. Chiumello D, Carlesso E, Cadringher P, Caironi P, Valenza F, Polli F, *et al.* Lung stress and strain during mechanical ventilation for acute respiratory distress syndrome. Am J Respir Crit Care Med 2008;178:346-55.
18. Ranieri VM, Giuliani R, Fiore T, Dambrosio M, Milic-Emili J. Volume-pressure curve of the respiratory system predicts effects of PEEP in ARDS: "occlusion" versus "constant flow" technique. Am J Respir Crit Care Med 1994;149:19-27.
19. Gerges FJ, Kanazi GE, Jabbour-Khoury SI. Anesthesia for laparoscopy: a review. J Clin Anesth 2006;18:67-78.
20. Fletcher D, Stamer UM, Pogatzki-Zahn E, Zaslansky R,

Tanase NV, Perruchoud C, *et al.* Chronic postsurgical pain in Europe: An observational study. Eur J Anaesthesiol 2015;32:725-34.

21. Murray A, Lourenco T, de Verteuil R, Hernandez R, Fraser C, McKinley A, *et al.* Clinical effectiveness and cost-effectiveness of laparoscopic surgery for colorectal cancer: systematic reviews and economic evaluation. Heal Technol Assess 2006;10:1-141, iii-iv.
22. Sutherasan Y, D'Antini D, Pelosi P. Advances in ventilator-associated lung injury: prevention is the target. Expert Rev Respir Med 2014;8:233-48.
23. Chiumello D, Algieri I, Grasso S, Terragni P, Pelosi P. Recruitment maneuvers in acute respiratory distress syndrome and during general anesthesia. Minerva Anestesiol 2016;82:210-20.
24. Rothen HU, Neumann P, Berglund JE, Valtysson J, Magnusson A, Hedenstierna G. Dynamics of re-expansion of atelectasis during general anaesthesia. Br J Anaesth 1999;82:551-6.
25. Futier E, Constantin JM, 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.
26. Serpa Neto A, Hemmes SN, Barbas CS, Beiderlinden M, Fernandez-Bustamante A, Futier E, *et al.* Incidence of mortality and morbidity related to postoperative lung injury in patients who have undergone abdominal or thoracic surgery: a systematic review and meta-analysis. Lancet Respir Med 2014;2:1007-15.
27. ART Investigators. Rationale, study design, and analysis plan of the Alveolar Recruitment for ARDS Trial (ART): study protocol for a randomized controlled trial. Trials 2012;13:153.
28. Tusman G, Bohm SH. Prevention and reversal of lung collapse during the intra-operative period. Best Pract Res Clin Anaesthesiol 2010;24:183-97.
29. Pelosi P, Goldner M, McKibben A, Adams A, Eccher G, Caironi P, *et al.* Recruitment and derecruitment during acute respiratory failure: an experimental study. Am J Respir Crit Care Med 2001;164:122-30.
30. Lachmann B. Open up the lung and keep the lung open. Intensive Care Med 1992;18:319-21.
31. Ferrando C, Mugarra A, Gutierrez A, Carbonell JA, García M, Soro M, *et al.* Setting individualized positive end-expiratory pressure level with a positive end-expiratory pressure decrement trial after a recruitment maneuver improves oxygenation and lung mechanics during one-lung ventilation. Anesth Analg 2014;118:657-65.
32. Mauri T, Yoshida T, Bellani G, Goligher EC, Carteaux G, Rittayamai N, *et al.* Esophageal and transpulmonary pressure in the clinical setting: meaning, usefulness and perspectives. Intensive Care Med 2016;42:1360-73.
33. Amato MB, Meade MO, Slutsky AS, Brochard L, Costa EL, Schoenfeld DA, *et al.* Driving pressure and survival in the acute respiratory distress syndrome. N Engl J Med 2015;372:747-55.
34. Neto AS, Hemmes SN, Barbas CS, Beiderlinden M, Fernandez-Bustamante A, Futier E, *et al.* Association between driving pressure and development of postoperative pulmonary complications in patients undergoing mechanical ventilation for general anaesthesia: a meta-analysis of individual patient data. Lancet Respir Med 2016;4:272-80.
35. Protti A, Maraffi T, Milesi M, Votta E, Santini A, Pugni P, *et al.* Role of Strain Rate in the Pathogenesis of Ventilator-Induced Lung Edema. Crit Care Med 2016;44:e838-45.
36. Grasso S, Terragni P, Birocco A, Urbino R, Del Sorbo L, Filippini C, *et al.* ECMO criteria for influenza A (H1N1)-associated ARDS: role of transpulmonary pressure. Intensive Care Med 2012;38:395-403.
37. Ferrando C, Soro M, Canet J, Unzueta MC, Suárez F, Librero J, *et al.* Rationale and study design for an individualized perioperative open lung ventilatory strategy (iPROVE): study protocol for a randomized controlled trial. Trials 2015;16:193.

Authors' contributions.—Davide D'Antini and Michela Rauseo contributed equally to this study. Davide D'Antini, Michela Rauseo, and Gilda Cinnella were responsible for conception and design, analyzing and interpretation, manuscript writing and final approval of the manuscript. Lucia Mirabella, Salvatore Grasso, and Michele Dambrosio were responsible for conception and design, data interpretation, and final approval of the manuscript. Antonella Cotoia performed data analysis and interpretation. Luigi Camporota, Savino Spadaro, Alberto Fersini, and Alberto Sciusco were responsible for manuscript writing and revision, and data analysis. Rocco Petta and Rosaria Menga performed data acquisition and manuscript revision. All authors read and approved the final manuscript.

Conflicts of interest.—The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Article first published online: July 5, 2017. - Manuscript accepted: June 24, 2017. - Manuscript revised: June 8, 2017. - Manuscript received: March 6, 2017.