Esophageal Pressure Versus Gas Exchange to Set PEEP During Intraoperative Ventilation

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BACKGROUND: Pneumoperitoneum and Trendelenburg position affect respiratory system mechanics and oxygenation during elective pelvic robotic surgery. The primary aim of this randomized pilot study was to compare the effects of a conventional low tidal volume ventilation with PEEP guided by gas exchange ($V_{Gas-guided}$) versus low tidal volume ventilation tailoring PEEP according to esophageal pressure ($V_{Pes-guided}$) on oxygenation and respiratory mechanics during elective pelvic robotic surgery. METHODS: This study was conducted in a single-center tertiary hospital between September 2017 and January 2019. Forty-nine adult patients scheduled for elective pelvic robotic surgery were screened; 28 subjects completed the full analysis. Exclusion criteria were American Society of Anesthesiologists physical status $\geq$ 3, contraindications to nasogastric catheter placement, and pregnancy. After dedicated naso/orogastric catheter insertion, subjects were randomly assigned to $V_{Gas-guided}$ (F_{IO_2} and PEEP set to achieve S_{pO_2} > 94%) or $V_{Pes-guided}$ (PEEP tailored to equalize end-expiratory transpulmonary pressure). Oxygenation (P_{aO_2}/F_{IO_2}) was evaluated (1) at randomization, after pneumoperitoneum and Trendelenburg application; (2) at 60 min; (3) at 120 min following randomization; and (4) at end of surgery. Respiratory mechanics were assessed during the duration of the study. RESULTS: Compared to $V_{Gas-guided}$, oxygenation was higher with $V_{Pes-guided}$ at 60 min (388 $\pm$ 90 vs 308 $\pm$ 95 mm Hg, P = .02), at 120 min after randomization (400 $\pm$ 90 vs 308 $\pm$ 81 mm Hg, P = .008), and at the end of surgery (402 $\pm$ 95 vs 312 $\pm$ 95 mm Hg, P = .009). Respiratory system elastance was lower with $V_{Pes-guided}$ compared to $V_{Gas-guided}$ at 20 min (24.2 $\pm$ 7.3 vs 33.4 $\pm$ 10.7 cm H_2O/L, P = .001) and 60 min (24.1 $\pm$ 5.4 vs 31.9 $\pm$ 8.5 cm H_2O/L, P = .006) from randomization. CONCLUSIONS: Oxygenation and respiratory system mechanics were improved when applying a ventilatory strategy tailoring PEEP to equalize expiratory transpulmonary pressure in subjects undergoing pelvic robotic surgery compared to a $V_{Gas-guided}$ approach. (ClinicalTrials.gov registration NCT03153592). *Key words: positive pressure respiration; pneumoperitoneum; respiratory mechanics; laparoscopy.* [Respir Care 2020;65(5):625–635. © 2020 Daedalus Enterprises]

Introduction

The laparoscopic robotic technique has gained a leading role in elective pelvic surgery by minimizing the surgical approach and improving clinical outcome.[1,2] Usually, Trendelenburg (head-down position) and carbon dioxide pneumoperitoneum are applied during robotic surgery to optimize the surgical field.[3] However, the increased abdominal pressure associated with the Trendelenburg

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position impairs respiratory function, decreasing the lung volume below functional residual capacity and increasing the risk of atelectasis in dependent lung regions.[3-5] These pathophysiologic changes amplify the risk of perioperative complications, such as hypoxemia, especially in obese patients.[6,7] Furthermore, atelectasis worsens the stress and strain of alveolar structures,[3,8] causing ventilator-induced lung injury.[9] Preventing ventilator-induced lung injury during surgery improves perioperative outcome.[10,11]

Several different ventilatory strategies have been proposed to optimize both oxygenation and respiratory mechanics during laparoscopy.[12-16] Application of PEEP increases functional residual capacity by reducing the cranial shift of the diaphragm during laparoscopic and robotic surgery.[16,17] Moreover, a ventilatory strategy using lung-recruitment maneuvers followed by the application of PEEP is effective in improving respiratory mechanics and oxygenation during laparoscopy in normal-weight and obese subjects.[12,14] A different approach to optimize ventilatory mechanics and oxygenation during laparoscopic surgery could use transpulmonary pressure, previously applied to manage ventilation during the course of ARDS.[18] In this regard, a comparison between a conventional low tidal volume ventilation with PEEP set according to gas exchange ($V_{Gas-guided}$) versus a low tidal ventilatory strategy tailoring PEEP to equalize or positivize expiratory transpulmonary pressure through a calibrated esophageal pressure (P_{es}) measurement ($V_{Pes-guided}$) has not been conducted yet. To our knowledge, when P_{es}-driven mechanical ventilation has been applied, no esophageal balloon calibration procedure has been employed during surgery,[13] leading to inappropriate levels of PEEP or lung overdistention.

The primary aim of this pilot, prospective, randomized study was to observe the effects of $V_{Gas-guided}$ and $V_{Pes-guided}$ on intraoperative oxygenation, assessed after definitive pneumoperitoneum and Trendelenburg achievement, in subjects undergoing elective pelvic robotic surgery. Furthermore, any changes on intraoperative respiratory mechanics, rate of lung recruitment maneuvers, perioperative lung aeration ultrasound score, rate and type of

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QUICK LOOK

Current knowledge

Pneumoperitoneum and Trendelenburg position, usually utilized in pelvic robotic surgery, negatively affect respiratory mechanics with a consequent worsening of oxygenation. Moreover, the increase in driving pressure associated with the aforementioned changes puts patients at risk for ventilator-induced lung injury, a well-defined cause of poor outcomes.

What this paper contributes to our knowledge

Tailoring PEEP to avoid negative end-expiratory transpulmonary pressure led to oxygenation improvement in subjects undergoing elective pelvic robotic surgery. Indeed, this approach improved respiratory mechanics and reduced driving pressure, and preserved a better lung aeration in the early postoperative period.

perioperative complications, and length of hospital stay were analyzed as secondary end points.

Methods

Subjects

The protocol was designed in accordance with Helsinki Declaration principles and approved (CE 62/17) by the ethical committee of Maggiore della Carità University Hospital, in Novara, Italy. Written informed consent was obtained from all subjects, according to local regulations. This manuscript adheres to the applicable CONSORT guidelines. Adult subjects undergoing elective laparoscopic surgery for radical prostatectomy or hysterectomy were included. Exclusion criteria were American Society of Anesthesiologists physical status $\geq$ 3, contraindications to nasogastric catheter placement, and pregnancy. This investigation was carried out in the Department of Anesthesiology and Intensive Care, Maggiore della Carità University Hospital, in Novara, Italy.

After subjects arrived in the operating room, a lung ultrasound assessment was performed to compute the lung ultrasound score using a 2–4 MHz or a 7.5–12 MHz probe (Mylab 30cv, Esaote spa, Milan, Italy) as previously proposed.[19-21] Subsequently, midazolam 0.02 mg/kg was administered intravenously, and the standard intraoperative vital parameter monitoring was applied (ie, electrocardiogram, pulse oximeter, noninvasive blood pressure measurement). After anesthesia induction via intravenous propofol 2 mL/kg, remifentanil 0.15–0.3 γ/kg/min, and rocuronium 0.6 mg/kg, orotracheal intubation was assured and mechanical ventilation was started in volume control

mode with an inspiratory square flow. Tidal volume ranged from 6 to 8 mL/kg ideal body weight,[18] F_{IO_2} was set to maintain $S_{pO_2} > 94\%$, and breathing frequency was set to achieve and maintain an end-tidal carbon dioxide concentration of 35–45 mm Hg. An inspiratory time, accounting for 33% of total mechanical respiratory time, was set while an inspiratory pause equal to 20% of inspiratory time was chosen. No PEEP was initially added. Inhalatory sevoflurane (1–2%), intravenous remifentanil 0.1–0.15 γ/kg/min, and extemporary rocuronium were administered according to the anesthesia maintenance plan. The radial artery was cannulated for continuous invasive blood pressure monitoring. Anesthesia depth was targeted to a bi-spectral index (Aspect A-2000; Aspect Medical System, Newton, Massachusetts) range of 40–60 throughout the surgery.

A gastric tube equipped with both esophageal and gastric balloons (Nutrivent Sidam, Mirandola, Italy) was advanced through the nose or mouth for 50–55 cm to reach the stomach, where the balloons were inflated to the recommended volume (ie, 4 mL). Before insertion, balloons were both deflated and secured with a 3-way stopcock. After the device was placed, esophageal and gastric balloons were connected via polyethylene tubes to a pressure transducer box system (KT1D-2, Kleistek, Bari, Italy). The catheter was slowly withdrawn into the lower third of the esophagus, as indicated by the appearance of cardiac artifacts on the esophageal trace, and the esophageal balloon filling volume was adjusted to obtain the optimal P_{es} transmission.[22,23] At this point, two external manual compressions on the rib cage were applied during an expiratory pause, and the simultaneous positive deflections of the airways and esophageal pressure traces were compared.[24-28] Finally, after the definitive catheter position was achieved, the end-expiratory and end-inspiratory calibrated P_{es} was computed.[23]

Once pneumoperitoneum and Trendelenburg position were achieved, a 1-min recruitment maneuver was applied.[14] The ventilator was switched to pressure control mode, an inspiratory/expiratory ratio of 1:1 was set, a peak inspiratory pressure gradient (above PEEP) was fixed at 20 cm H_2O, and PEEP was progressively applied to obtain a stepwise increase of peak inspiratory pressure to 30, 35, and 40 cm H_2O every 3 breaths. The final recruiting pressure of 40 cm H_2O was carried out over 6 breaths. The ventilator was then switched to volume control mode.

Study Protocol

After lung recruitment, subjects were randomly assigned to a treatment group using a computer-generated randomization sequence; the assignment was reported to the attending physician before the subject's admission to the operating room.

In the $V_{Gas-guided}$ group, PEEP and F_{IO_2} were chosen by the robotic surgery anesthesia staff to maintain a $S_{pO_2} > 94\%$ and a plateau respiratory system pressure (P_{plat}) < 30 cm H_2O according to our institutional protocol (F_{IO_2} to oxygenation target; PEEP of 0–5 cm H_2O for body mass index < 30 kg/m^2 and 5–10 cm H_2O for body mass index ≥ 30 kg/m^2). When S_{pO_2} decreased to ≤ 94%, F_{IO_2} was increased first, followed by PEEP, after excluding common possible causes such as endotracheal tube misplacement or airway secretions.[29,30] If S_{pO_2} persistently remained ≤ 94%, a recruitment maneuver was performed with continuous hemodynamic monitoring.

In the $V_{Pes-guided}$ group, PEEP was delivered to obtain an expiratory transpulmonary pressure ≥ 0 cm H_2O. Furthermore, an upper limit of 20 cm H_2O of inspiratory transpulmonary pressure was set.

Tidal volume was chosen based on ideal body weight (6–8 mL/kg), the inspiratory/expiratory ratio was 1:2, and the breathing frequency was set to maintain an end-tidal carbon dioxide value ≤ 55 mm Hg in both arms.[3,31] Furthermore, recruitment maneuvers, as previously described, could be delivered according to clinical judgment and if S_{pO_2} was < 94%. During recovery from anesthesia, subjects were transferred to the postanesthesia care unit while spontaneously breathing room air or, whenever required, oxygen via Venturi face mask, at which time they underwent a new lung ultrasound aeration evaluation.

Study steps were defined as follows (Figure 1): baseline, in the absence of external PEEP (T0), randomization immediately after recruitment maneuver (T1), 20 min (T2), 60 min (T3), and 120 min after application of the randomized ventilatory strategy (T4), and at the end of surgery, in a supine position, after elimination of pneumoperitoneum (T5).

Measurements

Demographic characteristics such as sex, age, ASA physical status, body mass index, and ideal body weight were obtained for each subject. Arterial pH, the ratio of arterial partial pressure of oxygen to the fraction of inspired oxygen oxygenation (P_{aO_2}/F_{IO_2}), arterial carbon dioxide partial pressure, and lactate were assessed at randomization, at 60 min, at 120 min, and at the end of surgery. Hemodynamic status was continuously assessed throughout the study; mean arterial blood pressure and heart rate were collected from T0 to T5.

Flow and airway pressure were obtained with a heated pneumotachograph (Fleisch no. 2; Fleisch, Lausanne, Switzerland) installed between the endotracheal tube and the respiratory circuit. Esophageal and gastric pressures, together with flow and airway pressure signals, were recorded, digitalized, and collected via a dedicated acquisition system and software on a personal computer (ICU Lab, Kleistek, Bari, Italy). Esophageal balloon calibration
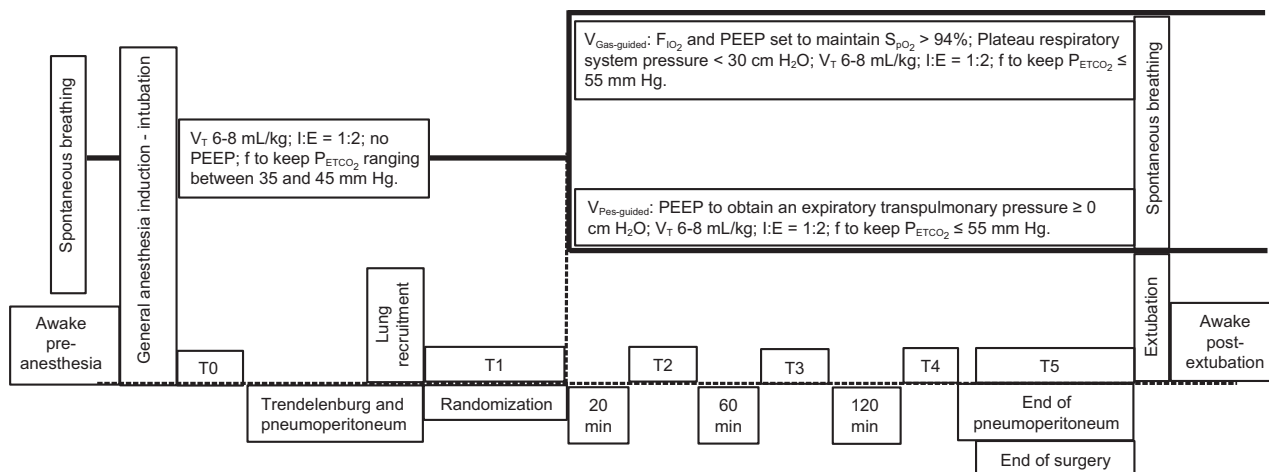
Fig. 1. Study time points. V_T = tidal volume; I:E = mechanical inspiratory-expiratory ratio; f = breathing frequency; P_{ETCO_2} = end-tidal carbon dioxide partial pressure; F_{IO_2} = inspiratory oxygen fraction; S_{pO_2} = peripheral oxygen saturation; $V_{Gas-guided}$ = conventional low-tidal ventilation with PEEP set according to gas exchange; $V_{Pes-guided}$ = low-tidal ventilation tailoring PEEP according to esophageal pressure.

was performed throughout the anesthesia period (T0–T5) during any change in PEEP, body position, or pneumoperitoneum pressure.[23] We created a dedicated spreadsheet (Excel, Microsoft, Redmond, Washington) to compute the calibrated esophageal pressure and respiratory mechanics at optimal filling volume.

At each step from T0 to T5, occlusion maneuvers at both end-expiration and end-inspiration were performed to measure static pressures in the airways ($PEEP_{tot}$, P_{plat}) and in the chest. These values were used to compute static expiratory and inspiratory transpulmonary pressures. Plateau elastance-derived transpulmonary pressure was also calculated.[32,33] Peak inspiratory pressure, tidal volume, and inspiratory flow were also noted. Airway resistance, elastance, and driving pressure of respiratory system, chest wall, and lung were calculated.

Lung ultrasounds were assessed before anesthesia induction and after recovery from anesthesia in the spontaneously breathing subjects.[19-21] On each hemithorax, 6 ultrasound regions were identified as follows: by using anterior and posterior axillary as anatomical landmarks, each side was divided into 3 zones that were furtherly partitioned into an upper and lower area. These zones were scanned with a linear or convex probe. For each explored region, the worst finding was reported according to the following rating: normal: 0; well-separated B-lines: 1; coalescent B-lines: 2; and consolidation: 3. The cumulative lung ultrasound score corresponds to the sum of each examined region score and ranged between 0 (minimum score, normal lungs) and 36 (maximum score, both consolidated lungs).

Anesthesiologic and surgical outcomes such as surgery, pneumoperitoneum, duration of Trendelenburg position, intraabdominal pressure applied, total number of lung recruiting maneuvers performed for each subject, the number of subjects in whom vasoactive drugs were administrated, diuresis, and fluids administration rate were acquired. Length of hospital stay was also recorded.

Statistical Analysis

To detect an average intraoperative P_{aO_2}/F_{IO_2} difference of 80 mm Hg and a standard deviation (SD) of 60 mm Hg (standardized mean difference = 1.3) at 120 min after randomization between the 2 study groups, considering the time needed for the PEEP to affect oxygenation,[34] a sample size of 28 subjects (14 per group, randomization ratio 1:1) was deemed suitable (power 80%, alpha 0.05). This difference considered the oxygenation improvement induced by PEEP as reported in previous studies.[17,35] Continuous variables were reported as mean ± SD. Comparison between groups was assessed using the Mann-Whitney test with the Holm-Sidak method correction. The Friedman test and the Dunn test correction were applied for trend analysis. Categorical variables were evaluated with the Fisher exact test. P values < .05 were considered statistically significant. Statistical analyses were conducted using Prism 6.0 software (Graph-pad, La Jolla, California).

Results

Demographic and Surgery Data

From September 2017 to January 2019, 49 nonconsecutive patients undergoing elective pelvic robotic surgery were considered eligible, of whom 31 were included in the study (Figure 2). Finally, 28 subjects successfully
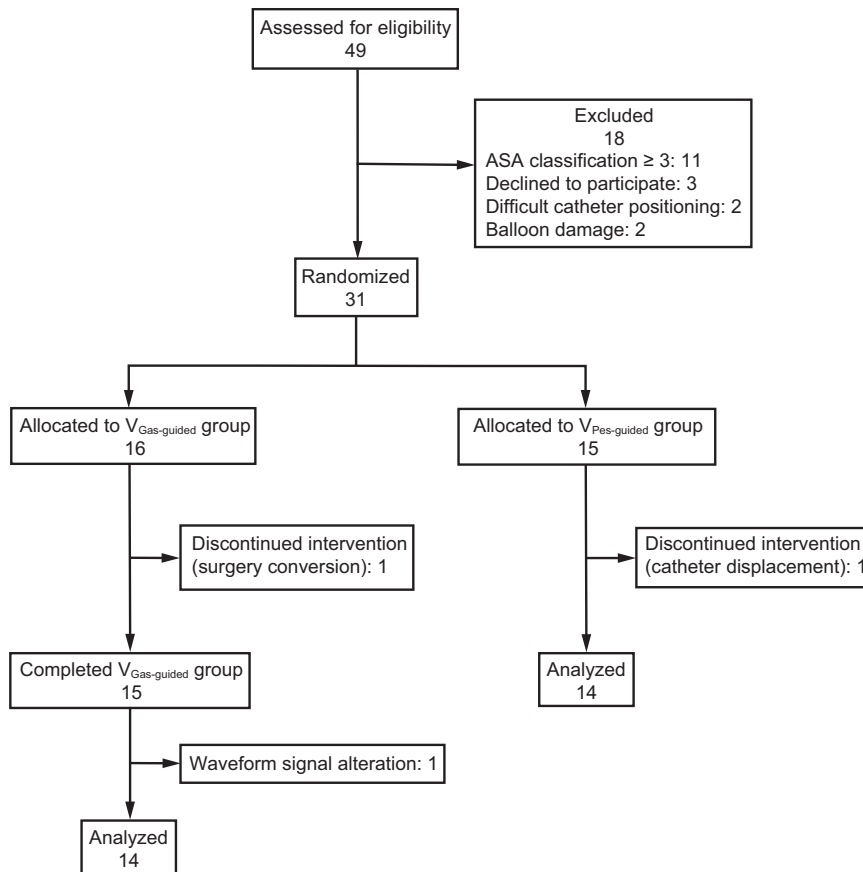
Fig. 2. Flow chart. ASA = American Society of Anesthesiologists; $V_{Gas-guided}$ = conventional low-tidal ventilation with PEEP set according to gas exchange; $V_{Pes-guided}$ = low-tidal ventilation tailoring PEEP according to esophageal pressure.

Table 1. Demographic Characteristics

Subjects	$V_{Gas-guided}$	$V_{Pes-guided}$	P
Male	8 (57.1)	7 (50)	.99
Age, y	62.5 ± 9.5	62.8 ± 11.4	.92
ASA classification II	12 (85.7)	11 (78.6)	.99
Body mass index, kg/m²	25.4 ± 2.6	24.1 ± 4.1	.25
Ideal body weight, kg	63.2 ± 9.0	61.9 ± 8.2	.74

Data are presented as n (%) or mean ± SD. n = 14 subjects in each group.
$V_{Gas-guided}$ = conventional low-tidal ventilation with PEEP set according to gas exchange
$V_{Pes-guided}$ = low-tidal ventilation tailoring PEEP according to esophageal pressure
ASA = American Society of Anesthesiologists

completed the study and were analyzed. Demographic characteristics were similar in the 2 groups (Table 1).

Ventilator Settings

As reported in Table 2, applied PEEP was lower in the $V_{Gas-guided}$ group compared to the $V_{Pes-guided}$ group at T2 ($P < .001$), T3 ($P < .001$), and T4 ($P = .002$). At T5, PEEP decreased compared to T2, T3 and T4 in the $V_{Pes-guided}$ group, without difference with respect to $V_{Gas-guided}$ group. Tidal volume, breathing frequency, and minute ventilation were comparable in both study groups. Breathing frequency and minute ventilation progressively increased from T0 to T3 in both ventilatory strategies.

Gas Exchange

The effects on arterial blood gases exerted by these ventilatory strategies are depicted in Table 3. After randomization, P_{aO_2}/F_{IO_2} progressively diverged in the subjects, and it was higher in the $V_{Pes-guided}$ group at T3 ($P = .02$), T4 ($P = .008$), and T5 ($P = .009$) compared to the $V_{Gas-guided}$ group; this difference was ascribed to an oxygenation improvement in the $V_{Pes-guided}$ group but not in the $V_{Gas-guided}$ group. F_{IO_2}, arterial carbon dioxide partial pressure, and lactate levels did not differ among groups.

Respiratory Mechanics

Static pressures, elastances, and driving pressures of the global respiratory system, chest wall, and lung are reported in Table 4. PEEP$_{tot}$ was lower at T2 ($P < .001$),

Table 2. Volume Control Mode Settings

Parameters	T0	T1	T2	T3	T4	T5
V_T, mL/kg						
$V_{Gas-guided}$	7.6 ± 0.3	7.6 ± 0.2	7.8 ± 0.2	7.8 ± 0.2	7.7 ± 0.2	7.7 ± 0.3
$V_{Pes-guided}$	7.6 ± 0.3	7.6 ± 0.3	7.7 ± 0.3	7.7 ± 0.4	7.7 ± 0.4	7.8 ± 0.3
Breathing frequency, breaths/min						
$V_{Gas-guided}$	14 ± 1	15 ± 2	17 ± 3†	18 ± 2†‡	18 ± 2†	18 ± 2†‡
$V_{Pes-guided}$	14 ± 1	15 ± 1	17 ± 3	19 ± 3†‡	20 ± 4†‡	20 ± 4†‡
Minute ventilation, L/min						
$V_{Gas-guided}$	6.1 ± 2.0	6.4 ± 2.2	7.1 ± †	7.7 ± 3.1†‡	8.2 ± 2.6†‡	8.2 ± 2.6†‡
$V_{Pes-guided}$	6.2 ± 1.8	6.3 ± 2.3	7.2 ± 3.2	7.9 ± 3.5†‡	8.3 ± 3.7†‡	8.1 ± 3.4†‡
PEEP, cm H_2O						
$V_{Gas-guided}$	0 ± 0	0 ± 0	5.1 ± 2.3*†‡	5.1 ± 2.0*†‡	5.2 ± 2.1*†‡	5.9 ± 2.6†‡
$V_{Pes-guided}$	0 ± 0	0 ± 0	11.2 ± 4.6†‡	11.6 ± 4.7†‡	10.4 ± 5.3†‡	5.5 ± 2.7§

Data are presented as mean ± SD.
* $V_{Gas-guided}$ vs $V_{Pes-guided}$ ($P < .05$).
† vs T0 ($P < .05$).
‡ vs T1 ($P < .05$).
§ vs T2, T3, and T4 ($P < .05$).
T0 = baseline
T1 = after recruitment maneuver, following pneumoperitoneum and definitive Trendelenburg position
T2 = 20 min after randomization
T3 = 60 min after randomization
T4 = 120 min after randomization
T5 = end of surgery, in supine position, after pneumoperitoneum elimination
$V_{Gas-guided}$ = conventional low-tidal ventilation with PEEP set according to gas exchange
$V_{Pes-guided}$ = low-tidal ventilation tailoring PEEP according to esophageal pressure
V_T = tidal volume

Table 3. Arterial Blood Gases

Parameters	Randomization	At 60 Min	At 120 Min	At End of Surgery
P_{aO_2}/F_{IO_2}, mm Hg				
$V_{Gas-guided}$	264 ± 66	308 ± 95*	308 ± 81*	312 ± 95*
$V_{Pes-guided}$	307 ± 102	388 ± 90†	400 ± 90†	402 ± 95†
F_{IO_2}				
$V_{Gas-guided}$	0.50 ± 0.06	0.47 ± 0.06	0.48 ± 0.07	0.48 ± 0.08
$V_{Pes-guided}$	0.47 ± 0.05	0.42 ± 0.07	0.41 ± 0.07	0.41 ± 0.07
P_{aCO_2}, mm Hg				
$V_{Gas-guided}$	47.1 ± 4.6	44.0 ± 2.9	42.3 ± 2.9†	42.0 ± 3.2
$V_{Pes-guided}$	44.5 ± 6.1	42.7 ± 5.1	41.1 ± 3.9	40.6 ± 3.7
pH				
$V_{Gas-guided}$	7.33 ± 0.04	7.33 ± 0.03	7.33 ± 0.03	7.32 ± 0.02
$V_{Pes-guided}$	7.33 ± 0.05	7.34 ± 0.04	7.35 ± 0.03	7.35 ± 0.04
Lactate, mmol/L				
$V_{Gas-guided}$	0.52 ± 0.12	0.59 ± 0.21	0.64 ± 0.21	0.73 ± 0.21†
$V_{Pes-guided}$	0.49 ± 0.12	0.55 ± 0.19	0.60 ± 0.21	0.64 ± 0.22†

Data are presented as mean ± SD.
* $V_{Gas-guided}$ vs $V_{Pes-guided}$ ($P < .05$).
† vs randomization ($P < .05$).
$V_{Gas-guided}$ = conventional low-tidal ventilation with PEEP set according to gas exchange
$V_{Pes-guided}$ = low-tidal ventilation tailoring PEEP according to esophageal pressure
P_{aO_2}/F_{IO_2} = ratio of arterial partial pressure of oxygen to the fraction of inspired oxygen

T3 ($P < .001$), and T4 ($P < .001$) in the $V_{Gas-guided}$ group compared to the $V_{Pes-guided}$ group. This difference was eliminated at T5 when $PEEP_{tot}$ was similar in both groups. Peak inspiratory pressure, P_{plat}, and inspiratory and expiratory chest wall pressure increased from T1 to T2, T3, and T4 with PEEP application and finally diminished at T5 to values similar to baseline in both groups. Expiratory transpulmonary pressure was lower at T2 ($P < .001$), T3 ($P < .001$), and T4 ($P = .002$) in the $V_{Gas-guided}$ group compared to the $V_{Pes-guided}$ group. Inspiratory transpulmonary pressure was lower in the $V_{Gas-guided}$ group than in the $V_{Pes-guided}$ group at T3 ($P = .003$) and T4 ($P = .005$).

Figure 3 depicts elastance and driving pressure trends during the study. Respiratory system and chest wall elastance and driving pressure worsened from T0 to T1 in both study groups. PEEP administration improved elastance and driving pressure from T4 to T5 in the $V_{Gas-guided}$ group and from T2 to the end of surgery in the $V_{Pes-guided}$ group. Respiratory system elastance was higher in the $V_{Gas-guided}$ group compared to the $V_{Pes-guided}$ group at T2 (33.4 ± 10.7 vs 24.2 ± 7.3 cm H_2O/L, $P = .001$) and T3 (31.9 ± 8.5 vs 24.1 ± 5.4 cm H_2O/L, $P = .006$), whereas chest wall elastance was greater only at T2 (18.2 ± 6.3 vs 13.2 ± 5.8 cm H_2O/L, $P = .007$). Respiratory system driving pressure was higher in the $V_{Gas-guided}$ group compared to the $V_{Pes-guided}$ group at T2 (15.8 ± 3.6 vs 11.3 ± 2.6 cm H_2O, $P < .001$), T3 (15.5 ± 3.4 vs 11.3 ± 2.0 cm H_2O, $P < .001$), T4 (14.5 ± 3.4 vs 11.3 ± 1.8 cm H_2O, $P = .005$), and T5 (10.8 ± 2.6 vs 8.5 ± 1.6 cm H_2O, $P = .01$), whereas chest wall driving pressure was greater only at T2 (8.7 ± 2.2 vs 6.0 ± 2.2 cm H_2O, $P < .001$), T3 (8.8 ± 2.7 vs 6.1 ± 1.9 cm H_2O, $P < .001$), and T4 (7.2 ± 2.3 vs 5.2 ± 1.6 cm H_2O, $P = .007$).

Lung Ultrasound and Outcomes

As shown in Figure 4, the lung ultrasound score worsened after extubation in both groups, reaching higher values

Table 4. Respiratory Mechanics

Parameters	Study Steps					
	T0	T1	T2	T3	T4	T5
PEEP$_{tot}$, cm H$_2$O						
V$_{Gas-guided}$	0.2 ± 0.8	0.6 ± 1.6	5.2 ± 2.4*†‡	5.3 ± 2.0*†‡	5.5 ± 2.2*†‡	6.1 ± 2.7†‡
V$_{Pes-guided}$	0.2 ± 0.6	0.9 ± 2.4	11.4 ± 4.8†‡	11.8 ± 4.9†‡	10.6 ± 5.5†‡	5.6 ± 2.7§
PIP, cm H$_2$O						
V$_{Gas-guided}$	15.1 ± 3.4	25.7 ± 9.4†	27.4 ± 5.5†	29.5 ± 5.8†‡	27.6 ± 5.8†	22.6 ± 4.1§
V$_{Pes-guided}$	14.8 ± 4.1	21.9 ± 5.7	29.2 ± 4.2†‡	31.3 ± 6.0†‡	29.0 ± 6.2†	20.4 ± 3.1§
P$_{plat}$, cm H$_2$O						
V$_{Gas-guided}$	9.8 ± 2.6	18.2 ± 4.0	21.0 ± 3.9†	20.8 ± 3.8†‡	20.0 ± 3.9†	16.9 ± 3.0§
V$_{Pes-guided}$	9.7 ± 2.9	15.9 ± 4.5	22.7 ± 4.3†‡	23.0 ± 4.9†‡	22.0 ± 5.8†‡	14.1 ± 3.1§
PE$_{CW}$, cm H$_2$O						
V$_{Gas-guided}$	4.4 ± 1.8	7.8 ± 5.0	9.7 ± 5.3†	9.1 ± 4.6†	9.1 ± 5.0†	7.5 ± 2.8
V$_{Pes-guided}$	3.6 ± 2.7	6.9 ± 4.9	11.6 ± 4.8†‡	11.1 ± 5.5†‡	10.0 ± 6.1†	5.8 ± 4.4§
PI$_{CW}$, cm H$_2$O						
V$_{Gas-guided}$	8.9 ± 1.6	17.3 ± 4.6†	18.3 ± 4.9†	17.9 ± 4.5†	16.3 ± 5.2†	11.5 ± 2.4‡§
V$_{Pes-guided}$	7.5 ± 3.2	15.0 ± 4.7†	17.6 ± 3.9†	17.2 ± 5.2†	15.2 ± 5.8†	9.0 ± 3.6§
PE$_L$, cm H$_2$O						
V$_{Gas-guided}$	-4.3 ± 1.6	-7.1 ± 4.7	-4.5 ± 5.3*	-3.8 ± 4.5*‡	-3.6 ± 4.7*‡	-1.4 ± 2.6†‡§
V$_{Pes-guided}$	-3.4 ± 2.6	-5.9 ± 3.3	-0.2 ± 2.0†‡	0.7 ± 1.3†‡	0.5 ± 1.3†‡	-0.2 ± 2.6‡
PI$_L$, cm H$_2$O						
V$_{Gas-guided}$	0.8 ± 1.9	0.9 ± 2.6	2.7 ± 3.6	2.9 ± 2.7*‡	3.7 ± 2.9*†‡	5.4 ± 3.0†‡
V$_{Pes-guided}$	2.2 ± 1.9	0.9 ± 1.8	5.1 ± 2.5‡	5.8 ± 1.9†‡	6.3 ± 1.9†‡	5.4 ± 2.7‡
PI$_{Lderived}$, cm H$_2$O						
V$_{Gas-guided}$	5.4 ± 2.3	8.3 ± 4.0	9.5 ± 4.0†	9.0 ± 4.1†	9.9 ± 4.1†	10.6 ± 4.3†
V$_{Pes-guided}$	5.8 ± 2.9	7.5 ± 3.9	10.8 ± 4.7†‡	10.7 ± 4.3†	11.8 ± 4.8†‡	9.5 ± 3.3
R$_{aw}$, cm H$_2$O/L/s						
V$_{Gas-guided}$	11.9 ± 3.8	13.1 ± 7.0	11.5 ± 4.9	13.9 ± 7.6	11.6 ± 6.8	8.7 ± 5.3†
V$_{Pes-guided}$	10.7 ± 3.3	12.8 ± 4.9	13.3 ± 3.6	13.2 ± 6.4	10.5 ± 5.0	10.0 ± 5.6§

Data are presented as mean ± SD.
* V$_{Gas-guided}$ vs V$_{Pes-guided}$ ($P < .05$).
† vs T0 ($P < .05$).
‡ vs T1 ($P < .05$).
§ vs T2, T3, and T4 ($P < .05$).
T0 = baseline
T1 = after recruitment maneuver, following pneumoperitoneum and definitive Trendelenburg position
T2 = 20 min after randomization
T3 = 60 min after randomization
T4 = 120 min after randomization
T5 = end of surgery, in supine position, after pneumoperitoneum elimination
V$_{Gas-guided}$ = conventional low-tidal ventilation with PEEP set according to gas exchange
V$_{Pes-guided}$ = low-tidal ventilation tailoring PEEP according to esophageal pressure
PEEP$_{tot}$ = respiratory system PEEP
PIP = peak inspiratory pressure
P$_{plat}$ = plateau respiratory system pressure
PE$_{CW}$ = expiratory chest wall pressure
PI$_{CW}$ = inspiratory chest wall pressure
PE$_L$ = expiratory transpulmonary pressure
PI$_L$ = inspiratory transpulmonary pressure
PI$_{Lderived}$ = inspiratory elastance-derived transpulmonary pressure
R$_{aw}$ = airway resistance

in the V$_{Gas-guided}$ group compared to the V$_{Pes-guided}$ group. Hemodynamic status was not different between study populations as represented in Figure 5. As described in Table 5, subjects in the V$_{Gas-guided}$ group and the V$_{Pes-guided}$ group experienced similar outcomes over the study duration. No difference in terms of length of hospital stay were noted between groups (4 ± 1 vs 4 ± 1 d).

Discussion

The main findings of our pilot investigation can be summarized as follows: intraoperative oxygenation improved in the V$_{Pes-guided}$ group while it remained stable in the V$_{Gas-guided}$ group; and respiratory system and chest wall mechanics were optimized with the V$_{Pes-guided}$
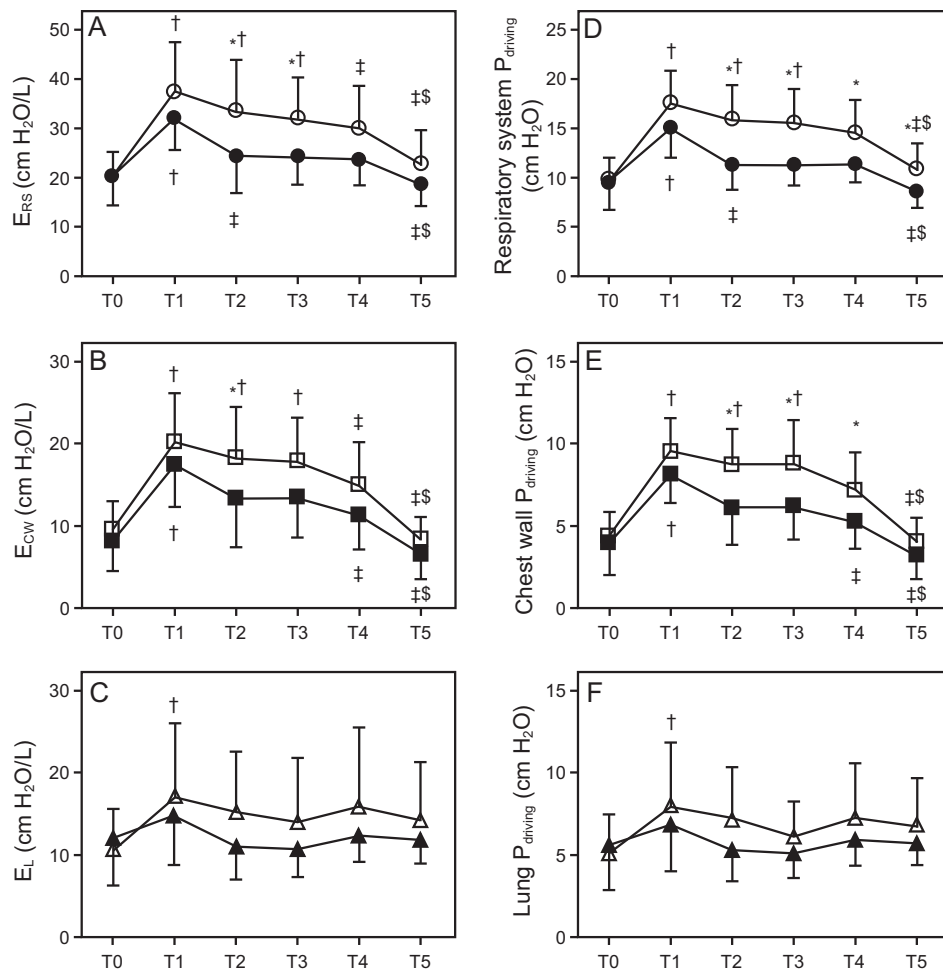
Fig. 3. Elastance and driving pressure. (A) Respiratory system elastance trend over entire study duration. (B) Chest wall elastance trend over entire study duration. (C) Lung elastance trend over entire study duration. (D) Respiratory system driving pressure trend over entire study duration. (E) Chest wall driving pressure trend over entire study duration. (F) Lung driving pressure trend over entire study duration. * $V_{Gas-guided}$ vs $V_{Pes-guided}$ ($P <.05$); † vs T0 ($P <.05$); ‡ vs T1, $P <.05$; $ vs T2, T3, T4 ($P <.05$). Data are presented as mean ± SD. White symbols = conventional low-tidal ventilation with PEEP set according to gas exchange; black symbols = low-tidal ventilation tailoring PEEP according to esophageal pressure. E = elastance; $P_{driving}$ = driving pressure; T0 = baseline; T1 = after recruitment maneuver, following pneumoperitoneum and definitive Trendelenburg position; T2 = 20 min after randomization; T3 = 60 min after randomization; T4 = 120 min after randomization; T5 = end of surgery, in supine position, after pneumoperitoneum elimination; E_{RS} = respiratory system elastance; E_{CW} = chest wall elastance; E_L = lung elastance.

approach, with a final reduction of the driving pressure applied during mechanical ventilation. In addition, this strategy had no impact on hemodynamic status and the clinical outcomes that we explored. In the $V_{Pes-guided}$ group, however, a nonsignificant incidence of higher vasoactive drug administration during the lung-recruiting maneuver, before randomization, was noted. This may be ascribed to a more pronounced propensity for hypotensive events observed in subjects in the $V_{Pes-guided}$ group compared to the control arm.

General anesthesia, pneumoperitoneum, and Trendelenburg position affect oxygenation by promoting atelectasis.[36] This phenomenon depends on a worsening of the functional residual capacity induced by a diaphragmatic cranial shift and stretch that usually occurs during

robotic surgery.[37-39] Moreover, the consequent impairment of respiratory mechanics and driving pressure can lead to ventilator-induced lung injury, which is a well-known risk factor for postoperative pulmonary complications.[10] Several trials have reported that PEEP application during pelvic robotic surgery improves oxygenation.[17,40] A recent investigation conducted in subjects undergoing laparotomic and laparoscopic surgery reported the benefit of electrical impedance tomography–guided PEEP on intraoperative oxygenation compared to a low-PEEP ventilation strategy.[35]

In keeping with previous work, P_{aO_2}/F_{IO_2} remained unchanged in the $V_{Gas-guided}$ group after randomization, whereas it increased progressively to higher values in the $V_{Pes-guided}$ group until the end of the surgery. Moreover, the
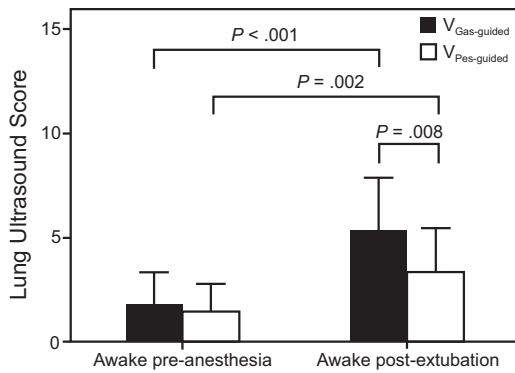
Fig. 4. Data are presented as mean ± SD. $V_{Gas-guided}$ = conventional low-tidal ventilation with PEEP set according to gas exchange; $V_{Pes-guided}$ = low-tidal ventilation tailoring PEEP according to esophageal pressure.
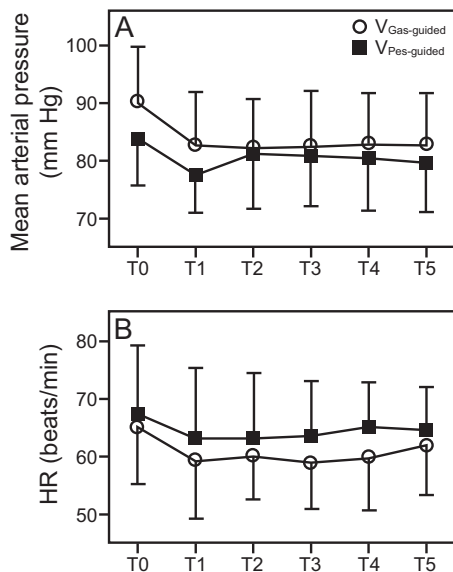

Fig. 5. Mean arterial blood pressure and heart rate. Data are presented as mean ± SD. T0 = baseline; T1 = after recruitment maneuver, following pneumoperitoneum and definitive Trendelenburg position; T2 = 20 min after randomization; T3 = 60 min after randomization; T4 = 120 min after randomization; T5 = end of surgery, in supine position, after pneumoperitoneum elimination.

oxygenation levels achieved through $V_{Pes-guided}$ PEEP were much higher compared to those obtained in the $V_{Gas-guided}$ group. The increase in P_{aO_2}/F_{IO_2} provided by the $V_{Pes-guided}$ approach could be ascribed to levels of PEEP that were similar to values previously applied via electrical impedance tomography–guided PEEP.[35] However, unlike the previous study, $V_{Pes-guided}$ PEEP provided a more restrained oxygenation improvement. Several factors most likely explain this result. First, in our series, P_{aO_2}/F_{IO_2} at randomization was similar between the study groups, whereas it was much higher in the electrical impedance tomography–guided group compared to

the control group. Second, in the $V_{Gas-guided}$ strategy, PEEP was not preset but was applied according to gas exchange. Finally, the lung-recruiting maneuver was planned after a decremental PEEP titration in the aforementioned investigation, whereas, in our study, it was applied following a PEEP-free volume-control stage. In this regard, lung recruitment was deemed mandatory in our study with the purpose of zeroing the lung history of each subject before PEEP application.[18]

PEEP has been proven to increase lung volume and counterbalance diaphragm cranial displacement induced by pneumoperitoneum and Trendelenburg position, improving chest wall and respiratory system mechanics with consequent reduction of driving pressure applied during mechanical ventilation.[14,35,38]

In this study, and in line with previous investigations, $V_{Pes-guided}$ PEEP, when compared to $V_{Gas-guided}$ PEEP, more incisively counteracted the negative effects of pneumoperitoneum and Trendelenburg position on chest wall and respiratory system reducing the respective elastance and driving pressure. Interestingly, under $V_{Pes-guided}$ PEEP, respiratory system driving pressure was constantly less than 12.5 cm H_2O, a well-defined limit of lower incidence of postoperative respiratory complications.[41] It is likely that PEEP set using the $V_{Pes-guided}$ strategy prevented substantial lung de-recruitment and worsening of global lung elastance, which was evident in the lung ultrasound scans after recovery from anesthesia. Conversely, negative values of expiratory transpulmonary pressure in $V_{Gas-guided}$ PEEP might have promoted both lung de-recruitment and tidal opening-closing of both alveoli and small airways, with opposite effects on lung elastance. De-recruitment increases lung elastance by diminishing the size of the lung, while cyclic opening and closing are associated with a tidal extra volume that decreases the measured lung elastance.[42] This may explain why lung mechanics and gas exchange were partially uncoupled in our study population. In addition, $V_{Pes-guided}$ PEEP appears to be a safe ventilatory plan because average plateau elastance-derived transpulmonary pressure never exceeded the overdistention threshold of the lung. On the contrary, a ventilatory scheme applying PEEP to equalize pneumoperitoneum pressure or providing periodical recruiting maneuvers could improve oxygenation and mechanical properties, although it may put subjects at risk for overdistention and hemodynamic instability.[43]

$V_{Pes-guided}$ PEEP, aiming to equalize expiratory transpulmonary pressure, could seem difficult to apply in routine laparoscopic surgery, but it could be particularly indicated in subjects who are at high risk of intraoperative lung de-recruitment and perioperative hypoxia to increase intraoperative oxygenation and ameliorate driving pressure.

Table 5. Clinical Outcomes

Subjects	$V_{Gas-guided}$	$V_{Pes-guided}$	P
Surgery duration, min	279 ± 57	263 ± 69	.42
Pneumoperitoneum and Trendelenburg duration, min	217 ± 69	214 ± 69	.99
Average pneumoperitoneum pressure, mm Hg	8.5 ± 3.1	8.4 ± 2.3	.92
Recruitment maneuver, n	1 ± 0	1 ± 0	> .99
Fluid administration, mL/kg/h	8.1 ± 3.1	8.5 ± 3.1	.72
Diuresis, mL/kg/h	1.8 ± 0.9	2.0 ± 1.2	.83
Vasoactive administration (during recruitment maneuver), n	6 (42.9)	11 (78.6)	.12

Data are presented as n (%) or mean ± SD. $n = 14$ subjects in each group.
$V_{Gas-guided}$ = conventional low-tidal ventilation with PEEP set according to gas exchange
$V_{Pes-guided}$ = low-tidal ventilation tailoring PEEP according to esophageal pressure

Our study has several limitations that make it impossible to draw definitive conclusions on the real benefits of $V_{Pes-guided}$ PEEP on oxygenation and respiratory mechanics. First, the study population was relatively small, although it was in line with a recent investigation conducted in an analogous laparoscopic setting.[35] Second, it could be argued that a standardized high-PEEP or an approach applying PEEP according to compliance or driving pressure was not adopted in the $V_{Gas-guided}$ group. However, our $V_{Gas-guided}$ strategy completely replicated the control arm of mechanical ventilation settings proposed in a recent investigation supporting the need to individualize PEEP in subjects undergoing general anesthesia for laparotomic or laparoscopic surgery.[35] Third, in the control group the administration of F_{IO_2} and PEEP were guided by gas exchange in agreement with our institutional protocol. However, a strategy that promotes PEEP modification over F_{IO_2} adjustment could have been more advantageous compared to that applied to our control group to improve respiratory function and gas exchange. Fourth, in evaluating chest wall and lung mechanics, it is worth considering the ventilation distribution between dependent and nondependent lung areas and the spatial pleural pressure gradients in the respiratory system.[44] Finally, some inhomogeneity in surgical procedures must be considered in interpreting our data.

Conclusions

In our setting, oxygenation, respiratory system mechanics, and driving pressure, improved when a $V_{Pes-guided}$ strategy was used, although no differences were detected in perioperative clinical outcomes. Our results need to be confirmed with future and larger investigations, conducted especially in subjects prone to develop intraoperative lung de-recruitment while undergoing elective pelvic robotic surgery.

ACKNOWLEDGMENTS

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