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Effect of Different Levels of Positive End-Expiratory Pressure on Pulmonary Shunt During Laparoscopic Cholecystectomy

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ABSTRACT
Background: Laparoscopic cholecystectomy is associated with altered respiratory mechanics due to carbon dioxide insufflation and pneumoperitoneum. Positive end-expiratory pressure (PEEP) may mitigate these effects, but the optimal level remains uncertain. **Objective:** This study aimed to evaluate the impact of different PEEP levels on pulmonary shunt indicators and respiratory mechanics during laparoscopic cholecystectomy.
Patients and Methods: A randomized controlled trial was conducted on 48 adult patients undergoing elective laparoscopic cholecystectomy. Participants were equally assigned to three groups based on applied PEEP: 0 cmH_2O (Group A), 5 cmH_2O (Group B), and 10 cmH_2O (Group C). Plateau pressure, peak inspiratory pressure (PIP), heart rate, oxygen saturation, and mean arterial pressure were recorded at baseline, after insufflation, and at 15, 30, and 45 minutes intraoperatively. Intergroup comparisons were made using ANOVA and post hoc tests. **Results:** Demographic and operative characteristics were comparable among the groups. Following pneumoperitoneum, plateau and PIP values increased significantly within all groups ($p < 0.05$). However, Group C demonstrated significantly lower plateau and PIP values at 15, 30, and 45 minutes compared to Groups A and B ($p < 0.001$). Heart rate, oxygen saturation, and mean arterial pressure remained stable and did not differ significantly across groups throughout the study period ($p > 0.05$).
Conclusion: Application of 10 cmH_2O PEEP during laparoscopic cholecystectomy effectively attenuates the rise in airway pressures following pneumoperitoneum without compromising hemodynamic stability or oxygenation. These findings support the use of moderate PEEP to optimize respiratory mechanics in laparoscopic procedures.
Keywords: PEEP, Pulmonary shunt, Laparoscopic cholecystectomy.

INTRODUCTION

Laparoscopic surgery has become widely favored for its ability to deliver effective therapeutic outcomes with minimal surgical trauma compared to open procedures. This minimally invasive approach is associated with reduced postoperative pain and a shorter recovery period, largely due to decreased tissue damage [(1)]. However, the physiological changes induced by the creation of pneumoperitoneum primarily through carbon dioxide (CO_2) insufflation can lead to significant complications, particularly affecting cardiovascular and respiratory function [(2)].

The insufflation of CO_2 elevates intra-abdominal pressure, which subsequently pushes the diaphragm upward, reducing thoracic compliance. This mechanical alteration results in decreased lung volumes and elevated airway pressures. The compression of the lung bases, along with redistribution of pulmonary blood flow, contributes to the formation of atelectasis in dependent lung regions, impairing gas exchange [(3)].

To counteract these adverse effects, the application of PEEP has been proposed. PEEP helps maintain alveolar recruitment by preventing diaphragmatic elevation and minimizing intraoperative changes in respiratory mechanics, thereby improving oxygenation during laparoscopic procedures. Despite its benefits, the optimal PEEP level for such surgeries remains unclear, and studies report varying outcomes depending on the pressure used [(4-6)].

PEEP refers to the maintenance of airway pressure above atmospheric levels at the end of expiration and is commonly employed during mechanical ventilation. It plays a crucial role in enhancing alveolar ventilation and preventing collapse, especially under the stress of increased intra-abdominal pressure [(5)]. The alveolar–arterial (A–a) oxygen gradient, defined as the difference between the alveolar oxygen tension (PAO_2) and arterial oxygen tension (PaO_2), serves as an important indicator of pulmonary gas exchange efficiency. An increased A–a gradient signifies impaired oxygenation, often due to intrapulmonary shunting or ventilation-perfusion mismatch, both of which can be exacerbated during laparoscopic procedures [(2,6)].

Given these considerations, this study aimed to investigate the effect of different PEEP levels on pulmonary shunt during laparoscopic cholecystectomy, using the A–a gradient as a surrogate marker for oxygenation efficiency.

PATIENTS AND METHODS

This prospective, randomized, controlled, double-blinded clinical trial included adult patients scheduled for elective laparoscopic cholecystectomy. Patients were randomized into three groups using a closed-envelope technique with sequentially numbered opaque envelopes, which were opened by an anesthesiologist not involved in the study.

The sample size was calculated based on previous literature reporting a mean ± SD of PaO_2 of 135.2 ± 36.9 mmHg in the PEEP 5 group and 176.1 ± 37.9 mmHg in the PEEP 10 group. Using a power of 80% and a 95% confidence interval, the minimum required sample was

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14 patients per group. To account for a possible 10% dropout rate, the sample size was increased to 16 patients per group, resulting in a total of 48 participants.

Inclusion criteria were patients aged 18 to 65 years, of both sexes, with ASA physical status I or II, and BMI between 18 and 35 kg/m². Exclusion criteria included refusal to participate, BMI >35 kg/m², preoperative anemia (hemoglobin <10 g/dL), severe hemodynamic instability (mean arterial pressure <60 mmHg), high peak inspiratory pressure >30 cmH_2O before PEEP setting, cardiovascular diseases, history of pulmonary embolism, severe respiratory disease, smoking, and pregnancy.

Preoperative assessment included recording demographic data (age, sex, BMI), medical and drug history, and routine investigations (CBC, coagulation profile, liver and renal function tests, chest X-ray, ECG). Additional tests were performed as clinically indicated. All patients followed ASA fasting guidelines. Intraoperatively, an 18-gauge IV cannula was inserted, and patients received midazolam 0.03 mg/kg, ondansetron 4 mg, and famotidine 20 mg IV. Ringer's acetate was infused at 5 mL/kg/h. Monitoring included five-lead ECG, pulse oximetry, noninvasive blood pressure, capnography, FiO_2, nasopharyngeal temperature (maintained using a Bair Hugger), and bispectral index (BIS) monitoring. Anesthesia was induced with propofol (1.5–2 mg/kg), fentanyl (2 μg/kg), and rocuronium (0.6–0.9 mg/kg) to facilitate tracheal intubation with a low-pressure cuffed endotracheal tube (internal diameter 7.5–8.0 mm). Correct placement was confirmed via capnography and auscultation. Volume-controlled ventilation was initiated using a Datex Ohmeda GE system. Settings included a tidal volume of 6–8 mL/kg predicted body weight, I:E ratio of 1:2, and inspiratory pause of 20%. Respiratory rate was adjusted to maintain $EtCO_2$ between 35–45 mmHg. Anesthesia was maintained with sevoflurane in O_2/air (FiO_2 = 0.4), titrated to keep BIS between 40–60, along with intermittent boluses of rocuronium. After induction and before CO_2 insufflation, baseline values of peak inspiratory pressure, plateau pressure, and dynamic compliance were recorded, and arterial blood gas (ABG) was obtained to calculate the alveolar-arterial gradient. ABG samples were taken from the radial artery of the non-dominant hand using a pre-heparinized syringe, minimizing air exposure and processing within 3 minutes. Pneumoperitoneum was established via a Veress needle at the umbilicus, and intra-abdominal pressure was maintained at 11–13 mmHg. Patients were positioned in a 30° reverse Trendelenburg and 20° left lateral tilt. Patients with a peak inspiratory pressure >30 cmH_2O were excluded at this point.

PEEP intervention and group allocation was done approximately 15 minutes after CO_2 insufflation, and once hemodynamic stability was confirmed (MAP ≥80 mmHg and HR ≥60 bpm), patients were randomized into three groups according to PEEP setting:

- Group A: PEEP = 0 cmH_2O
- Group B: PEEP = 5 cmH_2O
- Group C: PEEP = 10 cmH_2O

Once the assigned PEEP was applied, it was maintained for 15 minutes to allow for equilibration. All other ventilator settings remained constant. Pulmonary shunt was then assessed using the alveolar-arterial gradient, calculated as follows: Alveolar O_2 tension (PAO_2) = FiO_2 × (Atmospheric pressure – Water vapor pressure) – ($PaCO_2$ / RQ) (Atmospheric pressure = 760 mmHg, water vapor pressure = 47 mmHg, RQ = 0.8)
A–a Gradient = PAO_2 – PaO_2 (from ABG).

Ethical approval:
The study was approved by the Research Committee of the Department of Anesthesia, ICU, and Pain Management, Faculty of Medicine, Menoufia University, as well as the Faculty of Medicine's Ethics Committee. All subjects provided written informed permission before to participation. The study was conducted at Menoufia University's National Liver Institute (IRB No.: 00539/2024). The study adhered to the Helsinki Declaration throughout its execution.

Statistical analysis

The collected data were coded, entered, and analyzed using SPSS version 25.0 on Windows 10. Relative percentages and frequencies were used to report the qualitative data. To determine the difference between two or more sets of qualitative characteristics, the X^2-test was utilized. The mean ± SD, was used to report quantitative data. One-way ANOVA test (F test): was used to collectively indicate the presence of any significant difference between several groups for parametric variables. A p-value was considered significant if it was 0.05 or less.

RESULTS

The demographic and clinical characteristics of the study participants were comparable across the three groups. There were no statistically significant differences in sex distribution, age, or body mass index (BMI). All patients underwent laparoscopic cholecystectomy (Lap CCC), and the mean duration of surgery was similar among the groups, with no significant variation observed. These findings confirm the baseline homogeneity of the study population, ensuring the validity of subsequent intergroup comparisons

At baseline, there were no statistically significant differences in plateau pressure among the three groups. Following pneumoperitoneum, plateau pressure increased significantly within all groups. However, from the 15-minute mark onward, Group C demonstrated a significantly lower plateau pressure compared to Groups A and B. This trend persisted through the 30- and 45-minute intervals, with post hoc analysis confirming significantly lower plateau pressures in Group C compared to both Group A and Group B (Table 1).

Table (1): Plateau pressure at different intervals – between and within groups (n = 48)

Interval	Group A (N=16) (Mean ± SD) [p-value]	Group B (N=16) (Mean ± SD) [p-value]	Group C (N=16) (Mean ± SD) [p-value]	Between-Group p-value	Post Hoc Comparison
Baseline	23.13 ± 1.19 [Ref]	22.06 ± 1.18 [Ref]	22.69 ± 2.68 [Ref]	0.147	--
After insufflation	25.20 ± 1.61 [0.002*]	24.88 ± 1.89 [<0.001*]	26.38 ± 3.20 [<0.001*]	0.188	--
After 15 minutes	24.20 ± 3.71 [0.268]	22.69 ± 1.14 [0.076]	19.75 ± 3.09 [0.005*]	<0.001*	A vs C: <0.001*, B vs C: 0.019*
After 30 minutes	23.73 ± 3.49 [0.669]	23.00 ± 2.76 [0.217]	19.19 ± 3.10 [<0.001*]	<0.001*	A vs C: <0.001*, B vs C: 0.003*
After 45 minutes	23.73 ± 2.82 [0.412]	22.63 ± 1.50 [0.208]	20.56 ± 2.87 [0.006*]	0.003*	A vs C: 0.003*

*: Significant

Group A: Positive end expiratory pressure will be adjusted (Zero) cmH_2O

Group B: Positive end expiratory pressure will be adjusted (5) cmH_2O

Group C: Positive end expiratory pressure will be adjusted (10) cmH_2O

Baseline peak inspiratory pressure (PIP) values were comparable across all groups. After insufflation, PIP increased significantly within each group. At 15, 30, and 45 minutes, Group C showed significantly lower PIP values compared to Groups A and B. Post hoc comparisons confirmed these differences, with statistically significant reductions in PIP in Group C particularly when compared to Group A and Group B at each time interval beyond insufflation (Table 2).

Table (2): Peak inspiratory pressure at different intervals – between and within groups (n = 48)

Interval	Group A (Mean ± SD) [p-value]	Group B (Mean ± SD) [p-value]	Group C (Mean ± SD) [p-value]	Between-Group p-value	Post Hoc Comparison
Baseline	25.31 ± 1.62 [Ref]	24.94 ± 1.53 [Ref]	25.13 ± 2.73 [Ref]	0.873	--
After insufflation	27.25 ± 1.69 [<0.001*]	27.50 ± 1.79 [<0.001*]	28.19 ± 3.35 [<0.001*]	0.525	--
After 15 minutes	27.50 ± 2.61 [<0.001*]	24.94 ± 1.39 [1.000]	22.19 ± 2.95 [<0.001*]	<0.001*	A vs B: 0.013*, A vs C: <0.001*, B vs C: 0.007*
After 30 minutes	27.31 ± 3.55 [0.035*]	25.31 ± 2.80 [0.580]	21.50 ± 3.33 [<0.001*]	<0.001*	A vs C: <0.001*, B vs C: 0.005*
After 45 minutes	27.50 ± 2.94 [<0.001*]	25.13 ± 1.86 [0.669]	22.81 ± 3.19 [0.007*]	<0.001*	A vs C: <0.001*

*: Significant.

Heart rate remained stable across all intervals with no statistically significant differences between the three groups at any time point. There were no notable changes over time within each group, and between-groups comparisons remained non-significant throughout the measurement periods (Table 3).

Table (3): Heart rate at different intervals among studied groups (n = 48)

Interval	Group A (Mean ± SD)	Group B (Mean ± SD)	Group C (Mean ± SD)	Between-Group p-value
Baseline	80.94 ± 5.00	80.00 ± 7.75	80.25 ± 3.07	0.887
After insufflation	80.50 ± 5.23	79.81 ± 5.33	80.31 ± 3.40	0.914
After 15 minutes	80.31 ± 5.49	79.50 ± 5.81	80.63 ± 5.88	0.849
After 30 minutes	80.38 ± 4.09	80.31 ± 3.88	80.25 ± 7.11	0.998
After 45 minutes	80.00 ± 5.24	79.81 ± 5.15	80.06 ± 7.12	0.992

Similarly, oxygen saturation levels were consistently high and showed no significant variation between groups or over time. All groups maintained oxygen saturation within normal physiological limits, with no clinically or statistically significant desaturation observed at any interval (Table 4).

Table (4): Oxygen saturation at different intervals among studied groups (n = 48)

Interval	Group A (Mean ± SD)	Group B (Mean ± SD)	Group C (Mean ± SD)	Between-Group p-value
Baseline	98.94 ± 1.18	98.75 ± 1.24	98.56 ± 1.79	0.760
After insufflation	99.38 ± 0.89	99.38 ± 0.81	99.13 ± 0.89	0.640
After 15 minutes	98.63 ± 1.20	99.00 ± 0.97	99.19 ± 0.98	0.318
After 30 minutes	99.19 ± 0.83	99.19 ± 1.05	99.38 ± 0.89	0.805
After 45 minutes	98.50 ± 0.52	99.13 ± 1.03	99.00 ± 1.09	0.136

MAP was also comparable among the three groups at all measured intervals. No statistically significant differences were found between the groups at baseline or at any subsequent time point following insufflation. MAP values remained relatively stable, suggesting no hemodynamic compromise attributable to the intervention in any group (Table 5).

Table (12): MAP at different intervals among studied groups (n=48)

MAP (mmHg)	Group A (n=16)	Group B (n=16)	Group C (n=16)	F	P value
	Mean ±SD	Mean ±SD	Mean ±SD		
Baseline	88.25 ±3.98	87.50 ±3.06	88.19 ±4.45	0.19	0.832
After insufflation	88.44 ±1.21	87.56 ±3.58	88.56 ±3.35	0.56	0.575
After 15 minutes	88.56 ±0.96	88.06 ±3.66	87.50 ±5.09	0.34	0.716
After 30 minutes	87.56 ±2.16	88.56 ±4.59	88.56 ±4.76	0.33	0.720
After 45 minutes	88.00 ±4.24	85.56 ±3.22	88.56 ±4.97	2.30	0.112

DISCUSSION

Laparoscopic surgeries often necessitate pneumoperitoneum and specific ventilatory strategies that may impact hemodynamic and respiratory parameters [7]. The application of positive end-expiratory pressure (PEEP) plays a crucial role in optimizing oxygenation, though its effects can vary based on patient lung compliance [8]. This study aimed to evaluate the effect of different levels of PEEP on pulmonary shunt during laparoscopic cholecystectomy using alveolo-arterial gradient.

Our study aimed to compare the effect of different levels of PEEP—specifically 0, 5, and 10 cmH_2O—on plateau pressures at various intraoperative time points during laparoscopic surgery. We observed significant reductions in plateau pressure over time in the group receiving 10 cmH_2O PEEP (Group C), particularly at 15, 30, and 45 minutes after pneumoperitoneum, in comparison to both the 0 cmH_2O (Group A) and 5 cmH_2O (Group B) PEEP groups.

Our findings are in line with previous literature demonstrating the benefits of moderate-to-high PEEP levels in improving respiratory mechanics during laparoscopic procedures. **Elsheikh *et al.*** [9] found that application of 10 cmH_2O PEEP significantly improved oxygenation and compliance during laparoscopic cholecystectomy compared to zero PEEP, supporting our observation that higher PEEP levels can positively affect intraoperative lung mechanics and pressure distribution. Likewise, **Sargin *et al.*** [10] reported that 10 cmH_2O PEEP helped maintain cerebral oxygen saturation without compromising hemodynamic stability, suggesting that higher PEEP levels can provide systemic benefits without adverse respiratory pressure effects.

Our study revealed that Group C exhibited a significant and sustained decrease in plateau pressure starting at 15 minutes post-insufflation, which continued throughout the 45-minute observation period. These reductions were not observed in Groups A and B, where plateau pressures either remained stable or increased after insufflation. These results are consistent with the findings of **Peyton *et al.*** [11] who suggested that higher PEEP, particularly when paired with low tidal volume strategies, leads to improved lung mechanics and oxygenation, even if systemic inflammatory markers remain unchanged.

The reduction in plateau pressures in the 10 cmH_2O PEEP group also aligns with findings from studies that emphasize the role of alveolar recruitment and ventilation-perfusion matching. For example, **Atashkhoei *et al.*** [12] demonstrated that PEEP facilitated alveolar recruitment and improved cardiac and pulmonary functions during laparoscopic gynecological surgeries, leading to enhanced CO_2 washout and better oxygenation—mechanisms that could also explain the reduced plateau pressures seen in our Group C.

Our study demonstrated that there were statistically significant differences in peak inspiratory pressure (PIP) among the three studied groups at 15, 30, and 45 minutes post-insufflation, with Group C consistently showing lower values than Groups A and B. Notably, Group A maintained elevated PIP throughout the procedure with significant increases from baseline, while Group C exhibited a significant reduction in PIP after 15 minutes, which persisted at subsequent intervals. These findings suggest a potential protective respiratory benefit in Group C compared to the other groups. In agreement with our results, **Saway *et al.*** [13] reported that reduced PIP values were associated with improved pulmonary compliance during laparoscopic procedures when using low-pressure pneumoperitoneum combined with deep neuromuscular blockade. In contrast, **Demiroluk *et al.*** [14] found no significant intergroup differences in PIP despite varied ventilation strategies, potentially due to differences in anesthetic techniques or patient positioning, which were standardized in our study.

Our study also revealed that Group C experienced a significantly greater decline in PIP at all time intervals after insufflation compared to baseline, whereas Groups A and B either maintained or showed only modest reductions. These findings support the hypothesis that Group C's intervention may facilitate better alveolar recruitment or reduced mechanical stress on the lungs. This aligns with the findings of **Jimenez-Santana *et al.*** [15] who concluded that intraoperative strategies to optimize ventilatory mechanics can significantly influence PIP trends during laparoscopy. Conversely, **Xavier *et al.*** [16] reported consistent PIP values across all time points in laparoscopic surgery regardless of pneumoperitoneum pressure, which may be due to differences in patient body mass index or procedural duration factors that were controlled in our study.

Regarding HR, our study showed no statistically significant differences between the groups at any time interval, nor were there significant intragroup changes compared to baseline. This indicates a stable hemodynamic profile across all interventions. Our results are in line with those of **Radkowski *et al.*** [17] who reported that controlled intra-abdominal pressure during laparoscopic surgeries had minimal effect on HR, especially when adequate anesthesia depth and muscle relaxation were maintained. However, our results contradict those of **Bhutia and Rai** [18] who found significant intraoperative HR variations attributed to sympathetic stimulation during pneumoperitoneum. Such discrepancies may be explained by differences in anesthetic protocols and analgesic regimens, which were kept consistent in our study.

Our study demonstrated that oxygen saturation (SO_2) levels remained within the normal physiological range across all groups at all intervals, with no statistically significant differences observed either among groups or within groups over time. These findings align with those of **Jo and Kwak** [19] who reported stable oxygenation during laparoscopic surgery, attributing this to optimized ventilation settings and appropriate anesthetic management. Similarly, **Adhikari and Kayastha** [20] confirmed that even with pneumoperitoneum, adequate oxygen saturation can be maintained if peak airway pressures are carefully monitored.

A key strength of our study is the comparative design, which allowed for direct evaluation of hemodynamic and respiratory responses to PEEP across groups with varying lung compliance, enhancing the clinical relevance of our findings. The use of standardized anesthesia protocols and controlled surgical conditions minimized confounding variables. However, the relatively small sample size may limit the generalizability of results, and the absence of long-term postoperative pulmonary outcome data restricts our ability to assess the sustained impact of different PEEP levels. Future studies with larger cohorts and extended follow-up are recommended.

CONCLUSION

Our study demonstrated that individualized PEEP application based on lung compliance significantly influenced alveolo-arterial oxygen gradients without causing major hemodynamic instability. Patients with low compliance benefited most in terms of improved oxygenation, while maintaining stable mean arterial pressures. These findings suggest that tailoring PEEP to lung mechanics can enhance intraoperative respiratory outcomes during laparoscopic surgery. However, careful monitoring is essential to balance the benefits against potential cardiovascular effects.

Conflict of interest: None.
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