International Journal of Medical and Pharmaceutical Research

Online ISSN-2958-3683 | Print ISSN-2958-3675
Frequency: Bi-Monthly
Available online on: https://ijmpr.in/

Original Article

Comparison Of Inflammatory Markers in Low Presuure with Standard Pressure with Standard Pressure Laproscopic Cholecystectomy

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Received: 07-05-2026
Accepted: 29-06-2026
Available online: 04-07-2026

ABSTRACT

Laparoscopic cholecystectomy is the gold-standard treatment for symptomatic gallstone disease, but pneumoperitoneum creation may provoke inflammatory and stress responses affecting recovery. This prospective randomized comparative study, conducted in the Department of General Surgery at a tertiary care teaching hospital, compared low-pressure (8–10 mmHg) and standard-pressure (12–14 mmHg) pneumoperitoneum on inflammatory markers and postoperative recovery in 126 patients undergoing elective laparoscopic cholecystectomy, randomized into two equal groups. Preoperative and postoperative C-reactive protein (CRP), lactate dehydrogenase (LDH), and serum cortisol were assessed, alongside pain, analgesic requirement, bowel recovery, operative duration, and complications. Baseline characteristics were comparable between groups. Postoperative CRP and LDH were significantly higher in the standard-pressure group, indicating greater inflammatory and tissue stress response, while serum cortisol rose in both groups without significant difference. The low-pressure group experienced significantly lower postoperative pain, reduced analgesic requirement, and earlier bowel recovery. Operative duration was slightly longer with low pressure, but hospital stay and complications were comparable. Standard-pressure pneumoperitoneum and prolonged operative duration independently predicted greater inflammatory response and severe pain. Low-pressure pneumoperitoneum is a safe, effective alternative offering reduced inflammation, less pain, lower analgesic needs, and faster recovery without increasing complications.

Keywords: C-reactive protein; Inflammatory markers; Lactate dehydrogenase; Laparoscopic cholecystectomy; Pneumoperitoneum.

INTRODUCTION

Gallstone disease is among the most common gastrointestinal disorders worldwide and remains a major indication for elective abdominal surgery. Laparoscopic cholecystectomy has become the gold-standard treatment for symptomatic cholelithiasis because of its advantages of reduced postoperative pain, shorter hospital stay, faster recovery, and improved cosmetic outcomes compared with open surgery (1-3).

Creation of carbon dioxide (CO_2) pneumoperitoneum is essential for laparoscopic visualization and operative manipulation. Conventionally, intra-abdominal pressures of 12–14 mmHg are employed to provide adequate surgical exposure (4,5). However, increased intra-abdominal pressure is associated with important physiological alterations, including reduced venous return, increased systemic vascular resistance, impaired pulmonary compliance, decreased splanchnic perfusion, and transient renal hypoperfusion (6-8). Furthermore, peritoneal stretching, ischemia–reperfusion injury, and CO_2-induced acidosis may activate inflammatory pathways and neuroendocrine stress responses during surgery (9,10).
Inflammatory biomarkers such as C-reactive protein (CRP), lactate dehydrogenase (LDH), and serum cortisol are widely accepted indicators of tissue injury, cellular stress, and postoperative inflammatory response (11-13). Elevated

postoperative levels of these markers have been associated with increased surgical stress, greater postoperative discomfort, delayed recovery, and adverse clinical outcomes (14,15).

To minimize the physiological consequences of pneumoperitoneum, low-pressure laparoscopic cholecystectomy (8–10 mmHg) has been proposed as an alternative to standard-pressure techniques. Several randomized controlled trials and systematic reviews have demonstrated that low-pressure pneumoperitoneum is associated with reduced postoperative pain, lower analgesic requirements, improved cardiopulmonary stability, and enhanced postoperative recovery without compromising procedural safety (16-19). A recent randomized clinical trial further reported attenuation of postoperative inflammatory responses with low-pressure pneumoperitoneum (20).

Despite these encouraging findings, evidence comparing the effects of low- and standard-pressure pneumoperitoneum on inflammatory markers such as CRP, LDH, and serum cortisol remains limited. Therefore, the present study was undertaken to compare inflammatory marker responses and postoperative outcomes between low-pressure and standard-pressure laparoscopic cholecystectomy, with the objective of identifying a safer and physiologically less stressful surgical approach.

METHODOLOGY

Study Design and Setting

This prospective, randomized, comparative, interventional hospital-based study was conducted in the Department of General Surgery, Teerthanker Mahaveer Medical College and Research Centre (TMMC&RC), Moradabad, Uttar Pradesh, India. The study was carried out over a period of 18 months after obtaining approval from the Institutional Ethics Committee (IEC) and College Research Committee (CRC). Written informed consent was obtained from all participants before enrollment.

Study Population

Adult patients diagnosed with symptomatic gallstone disease and scheduled for elective laparoscopic cholecystectomy were screened for eligibility. Patients aged ≥18 years of either sex with ultrasonographically confirmed cholelithiasis who provided informed consent were included. Patients with common bile duct stones, acute cholecystitis, acute pancreatitis, biliary tract malignancy, chronic inflammatory disorders, endocrine disorders, severe systemic illness, anticipated difficult laparoscopic surgery, inadequate operative field at low pressure, or conversion to open cholecystectomy were excluded.

Sample Size and Randomization

The sample size was calculated using comparison of means between two independent groups with 95% confidence level and 80% study power. A minimum of 63 patients were required in each group, resulting in a total sample size of 126 participants. Eligible patients were randomized by simple random sampling (chit method) into two equal groups: Group A (standard-pressure pneumoperitoneum, 12–14 mmHg) and Group B (low-pressure pneumoperitoneum, 8–10 mmHg).

Study Procedure

All patients underwent elective laparoscopic cholecystectomy under general anesthesia using a standardized four-port technique. Pneumoperitoneum was maintained at 12–14 mmHg in the standard-pressure group and 8–10 mmHg in the low-pressure group throughout the procedure. Preoperative blood samples were collected for estimation of C-reactive protein (CRP), lactate dehydrogenase (LDH), and serum cortisol. Repeat measurements were obtained 24 hours postoperatively. Operative duration and intraoperative findings were recorded.

Outcome Measures

The primary outcomes were postoperative levels of CRP, LDH, and serum cortisol. Secondary outcomes included postoperative pain assessed using the Visual Analogue Scale (VAS), analgesic requirement, time to return of bowel sounds, duration of hospital stay, and postoperative complications including nausea, vomiting, port-site infection, and conversion to open surgery.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using Statistical Package for the Social Sciences (SPSS) software. Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 126 patients were included in the study, with 63 patients each in the standard-pressure and low-pressure laparoscopic cholecystectomy groups. Baseline demographic characteristics, body mass index, and comorbidity profiles were comparable between the groups, confirming their homogeneity at enrollment.

Patients undergoing low-pressure laparoscopic cholecystectomy experienced significantly better postoperative recovery. Mild postoperative pain (VAS score 1–3) was reported by 44.4% of patients in the low-pressure group compared with 15.9% in the standard-pressure group, while severe pain (VAS score 7–10) was more common in the standard-pressure

group (23.8% vs. 7.9%; p<0.001) (Table 1). In addition, return of bowel sounds occurred significantly earlier in the low-pressure group (16.8 ± 3.5 hours) than in the standard-pressure group (20.4 ± 4.2 hours; p<0.001). Analgesic requirements during the first 24 postoperative hours were also lower among patients receiving low-pressure pneumoperitoneum.
Preoperative inflammatory marker levels were similar in both groups. However, postoperative inflammatory responses differed significantly. The low-pressure group demonstrated significantly lower postoperative CRP levels (13.2 ± 3.8 vs. 18.4 ± 4.5 mg/L; p<0.001) and LDH levels (221 ± 40 vs. 265 ± 48 U/L; p<0.001) compared with the standard-pressure group (Table 2). Although postoperative serum cortisol levels were lower in the low-pressure group, the difference was not statistically significant (p=0.08).

Multivariate logistic regression analysis identified standard-pressure pneumoperitoneum and prolonged operative duration as independent predictors of severe postoperative pain (Table 3).

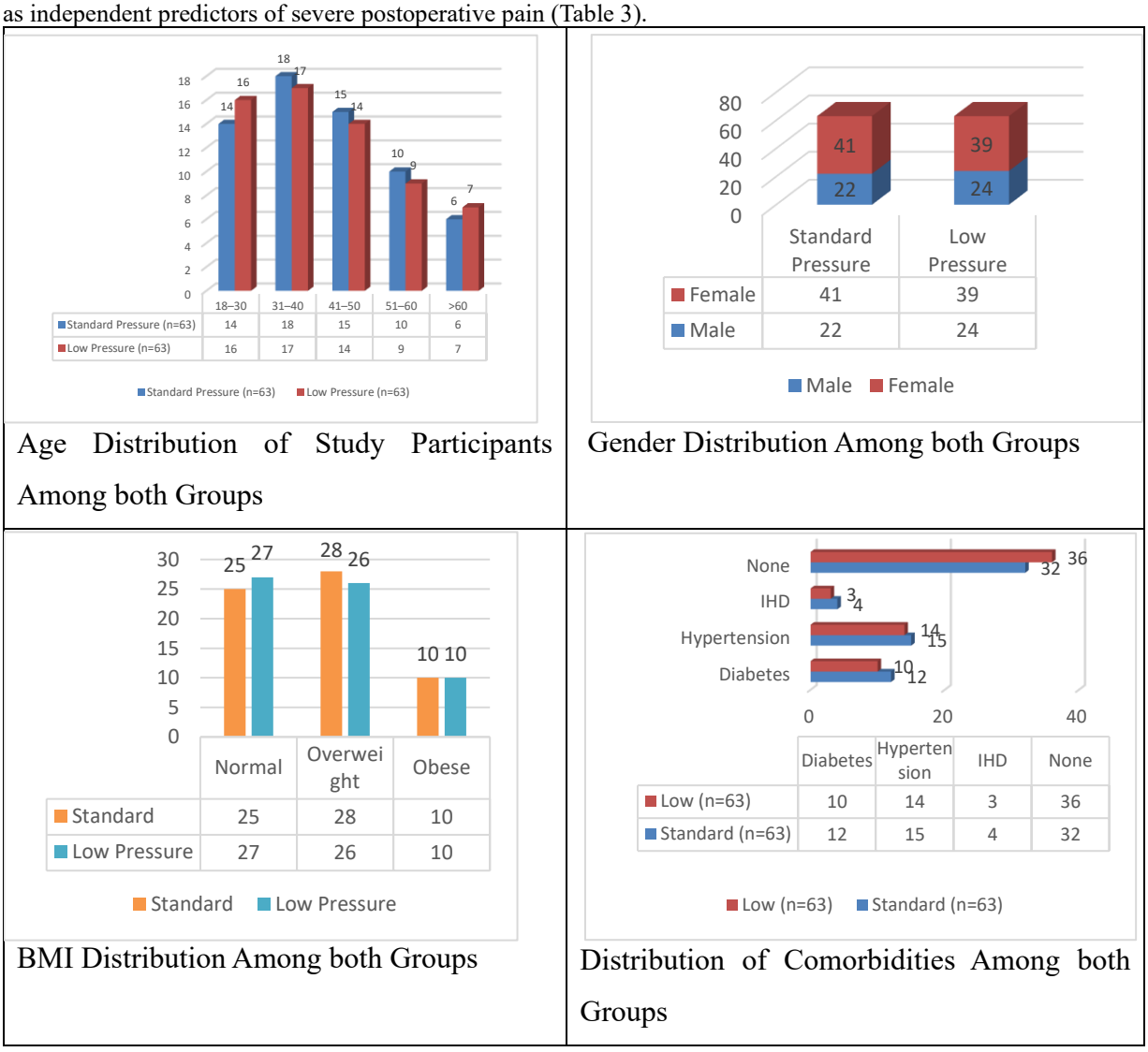

Figure 1. Baseline Characteristics , Comorbidities Among Standard-Pressure and Low-Pressure Laparoscopic Cholecystectomy Groups (N = 126)

Table 1. Comparison of Post-operative Pain, Shoulder Tip Pain, and Post-operative Complications Between Standard-Pressure and Low-Pressure Laparoscopic Cholecystectomy Groups (N = 126)

Variable	Category	Standard Pressure (n=63)	Low Pressure (n=63)	Total (n=126)	p-value
Post-operative Pain (VAS)	Mild (1–3)	10 (15.9%)	28 (44.4%)	38 (30.2%)	
	Moderate (4–6)	38 (60.3%)	30 (47.6%)	68 (54.0%)	
	Severe (7–10)	15 (23.8%)	5 (7.9%)	20 (15.9%)	<0.001*
Shoulder Tip Pain	Yes	4 (6.3%)	5 (7.9%)	9 (7.1%)	0.73
	No	59 (93.7%)	58 (92.1%)	117 (92.9%)	

Post-operative Complications	Nausea/Vomiting	10 (15.9%)	6 (9.5%)	16 (12.7%)	
	Port Site Infection	0 (0.0%)	1 (1.6%)	1 (0.8%)	
	Conversion to Open Surgery	2 (3.2%)	1 (1.6%)	3 (2.4%)	
	No Complications	51 (81.0%)	55 (87.3%)	106 (84.1%)	0.48†

*Statistically significant at $p < 0.05$.
†Chi-square/Fisher's exact test for overall comparison of postoperative complications.

Table 2. Comparison of Pre-operative and Post-operative Inflammatory Markers Between Standard-Pressure and Low-Pressure Laparoscopic Cholecystectomy Groups

Parameter	Standard Pressure (n=63) Mean ± SD	Low Pressure (n=63) Mean ± SD	p-value
CRP (mg/L)			
Pre-operative	4.8 ± 1.2	4.6 ± 1.1	0.42
Post-operative	18.4 ± 4.5	13.2 ± 3.8	<0.001*
LDH (U/L)			
Pre-operative	182 ± 35	179 ± 32	0.58
Post-operative	265 ± 48	221 ± 40	<0.001*
Serum Cortisol (µg/dL)			
Pre-operative	14.8 ± 3.2	15.1 ± 3.5	0.67
Post-operative	26.5 ± 5.1	24.3 ± 4.4	0.08

***Statistically significant at $p < 0.05$.**

Table 3. Multivariate Logistic Regression Analysis for Predictors of Severe Post-operative Pain (VAS ≥5)

Variable	Adjusted Odds Ratio (AOR)	95% CI	p-value
Age (>40 years)	1.29	0.61 – 2.71	0.50
BMI (>25 kg/m²)	1.41	0.71 – 2.79	0.32
Diabetes	1.22	0.49 – 3.01	0.67
Duration of Surgery (>55 min)	2.51	1.18 – 5.32	0.017*
Standard Pressure (vs Low Pressure)	5.47	2.53 – 11.82	<0.001*

***Statistically significant at $p < 0.05$.**

DISCUSSION

The present prospective randomized study compared the inflammatory response and postoperative recovery outcomes between standard-pressure (12–14 mmHg) and low-pressure (8–10 mmHg) pneumoperitoneum in patients undergoing elective laparoscopic cholecystectomy. The principal finding was that low-pressure pneumoperitoneum was associated with significantly attenuated postoperative inflammatory marker elevations, reduced pain intensity, lower analgesic consumption, and earlier return of gastrointestinal function, without any meaningful increase in operative complications.
Postoperative C-reactive protein (CRP), a sensitive acute-phase reactant synthesized by hepatocytes in response to tissue injury and cytokine release, was significantly lower in the low-pressure group compared with the standard-pressure group (13.2 ± 3.8 vs. 18.4 ± 4.5 mg/L; $p<0.001$). This finding aligns with the pathophysiological rationale that higher intra-abdominal pressures cause greater peritoneal stretch, ischemia–reperfusion injury, and carbon dioxide–mediated acidosis, each of which independently activates pro-inflammatory cascades (6,9). Rashdan et al. (15) similarly documented significantly lower postoperative CRP concentrations following low-pressure laparoscopic cholecystectomy, corroborating the mechanistic premise that reducing pneumoperitoneum pressure dampens the systemic acute-phase response.

Lactate dehydrogenase (LDH), a cytosolic enzyme released upon cellular membrane disruption, serves as a reliable biomarker of tissue and cellular injury (12). In this study, postoperative LDH levels were significantly elevated in the standard-pressure group relative to the low-pressure group (265 ± 48 vs. 221 ± 40 U/L; $p<0.001$). The higher LDH values in the standard-pressure group suggest greater mesothelial cell injury resulting from elevated intra-abdominal pressure, consistent with the findings of Shoar et al. (14), who reported augmented systemic stress responses under standard-pressure conditions. The extent of peritoneal ischemia and mechanical trauma appears to be proportional to the magnitude of pneumoperitoneum pressure, making LDH a clinically useful indicator for monitoring tissue stress in laparoscopic surgery.
Serum cortisol, a principal neuroendocrine stress mediator released from the adrenal cortex in response to surgical stimuli, rose significantly in both groups following surgery (13). However, the inter-group difference did not reach statistical significance (26.5 ± 5.1 vs. 24.3 ± 4.4 µg/dL; $p=0.08$). This observation suggests that pneumoperitoneum pressure alone may not be the predominant determinant of the hypothalamic–pituitary–adrenal axis response during laparoscopic cholecystectomy; anesthetic depth, surgical manipulation, and individual neuroendocrine variability likely contribute

substantially. Similar non-significant cortisol differences between pressure groups have been noted in prior investigations, reinforcing the view that cortisol responses in laparoscopic surgery are multifactorial in origin.

Postoperative pain scores demonstrated a highly significant difference between the two groups ($p<0.001$). Mild pain was reported by 44.4% of patients in the low-pressure group compared with only 15.9% in the standard-pressure group, while severe pain was nearly three times more prevalent in the standard-pressure cohort (23.8% vs. 7.9%). This gradient reflects the contribution of peritoneal distension and diaphragmatic irritation from elevated intra-abdominal pressure to visceral and somatic nociception. Yasir et al. (17) and Bhattacharjee et al. (20) similarly demonstrated superior pain outcomes in patients managed with lower pneumoperitoneum pressures, and a systematic review and meta-analysis by Ortenzi et al. (18) confirmed that low-pressure pneumoperitoneum consistently reduces postoperative pain across multiple randomized trials.

Multivariate logistic regression analysis revealed that standard-pressure pneumoperitoneum was the strongest independent predictor of severe postoperative pain (VAS ≥5), conferring an adjusted odds ratio of 5.47 (95% CI: 2.53–11.82; $p<0.001$). Prolonged operative duration exceeding 55 minutes was the second significant predictor (AOR 2.51; 95% CI: 1.18–5.32; $p=0.017$). Age, body mass index, and the presence of diabetes mellitus did not independently predict severe pain in this cohort. The markedly elevated odds ratio for standard-pressure pneumoperitoneum reinforces the causal relationship between elevated intra-abdominal pressure and postoperative pain burden.

Return of bowel sounds occurred significantly earlier in the low-pressure group (16.8 ± 3.5 vs. 20.4 ± 4.2 hours; $p<0.001$), reflecting less pneumoperitoneum-related splanchnic hypoperfusion (7,8) and faster resolution of postoperative ileus. Analgesic requirements during the first 24 postoperative hours were correspondingly reduced in this group. These recovery parameters have important practical implications; earlier return of gastrointestinal function facilitates oral intake, mobilization, and discharge, directly contributing to enhanced recovery pathways. The Cochrane systematic review by Gurusamy and Samraj (4) and the subsequent meta-analysis by Hua et al. (5) each documented benefits of low-pressure pneumoperitoneum on postoperative pain and recovery, consistent with the present findings.

The operative duration was marginally longer in the low-pressure group, which is an acknowledged trade-off of reduced pneumoperitoneum pressure owing to potentially diminished working space and surgical field visibility. However, this did not translate into increased intraoperative complications or conversions to open surgery, and the overall postoperative complication rates were comparable between groups ($p=0.48$). The incidence of shoulder-tip pain, a phenomenon ascribed to diaphragmatic irritation by residual CO2, was low and did not differ significantly between groups ($p=0.73$). The systematic review by Özdemir-van Brunschot et al. (19) similarly concluded that low-pressure pneumoperitoneum is feasible and safe provided appropriate patient selection and surgical expertise are in place.

Taken together, these results support the proposition that low-pressure pneumoperitoneum reduces the physiological burden of laparoscopic cholecystectomy while preserving surgical safety. The study's strengths include its prospective randomized design, standardized anesthetic and surgical protocols, systematic measurement of multiple inflammatory biomarkers, and a well-powered sample size. Limitations include the single-center design, which may constrain generalizability; the relatively short follow-up period limited to the immediate postoperative phase; and the exclusion of patients with anticipated technical difficulty, which may have introduced a selection bias toward less complex cases in the low-pressure arm. Future multicenter trials incorporating longer follow-up durations and patient-reported outcome measures would further substantiate these findings.

CONCLUSION

This randomized comparative study demonstrates that low-pressure pneumoperitoneum (8–10 mmHg) offers meaningful clinical and physiological advantages over standard-pressure pneumoperitoneum (12–14 mmHg) in patients undergoing elective laparoscopic cholecystectomy. Postoperative elevations in C-reactive protein and lactate dehydrogenase were significantly attenuated in the low-pressure group, indicating a reduced systemic inflammatory and tissue-injury response. Although serum cortisol rose in both groups, the difference between them was not statistically significant, suggesting that the neuroendocrine stress response to laparoscopic cholecystectomy is partially independent of pneumoperitoneum pressure.

Patients managed with low-pressure pneumoperitoneum experienced significantly less severe postoperative pain, required fewer analgesics during the first 24 postoperative hours, and recovered bowel function earlier. Standard-pressure pneumoperitoneum and prolonged operative duration were identified as the two independent predictors of severe postoperative pain on multivariate analysis. Despite a marginally longer operative duration in the low-pressure group, complication rates and hospital stay were equivalent between groups, confirming that low-pressure pneumoperitoneum does not compromise procedural safety.

In conclusion, low-pressure pneumoperitoneum represents a physiologically superior and equally safe technique for laparoscopic cholecystectomy, offering reduced inflammatory stress, improved pain control, and accelerated postoperative

recovery. Its adoption in routine practice is supported by the available evidence and warrants broader consideration, particularly in the context of enhanced recovery after surgery protocols, and future large-scale multicenter studies with enhanced surgical training are recommended to validate long-term benefits.

ACKNOWLEDGMENT
This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

CONFLICT OF INTEREST
The authors declare no potential conflicts of interest with respect to research, authorship and/or publication of this chapter.

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