

# Early Postoperative Pain Intensity after Laparoscopic Cholecystectomy and Associated Risk Factors

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## Abstract

**Background:** The present study was undertaken to evaluate the incidence of pain with severity  $\geq 50$  VAS points within 24 hours of LC and explore various factors that influence the early postoperative pain intensity after LC.

**Method:** 148 eligible adult patients ( $\geq 18$  years) of ASA physical status I and II undergoing elective uncomplicated LC for symptomatic cholelithiasis during the year 2018 were recruited for the study.

**Results:** Postoperatively, pain was the most frequent postoperative symptom and 49 (33.1%) of patients experienced severe postoperative pain during first 24 hours after surgery and opioids were consumed by 20.3% of patients to relieve pain. Multivariate regression analysis revealed that preoperative anxiety (aOR: 2.47, 95% CI: 1.53-3.97) and sensitivity to cold pressor induced pain (aOR: 1.52, 95% CI: 1.12-2.08) were the significant predictors for the intense early postoperative pain.

**Conclusion:** Intense pain is experienced by one third of patients in the early postoperative period after LC which can be effectively managed by properly addressing the preoperative risk factors as revealed in our study.

**Keywords:** Laparoscopy, Cholecystectomy, Pain intensity, Preoperative anxiety, Cold pressor.

## Introduction

Worldwide, Laparoscopic Cholecystectomy (LC) has replaced open cholecystectomy as the gold standard surgical procedure for symptomatic cholelithiasis. LC is safe, more effective, causes less pain and rapid recovery.<sup>1,2</sup> However, LC frequently results in significant early postoperative pain which warrants the need for rescue analgesia in PostAnaesthesiaCare

Unit (PACU).<sup>3,4</sup> Early pain is the dominant complaint after LC, most intense on the day of surgery and the main reason for prolonged hospital stay and prolonged convalescence after surgery thereby increasing treatment cost and decreasing quality of life of patients.<sup>5</sup>

Research regarding pain intensity and associated risk factors among patients undergoing LC is scarce in India. With this background, the present study was undertaken to address the following objectives: (1) to evaluate the incidence of pain with severity  $\geq 50$  VAS points within 24 hours of LC; and (2) to explore various factors that influence the early postoperative pain intensity.

## Method

A pilot study involving 18 patients undergoing LC and fulfilling the eligible criteria needed for the study

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was conducted to test the feasibility of the study and calculation of the sample size. Assuming prevalence of high intensity ( $\geq 50$  VAS points) early postoperative pain was assumed as 28% (result of pilot study), sample size was determined as 138 at absolute precision 7.5% and 95% level of confidence.

We conducted an observational prospective study during the period January – December, 2018 involving 148 eligible adult inpatients aged  $\geq 18$  years of ASA physical status I and II undergoing elective uncomplicated laparoscopic cholecystectomy for symptomatic cholelithiasis. Exclusion criteria included patients with diabetes mellitus; cardiovascular or respiratory or hepatic or renal insufficiency; psychiatric diseases or disturbance of central nervous system; substance abuse, chronic use of analgesics or steroids. In total, 158 eligible patients were approached for the study and 151 agreed to participate (95.6%). Two patients who underwent relaparotomy were excluded, and one patient with difficult surgical dissection underwent open cholecystectomy and thus excluded from the study leaving 148 patients for further analysis.

Previous studies have shown that pain after surgery is influenced by various factors such as age, gender, preoperative pain, type of surgery, duration of surgery<sup>6-8</sup> and preoperative anxiety seems to be an important predictor for acute postoperative pain intensity.<sup>7,9,10</sup> Also, preoperative sensitivity to cold pressor induced pain was identified as an independent risk factor for early postoperative pain.<sup>5</sup> After obtaining the written informed consent, relevant data regarding demographic characteristics, preoperative anxiety level, preoperative sensitivity to cold pressor induced pain, pre and post operative pain intensity, duration of surgery etc. were collected.

The day before the operation, a cold pressor test<sup>5</sup> was conducted among the patients to assess the subjective sensation of discomfort by immersing hand into the ice water. Two containers were filled with mixture of one third crushed ice and two thirds tap water. The resulting ice water mix stirred to maintain a constant temperature of  $1.0 \pm 0.3^\circ\text{C}$  throughout the study. The patients were told that the test would be terminated after 4 minutes. They were instructed to immerse one bare arm into each container with the palms resting on the bottom of the containers. All the patients were instructed that they could remove their hands at any time prior to 4 minutes if pain intensity was unbearable. Subjective assessment

of cold pressor test was recorded by Visual Analogue Scale (VAS) after the procedure. Each patient rated the subjective pain experience on a 100 mm VAS (0 mm = no discomfort and 100 mm = worst possible discomfort).

To assess the anxiety level of patients before anaesthesia and surgery, a Visual Analogue Scale (VAS) consisting of 10 items<sup>11</sup> was used. The VAS was based on a 100 mm scale: ranging from 0 indicating no preoperative anxiety to 10 indicating the maximal preoperative anxiety.

All patients received similar general anaesthesia, surgical and prophylactic analgesic regimens. Routine premedication with glycopyrrolate (0.01 mg/kg) and midazolam (0.2 mg/kg) was done. Standard protocol for general anaesthesia consisted of administration of propofol (1–2 mg/kg) for induction, butorphanol (0.02 mg/kg) for intraoperative analgesia and vecuronium (0.08 mg/kg) intravenous to facilitate tracheal intubation and obtain intraoperative muscle relaxation. Maintenance of anaesthesia was done with oxygen and nitrous oxide in the ratio of 1:2 along with isoflurane (0.6–0.8%) and intermittent dose of vecuronium for muscle relaxation. At the end of surgery, neuromuscular blockade was reversed with neostigmine (0.05 mg/kg) and glycopyrrolate (0.01 mg/kg). Prior to closure, ondansetron (0.08 mg/kg) and paracetamol (1 g) was administered. All the operations were conducted and supervised by the experienced laparoscopic surgeons using the standard 4-trocar technique of laparoscopic cholecystectomy. During laparoscopy, intra abdominal pressure was kept at 12 mm Hg and at the end of procedure CO<sub>2</sub> was evacuated by gentle abdominal pressure with open trocars. When VAS score was  $\geq 4$ , rescue analgesia was done with administration of tramadol (50 mg) or diclofenac (75 mg) as required by the patient. In surgery ward, pain was managed with combination of analgesics such as diclofenac (75 mg) + paracetamol (1 g) or tramadol (50 mg) + paracetamol (1 g) as needed by the patient. The pain assessment was done on the day before operation and the postoperative assessment was done at 6 hours, 12 hours, and 24 hours after the operation. Presence of high intensity pain, defined as VAS  $\geq 50$ , occurring at least once within the first 24 hours after arrival at the PACU was considered as the dependent variable of the study.

Data were analyzed by using SPSS version 21.0 software. Univariate analyses were done by the t test for continuous variables and the chi square test

for dichotomous variables. Variables significantly associated ( $p < 0.05$ ) with the dependent variable were tested with spearman rank correlation test. The variables found to have  $p < 0.2$  in univariate analyses were entered into the multivariate logistic regression model to identify the predictors for the early postoperative pain intensity. Values were expressed as mean  $\pm$  SD, absolute numbers, percentages with significance defined as  $p < 0.05$ .

**Results**

The mean age of the study population was  $43.2 \pm 14.3$  years and majority (63.5%) were females. Pre operatively, the mean intensity of pain was  $4.66 \pm 1.06$  VAS points and abdominal pain was the most frequent (139, 93.9%) symptom experienced by the patients. Pain was localized exclusively to the right upper abdomen in 93 (62.8%) patients and almost two third of patients (55.7%) reported that pain was radiating to back. Postoperatively, pain was the most frequent postoperative symptom and the mean intensity of post operative pain was  $4.34 \pm 1.33$  VAS points. Out of 148 patients, 73 (49.3%) localized pain to the incisional sites, 47 (31.7%) to the right upper abdomen, and 28 (18.9%) reported diffuse abdominal pain. Also, 23 (15.5%) patients reported that pain was radiating to the back and 34 (22.9%) experienced pain radiating to the shoulder area. However, when asked regarding the site of more intense pain, 55 (37.1%) indicated to the incisional sites, 34 (23%) to the right upper abdomen, 9 (6.1%) to the shoulder area, and 5 (3.4%) to the back.

The intensity of postoperative pain during first 24 hours after surgery was high ( $\geq 5$  VAS points) as experienced in one third of patients. In most of the

patients (79.7%), mild analgesics such as paracetamol or diclofenac or combination of both were used to relieve the pain whereas opioids were consumed by 30 (20.3%) patients (Table 1). Table 2 revealed the univariate analyses showing association between various factors and the outcome variable i.e. maximal VAS pain score during the first postoperative day. Multivariate regression analysis showed that preoperative anxiety and sensitivity to cold pressor induced pain were the significant predictors for severe postoperative pain during first 24 hours after LC (Table 3).

**Table 1: Postoperative symptoms, pain intensity, and analgesics used during first 24 hours after laparoscopic cholecystectomy (n = 148)**

| Characteristics            | Number | Percentage |
|----------------------------|--------|------------|
| <b>Symptoms</b>            |        |            |
| Pain                       | 148    | 100        |
| Feeling abdominal pressure | 78     | 52.7       |
| Loss of appetite           | 67     | 45.3       |
| Nausea                     | 47     | 31.7       |
| Vomiting                   | 15     | 10.1       |
| <b>Intensity of Pain</b>   |        |            |
| < 50 VAS* points           | 99     | 66.9       |
| $\geq 50$ VAS points       | 49     | 33.1       |
| <b>Analgesic Used</b>      |        |            |
| Paracetamol                | 35     | 23.6       |
| Diclofenac                 | 78     | 52.7       |
| Diclofenac + Paracetamol   | 05     | 3.4        |
| Tramadol                   | 19     | 12.8       |
| Tramadol + Paracetamol     | 11     | 7.4        |

\*VAS – Visual Analogue Scale

**Table 2: Univariate analyses showing association of factors with postoperative pain intensity (n = 148)**

| Characteristics                  | Postoperative Pain Intensity            |  | p value | r <sub>s</sub> |
|----------------------------------|---|--|---------|----------------|
|                                  | < 5 VAS points<br>[M $\pm$ SD or n (%)] | $\geq 5$ VAS points<br>[M $\pm$ SD or n (%)] |         |                |
| Age (in years)                   | 42.36 $\pm$ 13.66                       | 44.86 $\pm$ 15.67                            | 0.322   | -              |
| <b>Gender</b>                    |   |  |         |                |
| Male                             | 37 (68.5)                               | 17 (31.5)                                    | 0.750   | -              |
| Female                           | 62 (66.0)                               | 32 (34.0)                                    |         |                |
| Weight (in kg)                   | 58.19 $\pm$ 9.65                        | 57.22 $\pm$ 10.79                            | 0.582   | -              |
| Preoperative pain                | 4.75 $\pm$ 0.88                         | 4.47 $\pm$ 1.36                              | 0.186   | -              |
| Preoperative anxiety             | 4.58 $\pm$ 0.79                         | 5.24 $\pm$ 0.95                              | 0.000   | 0.33           |
| Cold pressure discomfort         | 6.11 $\pm$ 1.29                         | 6.78 $\pm$ 1.24                              | 0.003   | 0.14           |
| Duration of surgery (in minutes) | 81.90 $\pm$ 23.58                       | 86.7 $\pm$ 26.96                             | 0.262   | -              |

Note: M - Mean, SD - Standard Deviation; n – number,  $p < 0.05$  statistically significant; r<sub>s</sub> – Spearman correlation coefficient

**Table 3: Multivariate logistic regression analysis showing association of factors with postoperative pain intensity (n = 148)**

| Characteristics         | Postoperative pain intensity ( $\geq 5$ VAS points)* |             | p value |
|-------------------------|--|-------------|---------|
|                         | aOR  | 95% CI      |         |
| Preoperative pain       | 0.81   | 0.57 – 1.16 | 0.259   |
| Preoperative anxiety    | 2.47   | 1.53 – 3.97 | 0.000   |
| Cold pressor discomfort | 1.52   | 1.12 – 2.08 | 0.007   |

\*  $< 5$  VAS points is taken as reference

**Note:** aOR: adjusted Odds Ratio, CI: Confidence interval,  $p < 0.05$  statistically significant; Model  $\chi^2 = 27.406$ ,  $p < 0.001$  and Hosmer & Lemeshow  $p = 0.968$  indicates that the model fits the data. The classification table reports that overall expected model performance is 71.6%; that is 71.6% of the cases can be expected to be classified correctly by the model.

## Discussion

Our study demonstrated that pain was the most frequent complaint in patients during first 24 hours of LC and the mean intensity of postoperative pain was 43 VAS points. One third of patients reported severe pain ( $\geq 50$  mm VAS points) and nearly 20% of the patients needed opioids. This indicates the importance of addressing pain in the early postoperative period and thus designing effective strategies for better pain management. In accordance with our study, other studies have shown the pain scores in the range of 40 mm within 24 hours after surgery<sup>5,12</sup> and exceed 50 mm in up to one third of patients during early postoperative period.<sup>13</sup> Few studies have reported higher proportion (46–65%) of patients undergoing laparoscopic cholecystectomy experienced severe pain.<sup>4,6</sup> This might be due to methodological variation and difference in patient characteristics. In agreement with the findings of earlier studies,<sup>5,13</sup>

Our results showed that preoperative anxiety and preoperative sensitivity to cold pressor induced pain were found to be the significant independent predictors of early postoperative pain. However, the correlations were weak ( $r_s = 0.14 - 0.33$ ) indicating ( $r_s^2 = 0.02 - 0.11$ ) 2% and 11% of the variability of postoperative pain after LC could be predicted by sensitivity to cold pressor induced pain and preoperative anxiety respectively. It was observed that the odds of having high intensity early postoperative pain increases 2.5 times with one unit increase in preoperative anxiety score in the patients undergoing LC. Fear of postoperative pain or fear of poor outcome of operation/anaesthesia may act as a stressor

that stimulates increased anxiety response which in turn amplifies postoperative pain and thereby contributing to the continuity of cycle of pain and anxiety. Our result is in consistency with the findings of previous literatures which showed that fear of surgical procedure might increase in postoperative LC pain intensity.<sup>6,10</sup> Ali et al also reported that patients with high preoperative anxiety had higher postoperative VAS score.<sup>14</sup> In addition, Bakr et al revealed that the patients receiving preoperative anxiety intervention before surgery showed lower pain scores as compared to the patients who did not receive preoperative anxiety intervention.<sup>15</sup> This emphasizes the need of prior psychological preparation of patients undergoing LC which might be useful in reducing preoperative anxiety level thereby alleviating the intensity of postoperative pain.

In our study, the risk of experiencing high intensity postoperative pain among patients undergoing LC increases almost 1.5 times with one unit increase in sensitivity to cold pressor test. Although the relation between preoperative sensitivity to cold pressor induced pain and early postoperative pain intensity after LC reached statistical significance, the correlation was found to be weak. This suggests minor clinical importance of the cold pressor test in predicting the early postoperative pain intensity. In an earlier study, Bisgaard et al also observed similar result.<sup>5</sup> Further prospective research is needed to find the predictive power of the 4 minute cold pressor test.

The present study has few limitations that may affect the generalizability of the results. This study was a single center study and used cross-sectional design without a follow up. There might be introduction of bias as the data on pain and anxiety were based on the subjective perception of the patients. The strength of the study lies in the fact that all the patients were similarly prepared as per the institutional protocol and the type of surgery and anaesthesia was standardized which could eliminate the misleading effects.

## Conclusion

It was revealed in the study that pain was the most frequent complaint by the patients within 24 hours of LC and one third of patients experienced severe early postoperative pain. Our findings suggest that along with peri-operative multimodal analgesia approach, effective strategies can be planned to address the preoperative risk factors which could be beneficial in reducing the pain intensity in the early postoperative period.

**Ethical Clearance** was taken from the Institutional Ethics Committee of Kalinga Institute of Medical Sciences (No: KIMS/KIIT/IEC/09/2018)

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