

Persistence of Symptoms Following Laparoscopic Cholecystectomy for Symptomatic Cholelithiasis: A Prospective Observational Study

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Abstract

Introduction: Laparoscopic cholecystectomy is the standard surgical treatment for symptomatic cholelithiasis, but a proportion of patients continue to experience abdominal or gastrointestinal symptoms after surgery. This study evaluated the frequency of persistent symptoms and the resolution pattern of individual gastrointestinal symptoms following laparoscopic cholecystectomy.

Methods: This prospective longitudinal observational study was conducted at Pushpagiri Institute of Medical Sciences and Research Centre, Thiruvalla, Kerala. Eligible patients undergoing laparoscopic cholecystectomy for symptomatic cholelithiasis were prospectively enrolled and followed for one to six months after surgery through outpatient visits or telephone follow-up. Symptoms were recorded using a predefined structured proforma; no separate validated gastrointestinal symptom score was used. Of 70 enrolled patients, four who underwent open cholecystectomy were excluded, and eight were lost to follow-up, leaving 58 patients for final analysis. Paired preoperative and postoperative symptom status was compared using the exact McNemar test.

Results: Among the 58 patients who completed follow-up, 39 were female, and 19 were male. Persistent postoperative symptoms were observed in eight patients (13.8%), while 50 patients (86.2%) were symptom-free. Among patients with persistent symptoms, upper abdominal pain was present in all eight (100%), bloating in five (62.5%), and constipation in six (75%). Symptom resolution varied according to the presenting complaint. The resolution rates were 87.2% for nausea, 88.9% for vomiting, 88.2% for heartburn, 81.8% for early satiety, 92.6% for food intolerance, and 80.0% for bloating. Constipation showed comparatively poor resolution (44.4%).

Conclusion: Most patients experienced substantial symptomatic improvement after laparoscopic cholecystectomy, but approximately one in seven had persistence of at least one preoperative symptom during one- to six-month follow-up. Nonspecific gastrointestinal complaints, particularly bloating and constipation, may resolve less consistently. Preoperative counselling should distinguish typical biliary symptoms from potentially non-biliary symptoms and explain that complete symptom resolution cannot be guaranteed.

Categories: General Surgery, Gastroenterology

Keywords: cholelithiasis, dyspepsia, laparoscopic cholecystectomy, persistent symptoms, postcholecystectomy syndrome, symptomatic gallstones

Introduction

Gallstone disease is a common biliary disorder, and laparoscopic cholecystectomy is an established treatment for symptomatic cholelithiasis because it offers effective treatment with the advantages of minimally invasive surgery [1,2]. Nevertheless, the presence of gallstones does not establish that every abdominal or gastrointestinal complaint is gallbladder-related. Earlier prospective studies and systematic reviews have shown that a clinically relevant proportion of patients continue to report abdominal pain, dyspepsia, bloating, altered bowel habits, or other symptoms after cholecystectomy [3-9].

Persistent symptoms after cholecystectomy may reflect residual biliary disease, functional gastrointestinal disorders, gastroesophageal or peptic disease, physiological changes after cholecystectomy, psychological factors, or other coexisting conditions [8-10]. More recent prospective studies have reinforced the distinction between typical biliary colic and nonspecific gastrointestinal symptoms. Functional dyspepsia and irritable bowel syndrome are common in patients with gallstones and are associated with less favorable patient-reported outcomes after cholecystectomy [11]. Persistent and newly developed symptoms have also been demonstrated in contemporary prospective cohorts despite technically successful surgery [12].

These observations have direct implications for patient selection and preoperative counselling. Randomized and prospective data indicate that symptom outcomes after cholecystectomy are heterogeneous and that

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long-term pain-free status is not universal [10,13,14].

This prospective observational study aimed to determine the proportion of patients experiencing persistent preoperative gastrointestinal symptoms following laparoscopic cholecystectomy for symptomatic cholelithiasis. The study also aimed to evaluate the resolution of individual preoperative symptoms, including upper abdominal pain, nausea, vomiting, heartburn, early satiety, food intolerance, bloating, and constipation, during the postoperative follow-up period of one to six months.

Materials And Methods

Study design and setting

This prospective longitudinal observational study was conducted in the Department of General and Laparoscopic Surgery, Pushpagiri Institute of Medical Sciences and Research Centre, Thiruvalla, Kerala, India, over a period of 18 months. Eligible patients undergoing laparoscopic cholecystectomy for symptomatic cholelithiasis were enrolled prospectively during the study period.

The study protocol was approved by the Institutional Ethics Committee of Pushpagiri Institute of Medical Sciences and Research Centre, Thiruvalla (Ethical Clearance No. PMSRC/E1/388A/62/2022). Written informed consent was obtained from all participants before enrolment. Patient confidentiality and data security were maintained throughout the study.

Sampling and study population

Eligible patients presenting during the study period were enrolled prospectively in sequence as they were screened. Because no probability-based sampling frame was used, the recruitment approach was treated as consecutive non-probability sampling of eligible patients. The diagnosis of cholelithiasis was confirmed by ultrasonography of the abdomen as part of the preoperative evaluation. Both elective and emergency laparoscopic cholecystectomies performed for symptomatic gallstone disease were eligible.

Inclusion criteria were (1) symptomatic cholelithiasis confirmed on abdominal ultrasonography; (2) planned laparoscopic cholecystectomy, either elective or emergency; and (3) availability for postoperative symptom assessment within the study follow-up period. Exclusion criteria were (1) open cholecystectomy or conversion to open cholecystectomy; and (2) failure to complete postoperative follow-up. Patients were screened prospectively against these criteria; only those who underwent laparoscopic cholecystectomy and had postoperative outcome data were included in the final outcome analysis.

A total of 70 patients were initially enrolled. Four patients were excluded because they underwent open cholecystectomy, and eight patients were lost to follow-up. Therefore, 58 patients were available for final analysis.

Sample size

The sample size was estimated for a single proportion using the formula $n = \frac{Z^2 p(1-p)}{d^2}$, where Z is the standard normal deviate for the desired confidence level, p is the anticipated proportion of persistent symptoms, and d is the absolute precision. Based on the prospective study by Luman et al., an anticipated persistence proportion of 13% was used [5]. With Z = 1.96 for a 95% confidence level, p = 0.13, and d = 0.08, the calculated sample size was 67.9, which was rounded up to 68. A target sample of 70 patients was selected to allow for practical recruitment considerations.

Data collection and symptom assessment

Demographic characteristics, relevant laboratory investigations, clinical and imaging findings, preoperative symptoms, intraoperative findings, and postoperative symptoms were prospectively recorded using a predefined study proforma. The gastrointestinal symptoms assessed included upper abdominal pain, nausea, vomiting, heartburn, early satiety, food intolerance, bloating, constipation, and other relevant gastrointestinal complaints.

No separate validated gastrointestinal symptom questionnaire, symptom-severity score, or quality-of-life scale was used in this study. Symptoms were assessed using a structured symptom checklist incorporated into the predefined proforma and recorded according to their presence or absence. Accordingly, no score or scale citation was applicable to the primary symptom assessment used in this study.

Surgical treatment

All participants underwent laparoscopic cholecystectomy according to routine institutional surgical practice. Both elective and emergency laparoscopic procedures were included. Patients who underwent open cholecystectomy or conversion to open surgery were excluded from the final laparoscopic outcome cohort.

Postoperative follow-up

Patients were assessed preoperatively and subsequently during postoperative follow-up between one and six months after laparoscopic cholecystectomy. Follow-up was performed either during outpatient visits or by telephone when an in-person assessment was not available. At follow-up, patients were specifically questioned regarding the same gastrointestinal symptoms recorded preoperatively, allowing paired patient-level comparison of symptom status.

Definitions and outcome measures

A persistent postoperative symptom was defined as a gastrointestinal symptom that had been present before laparoscopic cholecystectomy and remained present during postoperative follow-up. A patient was classified as having persistent postoperative symptoms when at least one preoperative gastrointestinal symptom remained present. A symptom was considered resolved when it had been present preoperatively but was no longer reported at follow-up. Symptoms appearing for the first time after surgery were classified as new-onset postoperative symptoms and were distinguished from persistence of a pre-existing symptom.

The primary outcome was the proportion of patients experiencing persistence of preoperative gastrointestinal symptoms following laparoscopic cholecystectomy for symptomatic cholelithiasis. Patients reporting complete resolution of their preoperative symptoms during follow-up were classified as having no persistent symptoms, whereas patients continuing to experience one or more preoperative symptoms were classified as having persistent postoperative symptoms.

Secondary outcomes included the pattern and proportion of resolution of individual preoperative gastrointestinal symptoms during the postoperative follow-up period of one to six months.

Statistical analysis

Data were entered into Microsoft Excel (Microsoft Corp., Redmond, WA, USA) and analyzed using IBM SPSS Statistics for Windows, Version 27 (Released 2019; IBM Corp., Armonk, New York, United States). Continuous variables were summarized using appropriate descriptive measures, and categorical variables were expressed as frequencies and percentages. Because the principal symptom outcomes represented paired binary observations in the same patients before and after surgery, changes in individual symptom status were assessed using the two-sided exact McNemar test. A p-value <0.05 was considered statistically significant.

No multivariable predictor analysis was performed. Only eight patients had persistent postoperative symptoms, which was insufficient for a stable multivariable model and would have created a substantial risk of overfitting.

Results

Study population

Seventy patients were initially enrolled. Four patients who underwent open cholecystectomy were excluded, and eight patients were lost to follow-up, leaving 58 patients (82.9% of the enrolled cohort) for final analysis (Figure 1). Of these, 39 (67.2%) were female, and 19 (32.8%) were male. The mean age was 46 years. Forty patients (69.0%) had uncomplicated symptomatic gallbladder disease, while 18 (31.0%) had complicated disease. Acute cholecystitis was present in 13 patients (22.4%), choledocholithiasis in four (6.9%), and pancreatitis associated with common bile duct calculi in one (1.7%) (Table 1).

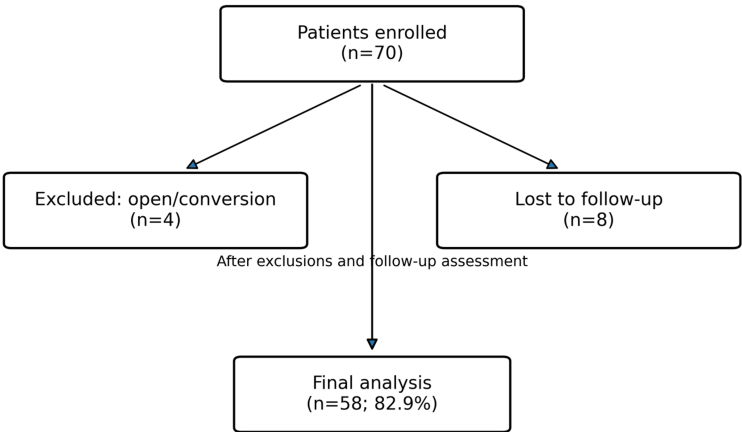


FIGURE 1: Flow of Participants Through the Study, Including Enrolment, Exclusions, Loss to Follow-Up, and the Final Analytic Cohort

Characteristic	Value
Age, mean, years	46
Female sex	39/58 (67.2%)
Male sex	19/58 (32.8%)
Uncomplicated symptomatic gallbladder disease	40/58 (69.0%)
Acute cholecystitis	13/58 (22.4%)
Choledocholithiasis	4/58 (6.9%)
Pancreatitis with CBD calculi	1/58 (1.7%)
At least one persistent preoperative symptom	8/58 (13.8%)
No persistent preoperative symptom	50/58 (86.2%)

TABLE 1: Baseline and Clinical Characteristics of the Study Population

Categorical variables are presented as n/N (%) and age as mean years.

CBD: common bile duct

Persistence of symptoms

At postoperative follow-up, 50/58 patients (86.2%) had no persistence of their preoperative gastrointestinal symptoms, whereas 8/58 (13.8%) had at least one persistent symptom. Among these eight patients, upper abdominal pain was reported by 8/8 (100%), constipation by 6/8 (75.0%), nausea by 5/8 (62.5%), and bloating by 5/8 (62.5%). Constipation persisted in five patients who had reported this symptom preoperatively. One additional patient developed new-onset constipation following surgery, resulting in six patients (10.3% of the total cohort) reporting constipation during postoperative follow-up. Vomiting, heartburn, early satiety, and food intolerance were each reported by 2/8 (25.0%). The same values corresponded to 13.8%, 10.3%, 8.6%, and 8.6% of the total analyzed cohort for upper abdominal pain, constipation, nausea, and bloating, respectively (Table 2).

Symptom	Among the Persistent-Symptom Cohort, n/8 (%)	Among the Total Cohort, n/58 (%)
Upper abdominal pain	8/8 (100.0)	8/58 (13.8)
Nausea	5/8 (62.5)	5/58 (8.6)
Vomiting	2/8 (25.0)	2/58 (3.4)
Heartburn	2/8 (25.0)	2/58 (3.4)
Early satiety	2/8 (25.0)	2/58 (3.4)
Food intolerance	2/8 (25.0)	2/58 (3.4)
Bloating	5/8 (62.5)	5/58 (8.6)
Constipation	6/8 (75.0)	6/58 (10.3)

TABLE 2: Pattern of Postoperative Symptoms Among Patients With Persistent Symptoms

Percentages in the second column are calculated using the eight patients with at least one persistent preoperative symptom as the denominator, whereas percentages in the third column are calculated using all 58 analyzed patients. These values represent descriptive postoperative symptom frequencies and should not be interpreted as symptom-specific persistence or resolution rates. Of the six patients reporting postoperative constipation, five had persistent preoperative constipation, and one developed new-onset constipation.

Resolution of preoperative gastrointestinal symptoms

Paired patient-level analysis demonstrated substantial resolution of most preoperative gastrointestinal symptoms (Figure 2). Nausea resolved in 34/39 patients (87.2%), vomiting in 16/18 (88.9%), heartburn in 15/17 (88.2%), early satiety in 9/11 (81.8%), food intolerance in 25/27 (92.6%), and bloating in 20/25 (80.0%). Constipation resolved in 4/9 patients (44.4%). Five of nine patients with preoperative constipation remained constipated, and one additional patient developed new-onset constipation after surgery, resulting in six patients with postoperative constipation overall. Exact McNemar testing demonstrated statistically significant reductions in nausea, vomiting, heartburn, early satiety, food intolerance, and bloating, whereas the change in constipation was not statistically significant (Table 3).

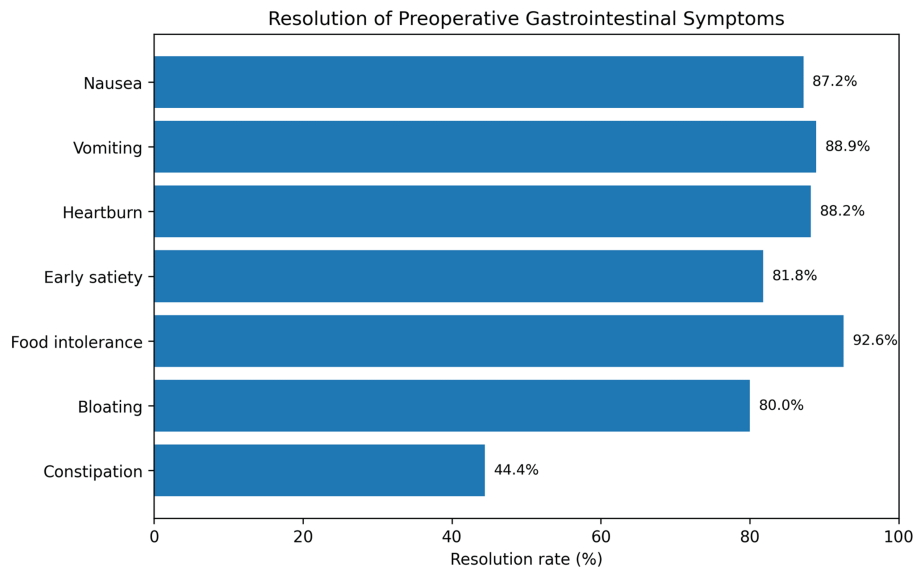


FIGURE 2: Resolution Rates of Preoperative Gastrointestinal Symptoms After Laparoscopic Cholecystectomy

Percentages were calculated using the number of patients with each symptom preoperatively as the denominator.

Symptom	Preoperative, n/58 (%)	Persistent, n/N Preop (%)	Resolved, n/N Preop (%)	Postoperative Total, n/58 (%)	Exact McNemar p-value
Nausea	39/58 (67.2)	5/39 (12.8)	34/39 (87.2)	5/58 (8.6)	<0.001
Vomiting	18/58 (31.0)	2/18 (11.1)	16/18 (88.9)	2/58 (3.4)	<0.001
Heartburn	17/58 (29.3)	2/17 (11.8)	15/17 (88.2)	2/58 (3.4)	<0.001
Early satiety	11/58 (19.0)	2/11 (18.2)	9/11 (81.8)	2/58 (3.4)	0.004
Food intolerance	27/58 (46.6)	2/27 (7.4)	25/27 (92.6)	2/58 (3.4)	<0.001
Bloating	25/58 (43.1)	5/25 (20.0)	20/25 (80.0)	5/58 (8.6)	<0.001
Constipation	9/58 (15.5)	5/9 (55.6)	4/9 (44.4)	6/58 (10.3)	0.375

TABLE 3: Resolution of Preoperative Gastrointestinal Symptoms Following Laparoscopic Cholecystectomy

N preop denotes the number of patients with the specified symptom preoperatively. Percentages for persistence and resolution use N preop as the denominator. Postoperative constipation includes five persistent cases plus one new-onset case. Two-sided exact McNemar tests were used for paired preoperative versus postoperative binary symptom status; $p < 0.05$ was considered statistically significant.

Discussion

In this prospective observational study, 8/58 patients (13.8%) had persistence of at least one preoperative gastrointestinal symptom during one- to six-month follow-up, while 50/58 (86.2%) had no persistent preoperative symptoms. This proportion is close to the 13% persistent pain reported by Luman et al. at six months, although differences in symptom definitions, populations, and follow-up intervals limit direct comparison [5]. Earlier studies similarly showed that most patients improve after laparoscopic cholecystectomy, but that complete disappearance of all abdominal or dyspeptic symptoms is not universal [3,4,6,7].

The symptom-specific analysis is clinically more informative than an overall success rate. Nausea, vomiting, heartburn, early satiety, food intolerance, and bloating demonstrated high resolution rates in the present cohort, while constipation improved less consistently. Systematic evidence has likewise shown wide variation in persistent and de novo symptoms after cholecystectomy, with upper abdominal pain usually improving but bowel and dyspeptic symptoms persisting or appearing de novo in a subset of patients [8]. In a contemporary analysis of 820 patients, Thunnissen et al. reported that persistent abdominal pain and symptoms such as flatulence remained clinically relevant after cholecystectomy despite high resolution of biliary colic [12].

The persistence of nonspecific gastrointestinal symptoms is important because gallstones and gastrointestinal complaints may coexist without a direct causal relationship. Latenstein et al. identified multiple potential explanations for long-term postcholecystectomy symptoms, including coexisting gastrointestinal diseases, residual or newly formed stones, physiological changes after cholecystectomy, psychological factors, surgical complications, and sphincter of Oddi dysfunction [9]. The PERFECT study further demonstrated that functional dyspepsia and irritable bowel syndrome are common among patients with gallstones and are associated with less favorable symptom outcomes after surgery [11].

These findings have direct implications for preoperative counselling. Patients should be informed that laparoscopic cholecystectomy is effective for typical biliary symptoms but may not eliminate every accompanying gastrointestinal complaint. Particular caution is appropriate when the predominant complaints are bloating, altered bowel habits, reflux-like symptoms, or other nonspecific symptoms. Contemporary randomized data reinforce the need for shared decision-making: the SECURE trial and its five-year follow-up demonstrated that a substantial proportion of patients remain symptomatic or not completely pain-free despite treatment, while the C-GALL trial showed that conservative management can be a reasonable alternative for selected patients with uncomplicated symptomatic gallstone disease [10,13,14].

Preoperative assessment should therefore actively consider alternative or coexisting causes of symptoms. Depending on the clinical presentation, these may include functional dyspepsia, irritable bowel syndrome, gastroesophageal reflux disease, peptic disease, constipation-related disorders, pancreatic disease, or other hepatobiliary pathology [9,11,15]. Persistent symptoms after surgery should similarly prompt a symptom-directed evaluation rather than automatic attribution to a generic postcholecystectomy syndrome.

Distinguishing persistent preoperative symptoms from genuinely new postoperative symptoms is also important, as the two may have different mechanisms and management implications [8,12].

This counselling approach is consistent with contemporary reviews emphasizing careful symptom characterization and selective treatment in symptomatic gallstone disease [16,17]. International guidance similarly supports cholecystectomy for appropriately selected symptomatic gallstone disease while recognizing the importance of evaluating other causes of abdominal symptoms when the clinical presentation is atypical [18].

The present study has several limitations. It was conducted at a single centre and included only 58 patients in the final analysis, with eight patients lost to follow-up, thereby limiting the precision and generalizability of the findings. Although the study followed a prospective observational design with predefined eligibility criteria and symptom assessment, certain methodological factors may affect its reproducibility. Laparoscopic cholecystectomies were performed by different surgeons, and variations in operative techniques, port placement, and perioperative management were not systematically standardized or evaluated. Additionally, symptom assessment was based on a structured study proforma rather than a validated gastrointestinal symptom questionnaire, and follow-up was conducted through either outpatient visits or telephone interviews. These differences in assessment methods may have introduced reporting and assessment bias.

Furthermore, the postoperative follow-up period varied between one and six months, potentially influencing the identification and reported persistence of gastrointestinal symptoms. The absence of a uniform follow-up time point and standardized symptom severity scoring limited the ability to objectively quantify symptom improvement. Although preoperative and postoperative symptoms were compared, variations in assessment timing and methodology may have affected the consistency of these comparisons. The relatively small number of patients with persistent symptoms also limited the ability to perform robust multivariable analyses to identify independent predictors of symptom persistence. These methodological limitations should be considered when interpreting the findings and attempting to reproduce the study in other clinical settings. Future multicentre prospective studies incorporating standardized operative protocols, validated symptom assessment instruments, uniform follow-up intervals, and larger sample sizes are warranted to improve reproducibility and establish more reliable predictors of persistent symptoms following laparoscopic cholecystectomy.

Since this was a single-arm observational study without a nonoperative comparison group, the observed improvements in gastrointestinal symptoms cannot be attributed exclusively to laparoscopic cholecystectomy, and causal relationships cannot be established.

Conclusions

Laparoscopic cholecystectomy was associated with substantial symptomatic improvement in this cohort, with 86.2% of patients reporting no persistence of preoperative gastrointestinal symptoms during one- to six-month follow-up. However, 13.8% had at least one persistent symptom. Most assessed symptoms showed high resolution rates, while constipation demonstrated comparatively poor resolution and bloating remained present in a subset of patients. Preoperative counselling should emphasize that nonspecific gastrointestinal symptoms may not be caused by gallstones and may persist despite technically successful cholecystectomy. Careful evaluation for alternative gastrointestinal causes is appropriate both before surgery in patients with atypical symptom patterns and after surgery in those who remain symptomatic.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Dalvin Devis, Manoj Gopal V., James Alex

Acquisition, analysis, or interpretation of data: Dalvin Devis, Manoj Gopal V., James Alex

Drafting of the manuscript: Dalvin Devis, Manoj Gopal V., James Alex

Critical review of the manuscript for important intellectual content: Dalvin Devis

Supervision: Dalvin Devis

Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. Institutional Ethics Committee, Pushpagiri Institute of Medical Sciences and Research Centre, Thiruvalla issued approval PIMSRC/E1/388A/62/2022. **Animal subjects:** All authors have

confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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