# High Incidence of Postcholecystectomy syndrome: Can We Reduce It?

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## Abstract

The incidence of postcholecystectomy syndrome (PCS) at Cipto Mangunkusumo Hospital, Indonesia, was previously found to be 54.29% (2012), which was higher than those reported in other countries. This research was undertaken to identify the risk factors for PCS in developing countries with limited resources and facilities.

This was a cross-sectional study of all patients who underwent cholecystectomy in our hospital during 2015. The variables included sex, body mass index, preoperative symptom duration, preoperative flatulence, level of education, preoperative symptoms, preoperative awareness, and preoperative ultrasound. All the data were analyzed through bivariate and multivariate analyses.

In total, 112 patients who underwent laparoscopic cholecystectomy were followed. We found the incidence of PCS to be 45.5%. Multivariate logistic regression analysis showed that preoperative flatulence (P ≤ 0.001, OR = 17.152), nonspecific preoperative symptoms (P = 0.012, OR = 3.984), and patients' poor preoperative awareness of PCS (P = 0.003, OR = 5.907) were independent predictive factors for PCS. Statistically significant correlation between patients' awareness and preoperative education (P ≤ 0.001, OR = 69.00) was found.

We concluded that preoperative flatulence, nonspecific preoperative symptoms, and poor preoperative awareness increased the incidence of PCS. Besides abdominal ultrasound, other examinations, such as upper GI endoscopy, for nonspecific preoperative symptoms that do not meet the Rome III criteria are recommended to rule out the diagnosis and avoid unnecessary surgeries. Adequate preoperative information and education may reduce the incidence of PCS.

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## Introduction

Postcholecystectomy syndrome (PCS) treatment rates remain unsatisfactory, and the patients may experience upper abdominal pain, dyspepsia, diarrhea, or food intolerance but may be free of symptoms after surgery. The incidence of PCS at Cipto Mangunkusumo Hospital, Indonesia, was previously been found to be 54.29% in 2012, which was higher than that reported in other countries (10%–15%).[1] More than 100 cholecystectomies are performed every year at our hospital; however, PCS remains a problem. A previous study by Mertens et al[2] showed that preoperative dyspeptic symptoms, notably bad taste and preoperative flatulence, were risk factors for PCS. Jensen et al[3] found that long duration of preoperative symptoms was related to PCS, whereas Murshid[4] found female sex and young age to be risk factors for PCS. As our incidence of PCS was higher, we suspected that there were different risk factors than those mentioned above. Our objective was to identify these risk factors in hope of reducing the incidence of PCS.

PCS can be diagnosed early or years after surgery and was first described by Womack and Crider.[1] The symptoms may actually be a continuation of symptoms that were interpreted as those resulting from gallbladder pathology or the development of new symptoms that might normally be attributed to the gallbladder.[1] The pathophysiology of PCS remains debatable;

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some authors found it to be biliary and others nonbiliary.[5] In 85% of the cases, PCS was caused by alteration of bile flow due to loss of the gallbladder's reservoir function after cholecystectomy. This increased bile flow into the upper gastrointestinal tract, thus causing esophagitis and gastritis. Within the lower gastrointestinal tract, it can cause diarrhea.[1,4]

Cholecystectomy is a standard treatment for cholecystolithiasis. Even with a low mortality rate, prophylactic asymptomatic cholecystectomy is not recommended.[6,7] The most specific symptom attributed to disorders of the gallbladder is biliary pain. Rome III criteria[8] compares biliary pain with other nonspecific abdominal complaints. It states that the pain must be pain located in the epigastrium and/or right upper quadrant and include all of the following: episodes lasting ≥30 min; recurrent symptoms occurring at different intervals (not daily);pain built-up to a steady level; moderate to severe pain enough to interrupt the patient's daily activities or lead to an emergency department visit; pain not relieved by bowel movements, postural changes, or antacids; and exclusion of other structural diseases that would explain the symptoms. The pain may present with one or more of the following: nausea and vomiting, radiation to the back and/or right infra subscapular region, or awakening from sleep in the middle of the night.

Transabdominal ultrasound of the entire upper abdomen is mandatory in patients with the previously mentioned symptoms, and has been widely used in our center. Even with its low false-positive rate (3.9%), it is possible that inaccurate ultrasound may be related to PCS.[9] Previously, upper GI endoscopy before cholecystectomy was controversial, but now it is used to rule out other diseases with similar symptoms such as peptic ulcers, and acute or chronic gastritis. It is routinely performed before cholecystectomy in health centers with adequate facilities to help avoid inappropriate surgeries in patients whose symptoms were not related to biliary stones.[10] However, as a developing country with limited resources and facilities, it is not applicable to our center where upper GI endoscopies cannot be routinely performed before surgery.

Egbert et al[11] showed that patients who were told before the surgery about postoperative pain, including how severe it would be and how long it would last, were able to reduce their postoperative narcotic requirements by half. We hypothesized that preoperative awareness could also influence perception of chronic pain, such as in PCS.

## Materials and Methods

This research was a cross-sectional study undertaken to determine the risk factors for PCS. The data were derived retrospectively from medical records and interviews with patients who underwent cholecystectomies at Cipto Mangunkusumo Hospital in 2015. Patients who underwent other procedures besides cholecystectomy (e.g. Whipple procedure, double bypass), patients with common bile duct or intrahepatic gallstones, and patients with insufficient data were excluded from the study. All data on patients' characteristic, preoperative symptoms, awareness of PCS, and postoperative conditions were collected from medical records and interviews. For preoperative symptoms, we used Rome III criteria to determine whether the symptoms were specific or nonspecific for biliary pain. To assess preoperative awareness of PCS, we asked the patients if they had preoperative knowledge about PCS and how they obtained that the information. We evaluate postoperative condition at a minimum of 6 months after surgery. Statistical analyses were performed using SPSS 22.0 to determine the relationships between PCS and (i) patients' characteristics, (ii) preoperative symptoms and (iii) awareness. For this type of study, formal consent was not required. This study was approved by the Ethical Committee of Health Research at Cipto Mangunkusumo Hospital.

## Results

In 2015, 119 patients underwent cholecystectomy at Cipto Mangunkusumo Hospital, but seven patients were excluded from this study due to insufficient data and loss at follow-up. Elective surgery was performed on all remaining 112 patients with indications of symptomatic cholecystolithiasis (96.4%), hydrops of the gallbladder (1.8%), gallbladder polyps (0.9%), and asymptomatic cholecystolithiasis (0.9%). No acute cholecystitis or pancreatitis were found. All procedures were performed laparoscopically but seven surgeries (6.2%) were converted to open cholecystectomy due to

adhesions and Mirrizi's syndrome. No cases of mortality were recorded. In addition, we found pigment gallstones in 52 patients (46.4%), cholesterol gallstones in 51 patients (45.4%), and no gallstones in the other patients.

Sixty-one patients (54.4%) experienced preoperative symptoms that did not meet the Rome III criteria as we classified them as nonspecific preoperative symptoms, and 58 patients (51.8%) experienced preoperative flatulence. Preoperative symptom duration was less than a year in 67 patients (59.8%), 1-5 years in 40 patients (35.7%), 6-10 years in four patients (3.6%), and more than 10 years in only one patient (0.9%). Most patients (97.3%) presented at the hospital with a chief complaint of upper abdominal pain; only a few patients reported experiencing nausea or jaundice without abdominal pain.

Abdominal ultrasound (USG) was done for all patients, but only 104 (92.9%) had intraoperative findings that were consistent with preoperative USG. Gallstones were seen in seven patients during the preoperative USG, but not intraoperatively, and gallbladder sludge was observed in one patient during preoperative USG, but pigment gallstones were found intraoperatively. In addition to USG, other imaging modalities were performed in a few patients: six patients underwent abdominal computed tomography (CT), 15 patients received magnetic resonance cholangiopancreatography (MRCP), endoscopic retrograde cholangiopancreatography (ERCP) was performed in five patients, and another five patients received MRCP together with ERCP. Oesophagogastroduodenoscopy (OGD) was performed in four (3.6%) patients who exhibited chronic dyspepsia. One patient with normal findings on OGD did not develop PCS, whereas the remaining three patients with pathologic findings on OGD (such as gastritis), all exhibited PCS after the surgery. Postoperative observation was done 6-20 months after surgery, with mean of 14.95±3.27 months.

The mean age of the patients was 47.69 (±11.33) years old, with most being 41- 60 years old (56.3%). The youngest was 22 years old and the oldest was 73 years old. In the entire sample, 73 patients (65.2%) were female, including the oldest and youngest subjects. Most patients were overweight (80.4%) and the mean body mass index (BMI) was 26.7 kg/m$^2$. In terms of education, 47 patients (42%) had studied at senior high school (middle education), 33 patients (29.5%) had only attended elementary school or junior high school (low education) and 32 patients (28.6%) had received higher education such as bachelor's degree or diploma.

PCS was found in 51 patients (45.5%) in various periods, ranging from soon after the surgery to 18 months after the surgery, with a mean period of 6.3 months. Most patients complained of upper abdominal pain (84.3%) and dyspepsia (78.4%), but none had icterus. Of the 51 patients with PCS, only 13.7% attended medical facilities, and none of them were evaluated for PCS due to resource limitations. Most patients felt relief following treatment with symptomatic therapies such as analgesics, H-2 receptor blockers, or proton pump inhibitors. Some patients with PCS did not seek medical treatment because of mild symptoms (35.3%) or preferring use of traditional or alternative medicines (51.0%).

| Variable | B | OR | *P-value* |
|---|---|---|---|
| Preoperative symptom duration >1 year | 0.811 | 2.251 (0.76–6.67) | 0.143 |
| Preoperative flatulence | 2.842 | 17.152 (5.31–55.42) | ≤0.001 |
| Nonspecific preoperative symptoms | 1.382 | 3.984 (1.36–11.69) | 0.012 |
| Poor preoperative awareness of PCS | 1.776 | 5.907 (1.86–18.75) | 0.003 |
| Inconsistent preoperative USG with intraoperative finding | 1.144 | 3.141 (0.07-135.16) | 0.551 |
| Constant | −3.673 | 0.025 | ≤0.001 |

**Table 1**. Multivariate analysis of risk factors for PCS.

The mean age for patients with PCS was 48.9±10.2 years and patients with no PCS were 46.6±12.1 years old. Most patients with PCS were 41-60 years old (62.7%), followed by 21-40 years old (25.5%). Data analysis showed no significant between-group differences in mean age between patients with and without PCS (P=0.279).

Bivariate analysis showed significant correlations between PCS and longer preoperative symptom duration (P=0.033),

preoperative flatulence (P≤0.001), nonspecific preoperative symptoms (P≤0.001), and preoperative awareness of PCS (P≤0.001). On logistic regression, only preoperative flatulence, nonspecific preoperative symptoms, and preoperative awareness showed a significant correlation with PCS (Table 1).

Of the total sample, 68 patients (60.7%) had good preoperative awareness of PCS, 69 patients (61.6%) had received preoperative explanation of PCS, but only 67 patients (59.8%) had received information from medical personnel (the others received information from other sources). There was one patient who had received a preoperative explanation but still had poor awareness of PCS. Male patients older than 60 years, with middle or high levels of education were found to better preoperative awareness of PCS. However, statistically there was no significant relationship between preoperative awareness and age, gender, or level of education, but a significant correlation was found with preoperative explanation (P≤0.001) (Table 2).

| Variable | Poor awareness n (%) | Good awareness n (%) | Total | OR | *P-value* |
|---|---|---|---|---|---|
| Age (years) | | | | | |
| 21–40 | 11 (31.4%) | 24 (68.6%) | 35 | reference | |
| 41–60 | 30 (47.6%) | 33 (52.4%) | 63 | 0.50 (0.21–1.20) | 0.120 |
| >60 | 3 (21.4%) | 11 (78.6%) | 14 | 1.68 (0.39–7.26) | 0.484 |
| Gender | | | | | |
| Female | 31 (42.5%) | 42 (57.5%) | 73 | 1.48(0.66–3.32) | 0.346 |
| Male | 13 (33.3%) | 26 (66.7%) | 39 | | |
| Level of education | | | | | |
| Low | 15 (45.5%) | 18 (54.5%) | 33 | reference | |
| Middle | 17 (36.2%) | 30 (63.8%) | 47 | 1.47 (0.59–3.64) | 0.404 |
| High | 12 (37.5%) | 20 (62.5%) | 32 | 1.39 (0.52–3.74) | 0.515 |
| Preoperative explanation | | | | | |
| No | 43 (100%) | 0 | 43 | 69.00 (9.86–482.90) | ≤0.001 |
| Yes | 1 (1.4%) | 68 (98.5%) | 69 | | |

**Table 2.** Patients' characteristic and awareness of PCS.

## Discussion

There was no significant difference in the incidence of PCS between this study and the previous study conducted in 2012 (45.5% vs 54.29%). We found our center's risk factors for PCS were preoperative flatulence, nonspecific preoperative symptoms, and preoperative awareness. Preoperative flatulence was previously mentioned by Mertens et al[2] as a PCS risk factor in their study. They also separated the patients into two groups based on preoperative symptoms: (i) patients with biliary pain and (ii) patients with dyspeptic symptoms without biliary pain. Of all the patients, 73.6% had biliary symptoms. Subjects with dyspepsia had greater risk for developing PCS. In this study, we used Rome III criteria to determine whether patients had specific or nonspecific preoperative symptoms, and only 45.5% patients presented with specific symptoms. We had more patients with nonspecific symptoms, and this may explain why our incidence of PCS was higher than other centers, where nonspecific symptoms were one of risk factors for PCS. As mentioned before, upper GI endoscopy was not routinely performed in our center due to limited facilities and resources. Only 3.6% of patients had endoscopic evaluations before surgery, given an indication of chronic dyspepsia. Although endoscopy could not be performed routinely with all patients, it should be considered for patients with nonspecific symptoms to avoid unnecessary surgeries, as they are more likely to develop PCS.

Preoperative explanation and education concerning PCS from medical staff should contain information on the disease itself, disease management, postoperative complications, and also what to do if there are complications. Patients' awareness was influenced by the provision of preoperative explanations. Good preoperative explanations provided by medical staff (i.e. doctors) can produce good awareness.

Statistically, good preoperative awareness will result in a lower possibility of developing PCS and may enhance patient satisfaction.

The results of these studies were influenced by the conditions specific to the various populations. Data on preoperative and postoperative conditions were all subjective and depended on the patient's intelligence and memory, although bias was minimized by also interviewing the family members to confirm the data.

## Conclusion

In conclusion, PCS was influenced by preoperative flatulence (17.1 times higher probability), poor preoperative awareness (5.9 times higher probability), and nonspecific preoperative symptoms (3.9 times higher probability). Beside abdominal ultrasound, patients with nonspecific preoperative symptoms who did not met Rome III criteria should have other examinations such as gastrointestinal endoscopy to rule out the diagnosis and avoid unnecessary surgeries. Giving complete preoperative information and education can produce good patient awareness, and potentially reduce the incidence of PCS.

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