

ORIGINAL ARTICLE

Colicky pain and related complications after cholecystectomy for mild gallstone pancreatitis

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Abstract

Background: Same-admission cholecystectomy is advised after gallstone pancreatitis to prevent recurrent pancreatitis, colicky pain and other complications, but data on the incidence of symptoms and complications after cholecystectomy are lacking.

Methods: This was a prospective cohort study during the previously published randomized controlled PONCHO trial on timing of cholecystectomy after mild gallstone pancreatitis. Data on healthcare consumption and questionnaires focusing on colicky pain and biliary complications were obtained during 6 months after cholecystectomy. Main outcomes were (i) postoperative colicky pain as reported in questionnaires and (ii) medical treatment for postoperative symptoms and gallstone related complications.

Results: Among 262 patients who underwent cholecystectomy after mild gallstone pancreatitis, 28 of 191 patients (14.7%) reported postoperative colicky pain. The majority of these were reported within 2 months after surgery and were single events. Overall, 25 patients (9.5%) required medical treatment for symptoms or gallstone related complications. Acute readmission was required in seven patients (2.7%). No predictors for the development of postoperative colicky pain were identified.

Discussion: Some 15% of patients experienced colicky pain after cholecystectomy for mild gallstone pancreatitis, which were mostly single events and rarely required readmission. These data may be used to better inform patients undergoing cholecystectomy for mild gallstone pancreatitis.

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Introduction

Cholecystectomy is among the most common surgical procedures in the Western World.¹ A recent systematic review reported that up to one third of patients who undergo this procedure for symptomatic gallbladder stones have persisting or new abdominal symptoms, such as upper abdominal pain.² These findings have raised concerns about the appropriateness of cholecystectomy in uncomplicated symptomatic gallstone disease.^{3,4}

In patients with complicated gallstone disease such as gallstone pancreatitis or acute cholecystitis, the risk of these gallstone related complications outweighs the risk of persisting symptoms.^{5–7} Several studies have demonstrated that cholecystectomy following gallstone pancreatitis does not completely eliminate the risk of recurrent disease, as this may occur in 5% of patients.^{8–12} Detailed data on the frequency and natural history of these recurrent symptoms after cholecystectomy for gallstone pancreatitis are lacking.¹³

To this end, we prospectively investigated the risk of colicky pain and related complications after cholecystectomy for mild gallstone pancreatitis, both from a patient and healthcare perspective. Furthermore, we explored potential risk factors for postoperative colic in these patients.

Methods

Study design

This was a prospective analysis of patients enrolled in the randomized controlled multicenter PONCHO trial on timing of cholecystectomy after mild gallstone pancreatitis.^{11,15} Patients were enrolled in the trial between December 2010 and August 2013 in 23 Dutch hospitals, including 7 university medical centers and 16 teaching hospitals. Adult patients admitted with a first episode of gallstone pancreatitis were screened for eligibility, excluding those with severe gallstone pancreatitis (*i.e.* organ failure for more than 48 h, pancreatic necrosis or peripancreatic fluid collections on imaging), chronic pancreatitis, pregnancy or *a priori* high risk of perioperative complications (American Society of Anesthesiologists [ASA] class III *and* age over 75 and all those with ASA class IV or V).^{16,17} Pancreatitis was diagnosed according to the Atlanta guidelines.¹⁶ At least two of the following three items had to be present: (i) epigastric pain, (ii) serum amylase or lipase levels exceeding three times the upper limit normal and (iii) if performed, characteristic findings of acute pancreatitis on cross-sectional imaging. Once discharge was foreseen within 48 h, participants were randomized to cholecystectomy within 3 days (*i.e.* same-admission cholecystectomy) or interval cholecystectomy after 25–30 days. Intraoperative cholangiography was not part of the study protocol, as very few Dutch surgeons perform this procedure routinely. The primary endpoint of the trial was mortality or acute readmission for gallstone-related complications during a 6-month follow-up period. In the present study, outcomes after cholecystectomy with a time horizon of 6 months were investigated from the perspective of both healthcare providers and patients.

Patient-reported postoperative colicky pain

Upon inclusion in the PONCHO trial, all patients were given questionnaires with instructions to prospectively document what they considered to be colicky pain during a 6-month period. Events were rated on a 0–10 numeric rating scale (NRS), with 0 representing ‘no pain’ and 10 ‘the worst pain imaginable’. Duration of the event was documented dichotomously as either under or over 30 min. We defined postoperative colicky pain as (i) persisting hypochondriac or epigastric pain of at least 30 min, corresponding with the Rome criteria, and (ii) pain with an NRS score of 5 or higher, which we considered a reasonable cut-off value.¹⁸ The trial study nurse contacted all participants by telephone approximately every 2 months and at the end of the 6-month follow-up period.

Healthcare based outcomes

Health care utilization of all participants was prospectively registered during the 6-month follow-up period. The following healthcare components were included in this study: hospital visits for gallstone-related disease (e.g. recurrent gallstone pancreatitis), diagnostics for suspected persisting common bile duct stones (e.g. ultrasound, endoscopic retrograde cholangiopancreatography). The focus of this study was postoperative gallstone-related complications. Therefore, hospital visits for surgical complications (such as wound infections) were excluded, as were patients in whom diagnostics revealed an unrelated cause of symptoms.

Risk factors for colicky pain

The following variables were examined for a potential effect on the development of colicky pain: age, sex, body mass index (BMI), overall health status based on ASA classification, a history of biliary colic, endoscopic sphincterotomy prior to surgery, the number of days between onset of pancreatitis and cholecystectomy, conversion to open cholecystectomy and difficulty of cholecystectomy according to the surgeon. This last variable was included as a difficult cholecystectomy, with much manipulation of the gallbladder, could theoretically increase the risk of gallbladder stones being forced into the common bile duct. Difficulty of cholecystectomy was assessed by the surgeon on a 0–10 NRS (10 being most difficult). Also, logistic regression analyses including those patients in whom cholecystectomy was performed per the PONCHO trial study protocol (*i.e.* same admission or interval cholecystectomy). Additionally, risk factors for common bile duct stones were assessed using the guidelines of the American Society for Gastrointestinal Endoscopy (ASGE).¹⁹ According to this stratification system, factors associated with high risk (*i.e.* >50%) for choledocholithiasis are (i) gallstones in the common bile duct on imaging, (ii) serum bilirubin levels exceeding 70 $\mu\text{mol/l}$, (iii) dilatation of the common bile duct ≥ 7 mm AND serum bilirubin levels between 30 and 70 $\mu\text{mol/l}$ or (iv) signs of cholangitis. Finally, the findings of patients who underwent intraoperative cholangiography (IOC) were evaluated.

Statistical analysis

Only investigations or hospital visits for (suspected) colic and related complications were included in this study. Patients were dichotomized based on post-cholecystectomy healthcare resource utilization. Patients who made a completely uneventful recovery were grouped as ‘no additional care’; those with postoperative symptoms needing additional medical care through diagnostics or treatment were grouped as ‘additional care’. In the latter category, all diagnostics and treatment for direct surgical complications such as bleeding or wound infections were excluded.

All continuous data was non-normally distributed and therefore reported as median with interquartile range (IQR). For

differences in distribution of categorical variables the χ^2 test was used. Relationships between the variables of interest and outcomes were tested through univariable logistic regression. Results from these analyses were reported as odds ratios (ORs) with 95% confidence intervals (CI) and *p* value. Regarding the patient-reported outcomes, these analyses included all patients who had returned the questionnaires. All analyses were performed in SPSS version 22 (Chicago, IL).

Results

Patients

Of the 266 participants in the PONCHO trial, 4 patients were excluded, for incorrect diagnosis of pancreatitis, declined cholecystectomy, withdrawn informed consent and death due to ischemic stroke. Baseline characteristics of the included patients are listed in Table 1.

Patient reported postoperative colicky pain

Questionnaires were returned by 191 of the 262 patients (72.9%). Baseline characteristics of these 191 patients are shown in Table 1. During the 6-month follow-up period, 28 patients (14.7%) reported postoperative colicky pain. This was one event in 14 patients, two events in 5 patients and the other 9 patients reported three or more events (range 1–12 events). Seven patients (25%) had a history of colicky pain prior to admission for pancreatitis. Of the 28 patients, 16 (8.3% of the respondents) developed colicky pain during the first month after

cholecystectomy, 6 (3.1%) in the second month and 2 (1%) in the third, fourth and fifth months (Fig. 1). One patient (3.6%) reported colicky pain in four consecutive months, 6 patients (21.4%) over the course of 2 months and the remaining 21 patients (75%) had colicky pain during 1 month. Only 4 (2.1%) of the 191 responding patients reported colicky pain during the final month of follow-up.

Healthcare based outcomes

Twenty-five out of the 262 patients (9.5%) needed postoperative hospital care for colicky pain or related complications. Table 2 presents an overview of the type and total number of diagnostic procedures and emergency room visits. Gallstone-related complications led to acute readmissions in seven of these patients (2.6%); four with recurrent pancreatitis (1.5%), two with colicky pain (<1%) and one with common bile duct stones (<1%). Two of these seven patients underwent post-operative ERCP (0.4%) for suspected bile duct stones, which was found in one. All other patients were treated conservatively. Recurrent pancreatitis was mild in all patients. All re-admissions occurred within one month after cholecystectomy.

In the remaining 18 patients, biochemical testing and imaging failed to confirm remnant common bile duct stones (*i.e.* cholelithiasis) as the cause of the complaints.

Common bile duct stones

Eighty patients had undergone preoperative biliary tract evaluation with endoscopic sphincterotomy prior to surgery, with documented stone extraction in 58. One patient had documented common bile duct stones on imaging prior to cholecystectomy. Endoscopic retrograde cholangiopancreatography was unsuccessful in this patient due to previous bariatric surgery and the patient was managed conservatively, making an uneventful recovery. One patient had raised serum bilirubin levels preoperatively, but also had an uneventful recovery. Another patient with slightly raised bilirubin levels was managed conservatively as these levels declined spontaneously. The patient recovered without needing additional care or reporting colicky pain. There were no patients with signs of cholangitis.

Intraoperative cholangiography (IOC) was attempted in 17 patients (6.5%). Cannulation of the cystic duct was unsuccessful in 2 patients. In 1 of the 15 remaining patients (6.7%) a filling defect was seen during IOC, which was managed conservatively. The patient made an uneventful recovery without reporting colicky pain.

Predictors of colicky pain or related complications

No predictors of colicky pain could be identified through univariate regression analysis (Table 3). Additional analyses were performed including only those patients who underwent cholecystectomy according to the treatment protocol of the PONCHO trial (*i.e.* same-admission cholecystectomy *vs.* interval cholecystectomy). No effect of treatment strategy was found in

Table 1 Baseline characteristics

	Total cohort (N = 262)	Questionnaire Respondents (N = 191)
Age; median (IQR)	53 (40–66)	54 (42–68)
Sex (male); N (%)	103 (39.3)	76 (39.7)
Body mass index; median (IQR)	28 (24–31)	27 (24–30)
ASA class; N (%)		
I	94 (35.8)	68 (35.6)
II	145 (55.3)	108 (56.5)
III	23 (8.7)	15 (7.9)
History of biliary colic; N (%)	77 (29.3)	54 (28.3)
Endoscopic sphincterotomy prior to cholecystectomy; N (%)	80 (30.5)	49 (25.7)
Days from onset of pancreatitis to cholecystectomy; median (IQR)	22 (7–33)	20 (7–33)
Difficulty of cholecystectomy; NRS score median (IQR)	6 (4–7)	6 (4–7)
Conversion ^a ; N (%)	9 (3.5)	6 (3.1)

IQR, interquartile range; ASA, American Society of Anesthesiologists; NRS, numeric rating scale.

No statistically significant differences between in baseline characteristics between the respondents and total cohort were found.

^a Excluding 4 patients in whom primary open cholecystectomy was performed.

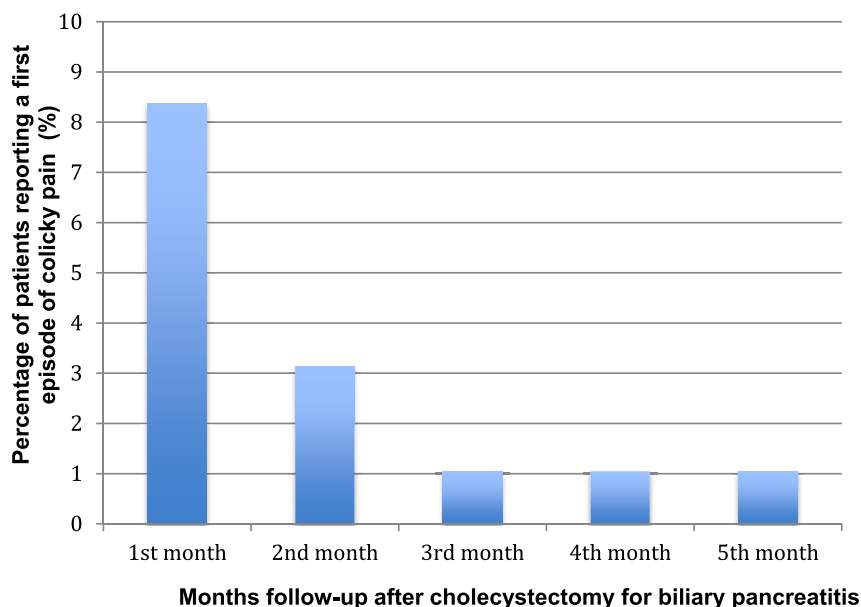


Figure 1 New patients reporting colicky pain per month

need for postoperative medical treatment: 14 out of 119 patients in the same-admission group (11.7%) vs. 5 out of 100 patients in the interval group (5%, odds ratio for interval cholecystectomy of 0.40, 95% confidence interval [CI] 0.14–1.14; $p = 0.09$). Likewise, no effect was found in patient reported colicky pain: 14 out of 91 responding patients (15.3%) reported colic after same-admission cholecystectomy vs. 13 of 70 patients (18.6%) in the interval group (odds ratio [OR] for interval cholecystectomy of 1.35, 95% CI 0.53–3.4; $p = 0.53$).

Discussion

This analysis performed within a randomized controlled multi-center trial found that 9.5% of patients after cholecystectomy for

Table 2 Health care consumption of the 25 patients who needed postoperative medical treatment during 6 months follow-up after cholecystectomy for biliary pancreatitis

Procedure	Total no. (% of patients)	Range per patient
Ultrasound	24 (9.2%)	1–3
CT	8 (3.1%)	1
ERCP	2 (0.8%)	1
MRCP	4 (1.5%)	1
Endoscopic ultrasound	1 (0.4%)	1
Emergency room visit	7 (2.7%)	1–2

CT Computed Tomography; MRCP Magnetic Resonance Cholangiopancreatography; ERCP Endoscopic Retrograde Cholangiopancreatography.

Note: This table does not include diagnostics performed postoperatively for (suspected) surgical complications or other, unrelated causes of symptoms.

mild gallstone pancreatitis required postoperative medical treatment, and some 15% of patients reported colicky pain during 6 months follow-up. Recurrent pancreatitis after cholecystectomy occurred in 2% of patients and was mild in all cases. Colicky pain was self-limiting and of short duration. No risk factors for the occurrence of either variable could be identified.

Previous studies in unselected cohorts have indicated that up to 33% of patients experience persisting upper abdominal pain after cholecystectomy.^{2,14} Along with cholecystitis, gallstone pancreatitis is generally considered a stringent indication for cholecystectomy. While this strategy reduces the risk of gallstone related complications, data are lacking on the incidence of colics or related complications after cholecystectomy for this indication.^{20,21} Although several studies have described postoperative symptoms in unselected cohorts *including* patients with pancreatitis or cholecystitis, the present study is the first to investigate this subgroup specifically.^{22,23} We found that a low but definite proportion of patients experienced colicky pain serious enough to warrant additional medical treatment. Obviously, these findings do not question the indication for cholecystectomy after gallstone pancreatitis: in the patients awaiting cholecystectomy in the interval group of the PONCHO trial, 51% reported colicky pain before surgery and 17% required re-admission for recurrent biliary events.¹¹ Other studies have reported recurrent gallstone-related morbidity in 16–61% of patients in whom cholecystectomy was delayed.^{24,25} Furthermore, a recurrent attack of pancreatitis may be more severe in up to 9% of patients and mortality rates of relapses are similar to those of the first attack.^{26,27}

There are several possible explanations for colicky pain or related complications after cholecystectomy. Although sphincter of Oddi dysfunction and neuropathic pain have been reported

Table 3 Univariable logistic regression analysis of factors predicting postoperative symptoms

Predictor	Postoperative colicky pain (N = 191)	p	Postoperative medical treatment (N = 262)	p
	OR (95% CI)		OR (95% CI)	
Age	0.99 (0.96–1.01)	0.33	0.98 (0.96–1.01)	0.15
Male Sex	0.68 (0.29–1.59)	0.37	0.70 (0.29–1.70)	0.43
Body Mass Index	0.95 (0.88–1.04)	0.27	1.02 (0.96–1.09)	0.50
ASA class I ^a	1.01 (0.44–2.32)	0.99	0.83 (0.34–1.99)	0.67
History of biliary colic	0.82 (0.33–2.07)	0.68	1.15 (0.47–2.78)	0.76
Endoscopic sphincterotomy prior to cholecystectomy	0.44 (0.14–1.33)	0.15	1.32 (0.56–3.12)	0.53
Days from admission to cholecystectomy	1.00 (0.97–1.03)	0.90	0.98 (0.96–1.01)	0.22
Difficulty of cholecystectomy	1.07 (0.87–1.32)	0.51	1.04 (0.85–1.27)	0.68
Conversion	1.14 (0.13–10.15)	0.91	1.16 (0.14–9.69)	0.89

ASA American Society for Anesthesiologists.

^a Compared with ASA class II and III patients.

among causes of post-cholecystectomy pain,²⁸ the most obvious cause is persisting common bile duct stones. These stones may already be present before operation or forced into the common bile duct by manipulation of the gallbladder during surgery. This is an interesting theory, especially when considering that this cohort included a large proportion (30%) of pre-cholecystectomy ERCP. The latter mechanism may explain why preoperative risk factors were not capable of predicting colicky pain. Therefore, the most appropriate moment for evaluating the presence of common bile duct stones is during or immediately following cholecystectomy. Intraoperative cholangiography allows for confirming suspected choledocholithiasis, after which the stones can be dealt with through transcystic stone extraction, laparoscopic bile duct exploration or postoperative ERCP with stone extraction. Notably, there is no consensus on managing asymptomatic common bile duct stones since most of these stones will pass spontaneously.²⁹ Whether all patients undergoing cholecystectomy for gallstone pancreatitis should be subjected to the procedural risks of laparoscopic bile duct exploration (*i.e.* bile leak) or ERCP (*i.e.* perforation, bleeding, post-ERCP pancreatitis) remains subject to debate. Moreover, multiple studies have found similar rates of recurrent gallstone-related complications in patients who had undergone IOC compared to patients who had not.^{30–32} Therefore, many have argued that since stones can be missed or patients may develop symptoms regardless of the procedure, IOC should be reserved for clinically or biochemically 'high-risk' patients.^{30,31,33} The question remains how to prevent postoperative gallstone complications. Despite all proposed strategies a small proportion of patients continue to develop symptomatic common bile duct stones or recurrent gallstone pancreatitis. Resolving this issue requires prospective studies documenting the presence of common bile duct stones shortly after surgery, using highly accurate imaging modalities such as endoscopic ultrasound or magnetic resonance

cholangiopancreatography. Combined with biochemical investigations, these patients can then be followed to study which features are predictive of developing symptoms.

This study has several strengths and limitations. We present a large, prospective cohort of patients with clear, uniform definitions of pancreatitis and other gallstone-related complications collected within the context of a randomized controlled trial. For all patients comprehensive pre- and postoperative clinical and healthcare usage information was available. Additionally, we had high response rates for the questionnaires describing the postoperative events in great detail. Some limitations also have to be addressed. First, since no validated questionnaire for colicky pain is available, such a questionnaire was designed by our study group. As trial participants already received two questionnaires to document pancreatitis-related sick leave in addition to 6 months worth of gallstone symptoms, no gastrointestinal quality of life form was included in the study. However, based on the postoperative healthcare use and patterns of colicky pain, only a very small proportion of patients had persisting postoperative symptoms and we expect the impact on quality of life to have been only minor. Secondly, all post-operatively recorded pain episodes fitting the definition of colicky pain were interpreted as caused by retained common duct stones. We do realize that this is an inference and we cannot exclude other causes for these pains. Furthermore, our data may be incomplete due to recall bias, although we believe it to be unlikely that we would have missed clinically relevant events, as our study nurse contacted patients frequently during follow up. Regarding the risk factor analysis, it is possible that no predictive factors were identified due to a type II error given the relatively low incidence of postoperative symptoms. Finally, it is possible that patients developed symptoms outside of the 6-month follow up period. Within the current follow up period, the majority of readmissions and reported postoperative colics occurred within the first month after cholecystectomy.

In conclusion, in this multicenter cohort of patients followed after cholecystectomy for mild gallstone pancreatitis, a substantial subset of patients (15%) reported one or more events of postoperative colicky pain, but the risk of readmission for biliary events after cholecystectomy was very low (3%). While these risks do not outweigh the benefit of cholecystectomy, they should be discussed during preoperative counseling.

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Conflicts of interest

None declared.

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