



# PRACTICE

## UNCERTAINTIES

# Can surgery be avoided in patients with symptomatic gallstone disease and no complications?

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### What you need to know

- Laparoscopic cholecystectomy is the current treatment of choice for people with symptoms of gallstone disease
- There is limited evidence from two randomised controlled trials that conservative management with pain medications and observation may be a safe alternative to surgery in patients with acute cholecystitis or biliary colic and no complications, as symptoms may subside over time and not recur
- A proportion of patients with uncomplicated gallstone disease who are initially treated conservatively may never require surgery

Cholelithiasis or gallstone disease affects between 5.3% and 25% of people, according to clinical survey reports from Europe, North and South America, and Asia.<sup>1-5</sup> In most people, gallstones are asymptomatic. About 20% of people with gallstones experience pain and complications.<sup>6</sup> Acute cholecystitis describes inflammation of the gall bladder, usually due to obstruction by a gallstone. It causes characteristic severe pain, known as biliary pain, in the right upper abdomen that can last from a few minutes to hours.<sup>7</sup> [Box 1](#) lists the complications of gallstone disease. Here, we focus on management of uncomplicated symptomatic gallstone disease.

### Box 1: Complications of gallstones which require immediate referral for surgical, radiological, or endoscopic intervention<sup>8 7</sup>

- Perforation or gangrene of the gallbladder
- Inflammation of the bile ducts (acute cholangitis)
- Obstructive jaundice due to obstruction of the common bile duct
- Inflammation of the pancreas (acute pancreatitis)
- Acute inflammation or infection of the gall bladder (severe acute cholecystitis), which may lead to complications such as empyema (collection of pus in the gallbladder)

Current clinical guidelines in the US and UK recommend laparoscopic cholecystectomy for patients with biliary pain or acute cholecystitis and radiological evidence of gallstones.<sup>8-10</sup> Surgical treatment carries the risk of complications. Some patients continue to experience symptoms after surgery. Persistent diarrhoea or constipation are often reported after cholecystectomy, and flatulence may arise de novo after surgery.<sup>11</sup> In a recent large prospective study in the UK (167 hospitals, 8909 patients) 7.1% and 10.8% of patients respectively were readmitted and had complications 30 days after cholecystectomy.<sup>12</sup> In the UK, more than 70 000 gall bladder surgeries are performed each year.<sup>13</sup> Laparoscopic cholecystectomy cost the NHS about £82 600 000 in 2015-16, and about £2700 per operation.<sup>14</sup>

Patients with biliary pain are sometimes placed on a waiting list and have elective surgery several months after the initial presentation. Around half of patients presenting with initial symptoms but no evidence of further complications may not experience further pain attacks.<sup>6</sup> There is uncertainty if conservative management with analgesics or anti-inflammatory drugs could be a safe and effective alternative to surgery in patients with uncomplicated symptomatic gallstone disease.

### What is the evidence of uncertainty?

There is limited evidence from two randomised controlled trials (201 patients),<sup>15 16</sup> which suggests that conservative management may be a safe alternative to surgery in some patients with uncomplicated symptomatic gallstone disease or acute cholecystitis. About 55% of patients randomised to conservative management in these trials did not eventually require surgery over a 14 year period. These patients may experience recurrent attacks of biliary pain, however. The studies are small, from a

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single population, and do not present outcomes by subgroups or patient characteristics to suggest which patients may be considered for conservative management. These findings seem to be in line with those from cohort studies on the natural course of gallstone disease that show that recurrent pain attacks may diminish or not happen again in up to half of symptomatic patients.<sup>6 17 18</sup>

**Box 2** describes our search strategy. Both trials were conducted in Norway by one research group and were judged to be at a low risk of bias using the Cochrane risk of bias tool.<sup>19</sup> Main outcomes were recurrence of symptoms (that is, pain attacks); gallstone related complications; hospital admissions due to gallstone related pain, surgery related complications, and people requiring surgery; and mortality. **Table 1** shows the main findings of these trials. Participants randomised to surgery experienced more surgery related complications than those who were treated conservatively and showed a slight, non-significant, increase in the rate of all-cause mortality. The participants allocated to observation had more episodes of cholecystitis but few other gallstone related complications. Out of 102 patients randomised to observation or conservative treatment, 56 (55%) did not require surgery during the 14 year follow-up period. The other 45% initially randomised to observation eventually underwent cholecystectomy.<sup>20</sup> Surgery was costlier than conservative management unless patients under observation developed complications or required emergency surgery.<sup>20</sup>

#### Box 2: Sources and selection criteria

As part of a Health Technology Assessment published in 2014, we searched major bibliographic electronic databases including Medline, Medline-in-process, EMBASE, Science Citation Index, BIOSIS, and the Cochrane Central Register of Controlled Trials using search terms cholecystitis, gallstones, biliary colic, cholecystectomy, and surgery. We included randomised controlled trials and non-randomised comparative studies published between 1980 and September 2012. Reports of relevant evidence syntheses were also sought from the Cochrane Database of Systematic Reviews and the Database of Abstracts of Review of Effects.

We identified 6779 potentially relevant citations, of which 73 reports were selected for full-text eligibility screening. After full-text assessment, two randomised controlled trials published in six reports were deemed suitable for inclusion. We updated the literature search in February 2019. No further randomised controlled trials comparing conservative management with cholecystectomy were identified.

## Is ongoing research likely to provide relevant evidence?

We are currently conducting a multicentre randomised controlled trial (C-Gall trial) comparing laparoscopic cholecystectomy with medical management (use of analgesics and anti-inflammatory drugs to relieve the biliary pain and generic lifestyle advice) for preventing recurrent symptoms and complications in adults with biliary colic or acute cholecystitis.<sup>21</sup> We are recruiting more than 430 adults from 21 trial centres in the UK. This trial is likely to provide information on patients who may benefit from a non-surgical approach and on the safety of such an approach. As part of this trial, we are formally developing a core outcome set comprising outcomes that matter most to patients and healthcare professionals.

We have searched the WHO International Clinical Trials Registry, Current Controlled Trials, Clinical Trials and the NIHR Portfolio for ongoing trials but found no other ongoing trials comparing surgery with conservative management.

#### Recommendations for future research

- In adults with uncomplicated symptomatic gallstone disease or acute cholecystitis is observation or conservative management a safe alternative to surgery for preventing recurrent symptoms and complications? Which patient may be suitable for conservative management?
- What is the clinical and cost effectiveness of observation or conservative management compared with cholecystectomy for preventing recurrent symptoms and complications in adults with uncomplicated symptomatic gallstone disease or acute cholecystitis?

## What should we do in the light of the uncertainty?

At present, cholecystectomy remains the default option in clinical guidelines for all people with symptomatic uncomplicated gallstone disease and acute cholecystitis,<sup>9 10</sup> with no attempt to identify people who might benefit from a conservative approach. People presenting with uncomplicated symptomatic gallstone disease do not require immediate medical or surgical treatment. It is not established yet if conservative management can be offered to all the patients, but we recommend doctors discuss the options with the patient. Inform your patient of the risks and benefits of either approach, including complications and the possibility of persistence of symptoms with surgery and repeated episodes of pain and gallstone related complications with conservative management. Take into consideration their preferences for immediate surgery as compared with observation with pain management.

#### Education into practice

- How would you discuss the options of surgery and conservative management with patients who have uncomplicated symptomatic gallstone disease or acute cholecystitis?

#### How patients were involved in the creation of this article?

No patients were involved in the creation of this article.

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## Table

Table 1 | Summary of results of the two identified randomised controlled trials comparing observation with cholecystectomy

	Schmidt 2011 <sup>15</sup> (n=137)				Schmidt 2011 <sup>16</sup> (n=64)			
	Observation (n=69, 83% women)		Surgery (n=68, 81% women)		Observation (n=33, 61% women)		Surgery (n=31, 55% women)	
	5 years	14 years	5 years	14 years	5 years	14 years	5 years	14 years
No of patients undergoing surgery	35 (51%)	35 (51%)	60 (88%)	60 (88%)	10 (30%)	11 (33%)	27 (87%)	27 (87%)
Pain attacks*	NR	23 (33%)	NR	8 (12%)	NR	3 (9%)	NR	4 (13%)
Gallstone related complications*:	3 (4%)	3 (4%)	1 (1%)	1 (1%)	13 (39%)	11 (33%)	3 (10%)	1 (3%)
Acute cholecystitis	1	1	0	0	9	8	1	0
CBD stones	2	1	0	0	4†	3	1‡	1
Acute pancreatitis	0	1	1	1	0	0	1	0
Surgery related complications:	6 (9%)	NR	10 (15%)	NR	3 (9%)	NR	10 (32%)	NR
Intra-abdominal infection or bile leakage	3	—	2	—	1	—	1	—
Wound infection or dehiscence	1	—	1	—	0	—	0	—
CBD stone, stenosis, bile duct injury, or pancreatitis	1	—	0	—	1	—	2	—
Re-operation	1	—	1	—	0	—	0	—
Minor complications	0	—	6	—	1	—	7	—
Admission due to gallstone-related paina	12 (17%)	NR	2 (3%)	NR	4 (12%)	NR	3 (10%)	NR
Mortality	NR§	8 (12%)	NR§	11 (16%)	0 (0%)	8 (24%)	4 (13%)	10 (32%)
Further surgical intervention needed	NR	NR	NR	4 (6%)¶	NR	NR	NR	NR

CBD = common bile duct.

\* For the 14 year data, events that took place before surgery in the group randomised to cholecystectomy were not included, unless as a result of dropout from surgery.

† n=7 late complication after surgery.

‡ Late complication after surgery.

§ Total 8/137 randomised participants had died.

¶ Endoscopic retrograde cholangiopancreatography (CBD stones in 1).