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A randomised controlled trial comparing surgery with watchful waiting for preventing recurrent symptoms and complications in adults with uncomplicated symptomatic gallstones

Submission date
27/05/2016

Recruitment status
No longer recruiting

Registration date
27/05/2016

Overall study status
Completed

Last Edited
01/07/2024

Condition category
Digestive System

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Gallstones are common, especially in women, but in many people they do not cause any symptoms. About one in three people with gallstones develop symptoms (symptomatic). Symptoms usually include a severe pain in the upper right-hand side of the abdomen (known as biliary colic), and sometimes nausea and vomiting. At times the pain is accompanied by inflammation of the gallbladder (cholecystitis). Once gallstones start giving symptoms, painkillers, anti-inflammatory medicines and antibiotics are usually prescribed initially and surgery is advised to medically fit patients. Surgery to remove the gallbladder, known as cholecystectomy, is the most common way to treat biliary pain or cholecystitis due to gallstones. About 70,000 cholecystectomies are performed every year in the UK, with significant costs for the NHS. In the UK, surgery is commonly offered to people who present at secondary care with pain or cholecystitis due to gallstones. However, it is known that some patients do not have any more symptoms after the initial episode of pain and that surgery may not be necessary. A policy of conservative management (painkillers/antibiotics and lifestyle advice) could therefore be appropriate in this group of people. A review of current evidence suggested that conservative management may provide a more efficient use of NHS resources. There were, however, great uncertainties in the data, with only two small studies run in Norway. There is a need for a definitive study to address these uncertainties. The aim of this study is to find out whether there any differences between conservative management and cholecystectomy in terms of patient quality of life and cost-effectiveness.

Who can participate?
Adult patients with symptomatic gallstone disease

What does the study involve?
Participants randomly allocated to either receive a surgical procedure to remove the gallbladder or to receive conservative management. Apart from treatment allocation and measurement of study outcomes, participants receive standard NHS follow up for at least 18 months. The main

outcome of the study is the effect of the two policies on the participants' quality of life. We assess this using a questionnaire. To assess any longer term benefits of either policy we use a mathematical model to give a prediction of quality of life over each participant's lifetime. We use the measurements we collect and the model to work out whether gall bladder removal is worthwhile to the NHS in terms of balancing any benefit to people's health against the added costs (cost-effectiveness).

What are the possible benefits and risks of participating?
Patients receive the same health care whether or not they choose to participate in the study. By taking part, they will be directly helping us to inform the future treatment of people with uncomplicated gallstones. The results of this study will help plan effective services offered by the NHS in the future. Risks and complications are possible from both surgical treatment and "watchful waiting" and participation in this study should not increase those risks. There are risks associated with surgical procedures and anaesthetics.

Where is the study run from?
1. NHS Grampian (UK)
2. Taunton and Somerset NHS Foundation Trust (UK)
3. Nottingham University Hospital NHS Trust (UK)

When is the study starting and how long is it expected to run for?
April 2016 to December 2021

Who is funding the study?
Health Technology Assessment Programme (UK)

Who is the main contact?
Karen Innes
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Study website
https://w3.abdn.ac.uk/hsru/C-GALL/

Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
Version 2.0, 20/05/2016; HTA 14/192/71

Study information

Scientific Title
A randomised controlled trial comparing laparoscopic cholecystectomy with observation /conservative management for preventing recurrent symptoms and complications in adults with uncomplicated symptomatic gallstones

Acronym
C-Gall

Study objectives
Is there any difference between observation/conservative management and cholecystectomy in terms of participant quality of life and cost-effectiveness in terms of incremental cost per QALY?

More details can be found at: http://www.nets.nihr.ac.uk/projects/hta/1419271

Ethics approval required
Old ethics approval format

Ethics approval(s)
North of Scotland Research Ethics Service (Committee 2), 23/05/2016, ref: 16/NS/0053

Study design
Pragmatic multi-centre parallel-group patient randomized superiority trial (with internal pilot phase)

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
https://w3.abdn.ac.uk/hsru/C-GALL/

Health condition(s) or problem(s) studied
Gallstones

Interventions
1. Laparoscopic cholecystectomy: the current standard surgical procedure for the management of symptomatic gallstone disease. The gall bladder is removed with the stones within it using keyhole techniques (laparoscopy). The procedure is undertaken under a general anaesthetic. It usually involves three to four small incisions in the abdomen, which allow the surgeon to dissect the gallbladder from its attachments and safely divide the key anatomical structures (the cystic duct and artery) that link it to the biliary tree. The gallbladder is then separated from the under surface of the liver. Usually the gallbladder (containing the stones) is removed within a retrieval bag via one of the small incisions. The operation takes between 45 and 120 minutes, many patients are admitted for one night, although day case laparoscopic cholecystectomy is safely undertaken in an otherwise fit patients with appropriate social support.

2. Observation/conservative management: observation/conservative management in the context of gallstone disease involves the prescription of analgesics to relieve the biliary pain. Typical therapy includes paracetamol, antispasmotics (e.g. Buscopan), nonsteroidal anti-inflammatory drugs (NSAIDs) (e.g. ibuprofen etc), narcotic analgesics (e.g. opiates) together with generic lifestyle advice. In the longer term, conservative management also may involve these strategies for symptom management if required, as well as advice to eat a healthy diet with regular meals (http://www.nhs.uk/Conditions/Gallstones/Pages/Treatment.aspx). For the purpose of this trial a standard protocol for conservative management will be agreed with the PPI group and used in all centres. Safety advice for patients in the observation/conservative management group will be aligned with the current advice given via the NHS choice website (www.nhs.uk).

Intervention Type
Procedure/Surgery

Primary outcome measure
The primary patient outcome measure will be quality of life as measured by area under the curve (AUC) at up to 18 months post-randomisation using the SF-36 bodily pain domain (AUC measures at 3, 9 and 18 months).

The primary economic outcome measure will be incremental cost per QALY.

Secondary outcome measures
Current secondary outcome measures as of 04/07/2023:
Measured at baseline, 3, 9, 12, 18 and 24 months:
1. Condition-specific quality of life (CSQ – The Otago gallstone condition-specific questionnaire)
2. SF-36 domains (excluding bodily pain domain) complications
3. Need for further treatment

4. Persistent symptoms
5. Healthcare resource use
6. Costs

The AUC at up to 24 months post-randomisation for the SF-36 bodily pain domain will be reported.

In addition, routinely collected national data on further surgery will be sought in the future to update longer-term estimates of cost-effectiveness.

Previous secondary outcome measures as of 10/09/2021:
Measured at baseline, 3, 9, 12 and 18 months:
1. Condition-specific quality of life (CSQ – The Otago gallstone condition-specific questionnaire)
2. SF-36 domains (excluding bodily pain domain) complications
3. Need for further treatment
4. Persistent symptoms
5. Healthcare resource use
6. Costs

The AUC at up to 24 months post-randomisation for the SF-36 bodily pain domain will be reported.

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In addition, routinely collected national data on further surgery will be sought in the future to update longer-term estimates of cost-effectiveness.

Overall study start date
01/04/2016

Completion date
01/12/2021

Eligibility

Key inclusion criteria
All adult patients with confirmed gallstones electively referred to a secondary care setting for consultation.

Clinical diagnosis of gallstone disease will be confirmed by imaging. Transabdominal ultrasonography is the standard imaging technique for the diagnosis of gallbladder stones, but diagnosis by any imaging technique is acceptable.

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
430

Total final enrolment
436

Key exclusion criteria
1. Unable to consent
2. ASA III and above
3. Pregnancy
4. Previous open major upper abdominal surgery
5. Gallstones in common bile duct or evidence of previous choledocholithiasis
6. A history of acute pancreatitis
7. Abnormal liver function tests (with the exception of GGT <90u/L)
8. Evidence of empyema of the gallbladder
9. Perforated gallbladder
10. Haemolytic disease

Date of first enrolment
01/09/2016

Date of final enrolment
01/09/2019

Locations

Countries of recruitment
England

Scotland

United Kingdom

Wales

Study participating centre
NHS Grampian
Department of Surgery
Aberdeen Royal Infirmary
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AB25 2ZN

Study participating centre
Taunton and Somerset NHS Foundation Trust
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Study participating centre
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Sponsor type
University/education

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http://www.abdn.ac.uk/

ROR
https://ror.org/016476m91

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Grampian Health Board

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Sponsor type
Hospital/treatment centre

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, HTA

Funding Body Type
Government organisation

Funding Body Subtype

National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal

Intention to publish date
30/08/2023

Individual participant data (IPD) sharing plan
The datasets generated during the current study will be available upon reasonable request from the Chief Investigator Irfan Ahmed (i.ahmed@abdn.ac.uk) after the publication of the current study.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		25/03/2021	29/03/2021	Yes	No
HRA research summary			28/06/2023	No	No
Results article		06/12/2023	18/12/2023	Yes	No
Results article		01/06/2024	01/07/2024	Yes	No