

Appendix A: Summary of evidence from surveillance

2018 surveillance of Gallstone disease: diagnosis and management (2014) NICE guideline CG188

Summary of evidence from surveillance

Studies identified in searches are summarised from the information presented in their abstracts.

Feedback from topic experts who advised us on the approach to this surveillance review, was considered alongside the evidence to reach a final decision on the need to update each section of the guideline.

Frequently used abbreviations

AGP	Acute gallstone pancreatitis
CBD	Common bile duct
CT	Computed tomography
DLC	Delayed laparoscopic cholecystectomy
ELC	Early laparoscopic cholecystectomy
EUS	Endoscopic ultrasound
ERCP	Endoscopic retrograde cholangiopancreatography
HIDA scan	Hepatobiliary iminodiacetic acid scan
LC	Laparoscopic cholecystectomy
IOC	Intraoperative cholangiography
LCBDE	Laparoscopic common bile duct exploration
LFTs	Liver function tests
MRCP	Magnetic resonance cholangiopancreatography

[1.1 Diagnosing gallstone disease](#)

Recommendations in this section of the guideline

- 1.1.1 Offer liver function tests and ultrasound to people with suspected gallstone disease, and to people with abdominal or gastrointestinal symptoms that have been unresponsive to previous management.

- 1.1.2 Consider magnetic resonance cholangiopancreatography (MRCP) if ultrasound has not detected common bile duct stones but the:
 - bile duct is dilated and/or
 - liver function test results are abnormal.
- 1.1.3 Consider endoscopic ultrasound (EUS) if MRCP does not allow a diagnosis to be made.
- 1.1.4 Refer people for further investigations if conditions other than gallstone disease are suspected.

Surveillance decision

This section of the guideline should not be updated.

2018 surveillance summary

Strategies for diagnosing gallstone disease

Liver function tests (LFTs) and ultrasound

A Cochrane review included 5 studies (n=523) assessing the diagnostic accuracy of abdominal ultrasound and LFTs in diagnosing common bile duct (CBD) stones in symptomatic patients. Presence of CBD stones were confirmed by either surgical or endoscopic extraction. Absence of CBD stones were confirmed by either surgical or endoscopic negative exploration of the CBD, or symptom-free follow-up for at least 6 months for a negative test result. The summary sensitivity for ultrasound was 0.73 (95% CI 0.44 to 0.90) and the specificity was 0.91 (95% CI 0.84 to 0.95). At the median pre-test probability of CBD stones of 0.408, the post-test probability associated with positive ultrasound tests was 0.85 (95% CI 0.75 to 0.91), and negative ultrasound tests was 0.17 (95% CI 0.08 to 0.33). One study reported the diagnostic accuracy of LFTs and ultrasound: ultrasound yielded a sensitivity of 0.32 (95% CI 0.15 to 0.54), bilirubin (cut-off greater than 22.23 µmol/L) was 0.84 (95% CI 0.64 to 0.95), and alkaline phosphatase (cut-off greater than 125 IU/L) was 0.92 (95% CI 0.74 to 0.99). The specificity for ultrasound was 0.95 (95% CI 0.91 to 0.97), bilirubin was 0.91 (95% CI 0.86

to 0.94), and alkaline phosphatase was 0.79 (95% CI 0.74 to 0.84). All studies were rated as having poor methodological quality. (1)

One observational study reported on the diagnostic utility of abdominal ultrasound in acute cholecystitis, using the intraoperative diagnosis as a reference standard. The sensitivity and specificity of ultrasound was 73.2% and 85.5% respectively. (2)

Magnetic resonance cholangiopancreatography (MRCP)

A systematic review included 25 studies (n=2,310 patients with suspected CBD stones and n=738 with CBD stones) investigating the diagnostic accuracy of MRCP in the detection of CBD stones. Patients had to be diagnosed with CBD based on endoscopic retrograde cholangiopancreatography (ERCP) and/or intraoperative cholangiography (IOC). Random effects models were used to generate pooled results for MRCP in detecting CBD stones: sensitivity = 0.90 (95% CI 0.88 to 0.92; p<0.001); specificity = 0.95 (95% CI 0.93 to 1.0; p<0.001); positive likelihood ratio = 13.28 (95% CI 8.8 to 19.94; p<0.001); negative likelihood ratio = 0.13 (95% CI 0.09 to 0.18; p<0.001); and diagnostic odds ratio = 143.82 (95% CI 82.42 to 250.95, p<0.001). (3)

Two observational studies reported on both the sensitivity and/or specificity of MRCP in detecting CBD stones, confirmed by ERCP

and/or IOC, clinical follow-up. (4,5) In one study MRCP yielded a sensitivity of 97% and specificity of 98% (4) whilst another study reported solely on the sensitivity of MRCP, which was 93.3%. (5)

Endoscopic ultrasound (EUS) and MRCP/ERCP

A Cochrane review included 18 studies (n=976 with CBD stones and n=1,390 without stones) assessing the diagnostic accuracy of EUS and MRCP in detecting CBD stones. Presence of CBD stones were confirmed by either surgical or endoscopic extraction. Absence of CBD stones were confirmed by either surgical or endoscopic negative exploration of the CBD, or symptom-free follow-up for at least 6 months for a negative test result. The pooled values of the 13 studies (n=1,537) which assessed EUS for sensitivity and specificity were 0.95 (95% CI 0.91 to 0.97) and 0.97 (95% CI 0.94 to 0.99) respectively. The pooled sensitivity of the 7 studies (n=996) which assessed MRCP for sensitivity and specificity were 0.93 (95% CI 0.87 to 0.96) and 0.96 (95% CI 0.90 to 0.98) respectively. There were no significant differences in sensitivity and specificity values between MRCP and EUS. At the median pre-test probability of CBD stones of 41%, for EUS the post-test probabilities associated with positive and negative EUS test results were 0.96 (95% CI 0.92 to 0.98) and 0.03 (95% CI 0.02 to 0.06) respectively and for MRCP the post-test probabilities associated with positive and negative MRCP test results were 0.94 (95% CI 0.87 to 0.97) and 0.05 (95% CI 0.03 to 0.09). The authors reported that none of the studies were of high methodological quality. (6)

A meta-analysis included 5 prospective cohort studies assessing the diagnostic accuracy of EUS and MRCP in detecting CBD stones. The reference standards used were ERCP, IOC, or clinical follow-up of more than 3 months for negative cases. The results found that the summary sensitivity and specificity values were 0.97 and 0.90 for EUS and 0.87 and 0.92 for MRCP respectively. The overall diagnostic

odds ratio of EUS was significantly higher than for MRCP (162.5 versus 79.0 respectively), mainly due to a significantly higher sensitivity of EUS compared with MRCP; however specificity values were not significantly different between both interventions. (7)

A model based cost-utility analysis taking a UK National Health Service (NHS) perspective with a 1 year time horizon for costs/outcomes compared the cost effectiveness of initial EUS or MRCP in patients with suspected CBD stones to reduce the risk of unnecessary ERCP. The results from the model found that MRCP was less costly compared to EUS for determining which patients required ERCP (\$1,299 versus \$1,753) and less costly than patients directly undergoing ERCP (\$1,781). Cost-effectiveness measured in quality-adjusted life years (QALYs) was similar for each option: 0.998 for EUS and MRCP and 0.997 for direct ERCP. Initial MRCP was the most cost effective method yielding the highest monetary net benefit, which was not sensitive to model parameters. MRCP was described as having a "61% probability of being cost-effective at \$29,000". (8)

Six observational studies assessed the diagnostic value of EUS in detecting CBD stones/sludge with ERCP undertaken in confirmed cases or high/intermediate risk patients. (9–14) The sensitivity of EUS reported in these studies ranged from 93.9% to 100%, and the specificity ranged from 79.5% to 100%.

Computed tomography (CT)

An RCT assessed the value of early abdominal non-enhanced CT in developing strategies for treating patients (n=102) with mild acute gallstone pancreatitis (AGP). All patients underwent non-enhanced CT within 48 hours of symptom onset and were randomised to receive early or delayed laparoscopic cholecystectomy. The study reported that non-enhanced CT had an accuracy of 89.2% in detecting gallbladder stones and was 87.8% accurate in detecting CBD stones. (15)

An observational study assessed the accuracy of intravenous (IV) contrast-enhanced multidetector CT in detecting CBD stones, in the presence and absence of positive intraduodenal contrast in patients (n=48) who underwent ERCP. Patients were divided into 2 groups based on the presence (n=17) or absence (n=31) of positive intraduodenal contrast, with independent radiologist assessment of CT results who were blinded to clinical and ERCP results. The positive intraduodenal contrast yielded a sensitivity range of 50-80%, specificity 57-71% and 59-71% accuracy compared with the group without contrast which yielded a sensitivity of 77-88%, 50-71% specificity and 71-74% accuracy. All diagnostic performance parameters (except for the positive predictive value) decreased in the positive intraduodenal contrast group, mostly affecting the negative predictive value (NPV) (71%-78% versus 50%-67%). (16)

An observational study with patients presenting with acute biliary pancreatitis (n=78) assessed the diagnostic value of MRCP in detecting CBD stones. ERCP or, when unavailable, IOC/clinical follow-up was used as the reference standard. All patients underwent MRCP and 30/78 patients had CBD stones. Sensitivity of MRCP in detecting CBD stones was significantly higher than the sensitivity of abdominal CT (93.3% versus 66.7%). The area under the receiver operating characteristic curve (AUC) of MRCP in detecting CBD stones was 0.882, which was significantly more accurate than the AUC for abdominal CT at 0.727. Out of the 38 patients who required ERCP, the dilation of the CBD did not impact the sensitivity and NPV of MRCP in detecting CBD stones, which were both 100%. (5)

Other investigative procedures

A Cochrane review included 5 studies (n=318) assessing the diagnostic accuracy of ERCP and IOC for diagnosing CBD stones (IOC is not included as a diagnostic tool in the scope of the guideline). Presence of CBD stones were confirmed by either surgical or endoscopic

extraction. Absence of CBD stones were confirmed by either surgical or endoscopic negative exploration of the CBD, or symptom-free follow-up for at least 6 months for a negative test result. The range of sensitivities of ERCP were 0.67 and 0.94, and the pooled sensitivity was 0.83 (95% CI 0.72 to 0.90). The range of specificities were 0.92 and 1.00, and the pooled specificity was 0.99 (95% CI 0.94 to 1.00). At the median pre-test probability of CBD stones of 0.35, for ERCP the post-test probabilities associated with positive test results was 0.97 (95% CI 0.88 to 0.99) and negative test results was 0.09 (95% CI 0.05 to 0.14). (17)

An observational study based on registry data on urgent cholecystectomies performed in acute cholecystitis patients assessed the diagnostic accuracy of CT and ultrasound for diagnosing acute cholecystitis. Patients were divided into 2 groups: ultrasound only (n=NR) or CT and ultrasound (n=101). CT was significantly more sensitive than ultrasound for the diagnosis of acute cholecystitis (92% versus 79%), whereas ultrasound was significantly more sensitive than CT for identification of gallstones (87% versus 60%). (18)

An observational study with patients (n=412) who underwent cholecystectomy evaluated the sensitivity of sonographic, hepatobiliary iminodiacetic acid scan (HIDA) scan and CT examination of acute cholecystitis to the pathology result. The following sensitivity values were reported: for HIDA scan: 84.2%, CT: 67.3%, and sonography: 59.8% with all differences between methods being significant. In samples with pathology results indicative of complicated acute cholecystitis, CT was significantly more sensitive than sonography in detecting acute cholecystitis (100% and 63.6% respectively) irrespective of whether complications were identified (a HIDA scan was not done). In terms of identifying complications of acute cholecystitis, CT had a sensitivity of 35.71%, whereas sonographic

examination was unable to detect any of the complications. (19)

An observational study with patients (n=406) who underwent cholecystectomy for acute cholecystitis, assessed the utility of abdominal ultrasound, HIDA scan or both. One hundred and thirty two patients underwent abdominal ultrasound, 46 patients underwent HIDA scan and 228 patients had both modalities performed, with 214/406 patients having histopathological confirmed acute cholecystitis. The sensitivity values for diagnosing acute cholecystitis were for abdominal ultrasound 73.3% (95% CI 66.3% to 79.5%), HIDA 91.7% (95% CI 86.2% to 95.5%), and for abdominal ultrasound combined with HIDA for acute cholecystitis 97.7% (95% CI 93.4% to 99.5%). During abdominal ultrasound, sonographic Murphy sign, gallbladder distension, and gallbladder wall thickening were associated with a diagnosis of acute cholecystitis. (20)

Intelligence gathering

One topic expert highlighted an ongoing pragmatic RCT known as [The Sunflower Study](#) which will compare expectant management (no imaging) versus preoperative imaging with MRCP in patients undergoing laproscopic cholecystectomy or gallstones at low or moderate risk of CBD stones. This ongoing study will be monitored and results considered for impact on the guideline when available. Another topic expert noted that “adoption of and access to diagnostic studies, including endoscopic ultrasound, is widespread”.

Regarding specific subgroups of the population, a topic expert asked whether the recommendations apply to pregnant women. No evidence on diagnosis of gallstone disease relating to this subgroup was identified.

Impact statement

A large body of evidence (21 studies consisting of 3 Cochrane reviews, 1 systematic review, 1 meta-analysis, 1 RCT, 1 cost-utility analysis and

14 observational studies) was identified on diagnosis of gallstone disease.

Liver function tests (LFTs) and ultrasound

Evidence was identified on the diagnostic accuracy of liver function tests (LFTs) and abdominal ultrasound in diagnosing gallstone disease that indicates these measures have, overall, good sensitivity and specificity for identifying gallstone disease. There was some indication that abdominal ultrasound may not be as good as other tests for picking up cases of common bile duct (CBD) stones, as reported in a Cochrane review, which highlights the potential need for additional tests. As such, the evidence supports current recommendations to initially offer LFTs and abdominal ultrasound to patients with suspected gallstone disease, but to also consider the use of other diagnostic techniques.

Endoscopic ultrasound (EUS) and MRCP/ERCP

Evidence was identified that indicated endoscopic ultrasound (EUS) and magnetic resonance cholangiopancreatography (MRCP) had high sensitivity and specificity for diagnosing CBD stones. There appears to be no significant differences between investigations in terms of sensitivity and specificity in diagnosing CBD stones as indicated by findings from a Cochrane review. Initial MRCP was found to be more cost effective compared with EUS, based on evidence from one cost-utility analysis. The new evidence supports current recommendations concerning the use of both investigations and highlights that first approach MRCP and EUS can prevent the use of endoscopic retrograde cholangiopancreatography (ERCP) as a diagnostic tool.

There was some indication that ERCP may be of value in diagnosing CBD stones and guiding further invasive treatment as indicated by findings from a Cochrane review. ERCP is currently not included under recommendations for diagnosing gallstone disease but instead

under the therapeutic management of CBD stones. As such, it is not anticipated that such evidence will impact current recommendations.

Other investigative procedures

A small body of evidence (6 studies consisting of 1 RCT and 5 observational studies) was identified on the diagnostic accuracy of computed tomography (CT) and hepatobiliary iminodiacetic acid (HIDA) scans. The evidence indicates that HIDA scans have a higher sensitivity for diagnosing acute cholecystitis

compared with ultrasound. There was mixed evidence concerning the diagnostic performance for CT scans, however two observational studies noted that CT scans were more sensitive in detecting acute cholecystitis compared to ultrasound. At present, there is insufficient consistent evidence in these areas to impact on the recommendation.

New evidence is unlikely to change guideline recommendations.

1.2 Managing gallbladder stones

Recommendations in this section of the guideline

- 1.2.1 Reassure people with asymptomatic gallbladder stones found in a normal gallbladder and normal biliary tree that they do not need treatment unless they develop symptoms.
- 1.2.2 Offer laparoscopic cholecystectomy to people diagnosed with symptomatic gallbladder stones.
- 1.2.3 Offer day-case laparoscopic cholecystectomy for people having it as an elective planned procedure, unless their circumstances or clinical condition make an inpatient stay necessary.
- 1.2.4 Offer early laparoscopic cholecystectomy (to be carried out within 1 week of diagnosis) to people with acute cholecystitis.
- 1.2.5 Offer percutaneous cholecystostomy to manage gallbladder empyema when:
 - surgery is contraindicated at presentation and
 - conservative management is unsuccessful.
- 1.2.6 Reconsider laparoscopic cholecystectomy for people who have had percutaneous cholecystostomy once they are well enough for surgery.

Surveillance decision

This section of the guideline should not be updated.

2018 surveillance summary

Laparoscopic cholecystectomy (LC) versus conservative management

Two systematic reviews included 2 RCTs (n=201) investigating the clinical and cost effectiveness of cholecystectomy compared with observation/conservative management in patients with symptomatic gallstones or acute cholecystitis. Patients randomised to observation/conservative management had a significantly greater likelihood of gallstone-related complications (RR 6.69, 95% CI 1.57 to 28.51) particularly acute cholecystitis (RR 9.55, 95% CI 1.25 to 73.27), were significantly less likely to have surgery (RR 0.50, 95% CI 0.34 to 0.73) and to have surgery-related complications (RR 0.36, 95% CI 0.16 to 0.81) compared to those patients randomised to cholecystectomy. The cost-analysis based on a Markov model, found that LC was more costly (£1,236 more per patient) and effective compared to observation/conservative management, however there was uncertainty around some of the parameters used in the economic model. A rise in the number of patients who required surgery during conservative treatment, resulted in a reduction in the cost effectiveness of the conservative management strategy. (21,22)

LC compared with LC and Intraoperative cholangiography (IOC)

A randomised trial including symptomatic patients (n=371) with suspected gallstones were randomised to either receive routine LC alone or LC and IOC. The results found no significant differences in the rates of successful LC (98.38% versus 97.85%), CBD stone retainment (0.54% versus 0.00%), CBD injury (0.54% versus 0.53%) and other complications (2.16% versus 2.15%), as well as length of hospital stay (5.10+/-1.41 days versus 4.99+/-1.53 days). The authors reported no fatal complications for either interventions. At 1 year follow-up, 1 case of diarrhoea lasting for 3 months post routine LC and 1 case of intermittent epigastric discomfort post LC and

IOC were reported, however no abnormalities were identified during radiological examination. (23)

LC compared with percutaneous cholecystostomy

A systematic review and meta-analysis included 6 studies (n=337,500) assessing the benefit of percutaneous cholecystostomy compared with LC in the management of critically ill patients with acute cholecystitis. The results, found that LC was significantly superior in terms of mortality (OR 4.28, 95% CI 1.72 to 10.62), length of hospital stay (OR 1.41, 95% CI 1.02 to 1.95) and rate of readmission for biliary complaints (OR 2.16, 95% CI 1.72 to 2.73) compared to percutaneous cholecystostomy. There were no significant differences between both interventions in terms of complications or re-interventions. (24)

Day-case LC versus inpatient LC

A systematic review that undertook a meta-analysis included 12 studies comparing the safety and feasibility of day LC compared to overnight stay LC. The results found no significant differences between both groups in terms of morbidity, prolonged hospitalisation, readmission rate, consultation rate, postoperative nausea and vomiting scale, time to return to activity and work. (25)

An RCT with data from symptomatic gallstone patients (n=65) randomised to undergo day-case LC or routine (conventional) LC procedure compared the feasibility and safety of both procedures. The results found no significant differences between both procedures in terms of complications, quality of life, satisfaction, postoperative nausea and vomiting and pain outcomes. The authors reported that 97% of day-case LC patients were successfully discharged with a lower mean duration of stay of 8.9+/-4.54 hours compared with those patients who underwent routine procedure at 3.33+/-1.45 days. (26)

Timing of interventions in the management of gallbladder disease

A systematic review of RCTs (n=NR) assessed the optimal timing for LC in acute cholecystitis patients. The review reported that there was a preference for early LC in patients with acute cholecystitis although there was a lack of consistency in defining "early". The review indicated that immediate LC within 24 hours after admission is the best approach in American Society of Anesthesiologists physical status classification system (ASA) I-III patients with acute cholecystitis compared to delayed LC after initial antibiotic therapy. This was in relation to morbidity, duration of hospital stay and treatment cost outcomes. The authors stated that "concerning critically ill patients suffering from acute calculous or acalculous cholecystitis, there is no consensus in treatment due to missing data in the literature". (27)

A meta-analysis included 15 RCTs comparing outcomes between early and delayed cholecystectomy for acute cholecystitis. The results found no differences in mortality, bile duct injuries, bile duct leaks, risk of conversion to open surgery between both early and delayed groups. A proportion of patients in the delayed group (9.7%) failed initial non-operative management and underwent emergency LC, whereas early surgery patients had a significantly shorter hospital stay, lower risk of wound infections and lower mean hospital costs when compared with delayed cholecystectomy. Definitions of time periods for early and delayed LC were not provided in the abstract. (28)

A meta-analysis included 16 studies (reporting on 15 RCTs, n=1,625) comparing early laparoscopic cholecystectomy (ELC) performed within 1 week of onset of symptoms with delayed laparoscopic cholecystectomy (DLC) performed at least 1 week after symptoms had subsided for acute cholecystitis. The results found that ELC groups demonstrated significant reductions in days lost from work (MD -11.07, 95% CI -16.21 to -5.94), risk of

Appendix A: Summary of evidence from 2018 surveillance of Gallstone disease: diagnosis and management (2014)

wound infection, and length of hospital stay (MD -3.38 days, 95% CI -4.23 to -2.52). ELC was associated with reductions in hospital costs, higher patient satisfaction and quality of life compared with DLC. No significant differences were identified in terms of mortality, bile duct injury, bile leakage, conversion to open surgery or overall complications. (29)

A meta-analysis included 9 RCTs comparing the length of hospital stay between ELC and DLC in patients following acute cholecystitis. Included patients underwent ELC (n= 617) or DLC (n=603) after acute cholecystitis and the mean hospital stay was shorter in the ELC compared with the DLC group (5.4 versus 9.1 days respectively). The results from the meta-analysis showed a significantly shorter mean hospital stay (MD 3.24, 95% CI 1.95 to 4.54) in the ELC group and the rate of major biliary duct injury was 0.8% versus 0.9% for ELC compared to the DLC group respectively. The authors reported no significant differences between both groups. Definitions of time periods for early and delayed LC were not provided in the abstract. (30)

A meta-analysis included 7 RCTs (n=1,106) assessing the safety and outcomes of ELC and DLC in the management of acute cholecystitis. The results found no significant differences in terms of bile duct injury and conversion to open surgery between both groups. The total duration of hospital stay was significantly lower for the ELC group compared with DLC (MD -4.12 days, 95% CI -5.22 to -3.03). Definitions of time periods for early and delayed LC were not provided in the abstract. (31)

An RCT with acute cholecystitis patients (n=62) were randomised to receive either ELC within 72 hours after the onset of symptoms or initial antibiotic treatment followed by DLC after 6-8 weeks. The results found ELC was associated with a lower conversion rate to open surgery, duration of hospital stay,

postoperative recovery and reduced cost of hospitalisation compared with DLC. (32)

An RCT with acute cholecystitis patients (n=86) experiencing more than 72 hours of symptoms were randomised to receive either ELC (performed following hospital admission) or DLC (at least 6 weeks post initial antibiotic treatment). The results found that median length of hospital stay was significantly lower (4 versus 7 days) in the early surgery compared to delayed surgery group. The duration of antibiotic therapy was also significantly lower in the early surgery group at 2 days compared to 10 days in the delayed surgery group. Overall morbidity (6 versus 17 patients) and total hospital costs were also significantly lower in the early surgery group whereas there were no significant differences in postoperative complications between both groups. (33)

An RCT compared either ELC within 24 hours of admission or DLC 6-8 weeks after initial conservative management in people with acute cholecystitis (n=50). The study results found that postoperative complications for ELC were 24% versus 8% for DLC and that ELC had significantly shorter length of hospital stay (4.1 days versus 8.6 days). The conversion rate to open surgery in ELC was 16% and 8% in DLC and blood loss was 159.6 mL in ELC versus 146.8 mL for DLC. The authors concluded that ELC "should be offered to the patients with acute cholecystitis, provided that the surgery is performed within 96hrs of acute symptoms by an experienced surgeon." (34)

An RCT compared either ELC (within 24 hours of admission) or DLC (after 6-8 weeks of conservative treatment) in patients (n=60) with acute cholecystitis. The results found that length of hospital stay (5.2 +/- 1.40 versus 7.8 +/- 1.65 days) and total costs (2,500.97 +/- 755.265 versus 3,713.47 +/- 517.331 Turkish Lira) were both significantly greater in the delayed compared to the early surgery groups. Intraoperative and postoperative complications were significantly greater in the early surgery

group (8 patients) compared to the delayed surgery group where no patients experienced complications. (35)

A cost-utility analysis based on a model with a 5 year time horizon to compare costs and QALYs gained from 3 treatment strategies for acute cholecystitis: early cholecystectomy (within 7 days of presentation), delayed elective cholecystectomy (8 to 12 weeks from presentation), and watchful waiting (surgery is performed urgently only if recurrent symptoms arise). The results found that early cholecystectomy was superior in terms of costs (6,905 Canadian dollars per person) compared to delayed cholecystectomy (8,511) and watchful waiting (7,274). Early cholecystectomy was also more effective in terms of QALYs gained per person at 4.20 compared to delayed surgery at 4.18 and 3.99 for watchful waiting. Uncertainty was evaluated using probability sensitivity analysis which found that early cholecystectomy was the preferred management of acute cholecystitis in 72% of model iterations, based on the cost-effectiveness threshold of 50,000 Canadian dollars per QALY. (36)

A cost-utility analysis (using data from a prospective cohort study from the UK NHS perspective) with a 1 year time horizon for costs/outcomes aimed to determine the cost effectiveness of emergency cholecystectomy (performed during an emergency surgical admission) compared to delayed cholecystectomy (patients were discharged and then readmitted for a planned procedure) for acute gallbladder disease. The results found that emergency surgery was less expensive (£4,570 versus £4,720) and more effective (0.8868 versus 0.8662 QALYs) than delayed surgery. Probabilistic sensitivity analysis demonstrated that emergency cholecystectomy has greater than 60% likelihood of being cost-effective across willingness-to-pay values for the QALY from £0 to £100,000. (37)

An economic evaluation using data from 6 RCTs using a UK NHS perspective aimed to determine the incremental cost effectiveness of ELC compared to DLC in the treatment of acute cholecystitis. The results found that DLC was more costly with an average net present value of £4,565 compared to £3,920 for ELC, which when scaled to a population level may result in potential savings of £30,000,000 per annum for the NHS. Definitions of time periods for early and delayed LC were not provided in the abstract. (38)

An economic evaluation using records of inpatients (n=191,032) who underwent LC for acute cholecystitis assessed the impact on costs in delaying LC. The results found that approximately 65% of subjects underwent LC within 24 hours of admission with the average cost of care for LC at \$11,087 on the day of admission. Costs progressively increased by 22% on the second hospital day, 37% on day 3, 52% on day 4, 64% on day 5, 81% on day 6, and by 100% on day 7, when compared to the cost of care for LC within 24 hours. (39)

Timing of interventions in the management of gallstone-related pancreatitis

A systematic review that undertook a meta-analysis included 13 studies (n=2,291) comparing the safety of ELC and DLC in patients with mild biliary pancreatitis. The results found that rates of readmissions and complications were higher for DLC than ELC group (complication rate 13.45% versus 6.8%; significance not reported). The duration of hospital stay was shorter in ELC compared with the DLC group and no significant differences were identified in terms of conversion to open surgery between both groups. Definitions of time periods for early and delayed LC were not provided in the abstract (40)

A multicentre RCT superiority trial with hospital patients (n=266) recovering from mild gallstone pancreatitis were randomised to receive either interval cholecystectomy

(discharge, followed by surgery 25-30 days after randomisation) or same-admission cholecystectomy (within 72 hours of randomisation); the primary endpoint was a composite of readmission for recurrent gallstone-related complications or mortality within 6 months following randomisation. The primary endpoint occurred in 23/136 patients in the interval group and in 6/128 patients in the same-admission group (RR 0.28, 95% CI 0.12 to 0.66; p=0.002). Four incidences of serious surgery-related adverse events including bile duct leakage and postoperative bleeding occurred for both groups, but did not result in death. (41)

A multicentre RCT with patients (n=264) diagnosed with mild gallstone pancreatitis were randomised before discharge to receive either early cholecystectomy within 72 hours (same-admission surgery) or delayed cholecystectomy after 25-30 days (interval surgery). The results found that same-admission surgery significantly lowered the risk of acute readmission for recurrent gallstone-related complications from 16.9% to 4.7%. Cost-effectiveness analyses from a societal perspective with costs per readmission prevented as the main outcome over a time horizon of 6 months, found that mean costs were €234 (95% CI -1,249 to 738) less per patient in the same-admission group. Same-admission was less expensive and more effective than interval surgery, with a societal incremental cost-effectiveness ratio of -€1,918 to prevent one readmission for gallstone-related complications. (42)

An RCT with patients (n=72) diagnosed with mild to moderate acute biliary pancreatitis were randomised to receive either early cholecystectomy or delayed cholecystectomy. The results found no significant differences in perioperative complications or conversion to open surgery between groups. The delayed group demonstrated a significantly greater number of recurrent biliary events (44.12% versus 0%) and significantly longer duration of hospital stay compared to the early group (9

days versus 8). Definitions of time periods for early and delayed cholecystectomy were not provided in the abstract. (43)

An RCT assessed the value of early abdominal non-enhanced CT in developing strategies for treating patients (n=102) with mild AGP. All patients underwent non-enhanced CT within 48 hours of symptom onset and were randomised to receive ELC (within 7 days after pancreatitis attack with AGP symptoms) or DLC (performed at or after 7 days following an attack, with the patient being completely free of AGP symptoms). Patients in both groups were successfully treated with no surgery-related complications and there were no instances of increased AGP severity post-surgery. The mean duration of hospital stay was significantly less in the early LC group compared with delayed LC group. (15)

A model based cost-utility analysis for mild AGP (from the UK NHS perspective with a 1 year time horizon for costs/outcomes) assessed the cost effectiveness of LC within 72 hours of admission (group A) or during the same-admission but after 72 hours (group B) or electively in another admission (group C). The results found that the mean costs of LC for group A was €2,748 and group B was €3,543, with QALYs per patient for both groups at 0.888, the cost and QALY values for group C were €3,752 and 0.884 respectively. ELC (within 72 hours of admission) showed a 91% probability of being cost-effective at the maximum willingness-to-pay threshold for a QALY commonly used in the UK. The authors reported that hospitals may not have access to certain interventions such as MRCP and ERCP, particularly at certain times/weekends therefore implementing a target timespan for completing LC within 72 hours may not be feasible without the assignment of further resources that would essentially diminish the cost-effectiveness. The investigators concluded "after 3 days there is little financial advantage to same-admission operation." (44)

Intelligence gathering

One topic expert highlighted an ongoing study: [A randomised controlled trial comparing laparoscopic cholecystectomy with observation/conservative management for preventing recurrent symptoms and complications in adults with uncomplicated symptomatic gallstones](#). This topic expert commented "there is evidence that patients with an episode of acute cholecystitis may not have a further attack of gallstone symptoms" and suggested that "the uncertainty on which the [ongoing] study is based on is incorporated into any NICE CG188 update". This ongoing study will be monitored and results considered for impact on the guideline when available. The topic expert also commented that the recommendation to do cholecystectomy within one week of acute cholecystitis "needs updating" based on the reference provided and that there is an increasing rate of cholecystectomies performed in the NHS and the guidance should consider how this could be lessened.

Regarding specific subgroups of the population, a topic expert asked whether the recommendations apply to pregnant women. No evidence on management of gallbladder stones relating to this subgroup was identified.

Correspondence was received based on a coroner's report. This formed the basis of a request to consider the timing of surgery following the diagnosis of gallstone pancreatitis as an additional area in this surveillance review.

Initial intelligence gathering identified NICE clinical knowledge summary (CKS) on the secondary care [management of suspected acute pancreatitis](#) (revised in May 2016) caused by suspected or proven gallstones. The CKS includes detail on the timing of cholecystectomy either during the same-admission for uncomplicated cases, or possibly delayed in severe cases until clinically appropriate. It also states that management may include ERCP within 72 hours of the onset of pain in patients with cholangitis.

NICE quality standard [QS104 on gallstone disease](#) uses the [Commissioning guide: gallstone disease](#) (2013, reviewed October 2016) from the Royal College of Surgeons (RCOS) as an evidence source. The guide was NICE accredited from September 2012 for a period of 5 years. RCOS guidance provides secondary care management recommendations which may be applicable to the issue raised: AGP patients should undergo definitive treatment within 2 weeks of recovery from the incident episode.

This evidence is also of relevance to [Pancreatitis: diagnosis and management](#) NICE guideline currently in development.

Impact statement

Laparoscopic cholecystectomy (LC) versus conservative management

The new evidence indicated that conservative management resulted in poorer outcomes among patients with symptomatic gallstones or acute cholecystitis compared with LC, although LC was more costly. Overall, this evidence supports the current recommendation to offer LC in people diagnosed with symptomatic gallbladder stones.

LC compared with LC and Intraoperative cholangiography (IOC)

One identified study found no difference in outcomes between routine LC alone or LC and IOC in symptomatic patients with suspected gallstones. No impact on the guidelines is anticipated as there is uncertainty about whether the addition of IOC was beneficial or not since there were no significant differences between the groups on any of the outcomes.

LC compared with percutaneous cholecystostomy

A systematic review indicated that LC was significantly superior to percutaneous cholecystostomy in a number of outcomes including mortality and length of hospital stay. As LC is the recommended approach for

managing acute cholecystitis, no impact on the guideline is expected.

Day-case LC versus inpatient LC

New evidence comparing day-case with inpatient LC found no significant differences in outcomes including morbidity and complications. However, as none of the studies reported on costs, which was an important consideration in developing the recommendation on day-case LC, it would be pertinent to wait for further evidence before considering this area for update.

Timing of interventions in the management of gallbladder disease

A large body of evidence (13 studies consisting of 1 systematic reviews, 4 meta-analyses, 2 cost-utility analyses, 2 economic evaluation studies and 4 RCTs) was identified regarding the timing of LC in acute cholecystitis. Overall the evidence supports the use of early LC over delayed LC, which is in line with current recommendations to offer early laparoscopic cholecystectomy (to be carried out within 1 week of diagnosis) to people with acute cholecystitis.

Timing of interventions in the management of gallstone-related pancreatitis disease

The management of gallstone-related pancreatitis is not within the scope of NICE guideline CG188. However, correspondence was received based on a coroner's report. This formed the basis of a request to consider the timing of surgery following the diagnosis of gallstone pancreatitis as an additional area in this surveillance review.

Six studies (1 systematic review, 4 RCTs, 1 cost-utility analysis) were identified that assessed the optimal timing of cholecystectomy in gallstone pancreatitis patients. Several studies noted the benefits of early surgery on a range of outcomes, however the timing of early surgery differed, including 7 days after onset of symptoms, within 3 days

following admission (same-admission), whilst other studies did not specify.

Although the evidence indicates that performing early surgery within the same-admission is good for patient outcomes and reduces costs, an optimal timing for surgical treatment of gallstone pancreatitis following diagnosis/onset of symptoms was not

demonstrated in the evidence identified through surveillance. At present, it would therefore not be feasible to define operation intervals.

New evidence is unlikely to change guideline recommendations.

1.3 Managing common bile duct stones

Recommendations in this section of the guideline

- 1.3.1 Offer bile duct clearance and laparoscopic cholecystectomy to people with symptomatic or asymptomatic common bile duct stones.
- 1.3.2 Clear the bile duct:
 - surgically at the time of laparoscopic cholecystectomy **or**
 - with endoscopic retrograde cholangiopancreatography (ERCP) before or at the time of laparoscopic cholecystectomy.
- 1.3.3 If the bile duct cannot be cleared with ERCP, use biliary stenting to achieve biliary drainage only as a temporary measure until definitive endoscopic or surgical clearance.
- 1.3.4 Use the lowest-cost option suitable for the clinical situation when choosing between day-case and inpatient procedures for elective ERCP.

Surveillance decision

This section of the guideline should not be updated.

2018 surveillance summary

Managing common bile duct stones

Pre/intra/postoperative ERCP +LC compared with bile duct exploration + LC

A Cochrane review compared the benefits and harms of different approaches to the management of CBD stones. The review included 5 RCTs (n=580) comparing LC and laparoscopic common bile duct exploration (LCBDE) versus preoperative ERCP and LC, which found no significant differences in

mortality, morbidity or number of people with retained stones between both groups. Two RCTs (n=166) compared LC and LCBDE with LC and postoperative ERCP, which found no significant difference in terms of morbidity whilst mortality was not reported in either group. A significant difference was found in the number of participants with retained stones between laparoscopic surgery (9%) and postoperative ERCP (25%) groups (OR 0.28, 95% CI 0.11 to 0.72). Seven RCTs (n=746) compared single-stage LC and LCBDE versus two-stage pre/postoperative ERCP and LC, with no statistically significant differences

reported in terms of mortality, morbidity or number of retained stones between both intervention groups. One RCT (n=234) compared LC and LCBDE versus LC and intraoperative ERCP, which found no significant differences in terms of morbidity, retained stones or procedure failure rates between both groups. No cases of mortality were reported in either intervention group. Comparison of LCBDE with pre/intra/postoperative ERCP procedures found no significant differences in conversion rates to open surgery. (45)

A systematic review included 4 studies comparing single-stage surgical management (involving LC with CBD exploration) versus two-stage surgical management (involving LC with pre/postoperative ERCP) in patients with symptomatic gallstones and concomitant CBD stones. The review included 1 meta-analysis which reported no significant differences in the effectiveness or frequency of complications between management strategies (details of complications recorded not provided in abstract). Three smaller studies also concurred with these findings, however each study found that single-stage management was more cost-effective. (46)

A systematic review that undertook a meta-analysis included 11 studies (n=1,513) comparing single-stage laparoscopic common bile duct exploration (LCBDE) and cholecystectomy with two-stage preoperative endoscopic stone extraction followed by cholecystectomy (ERCP and LC). The results found that LCBDE was associated with a significantly lower rate of technical failure and shorter hospital stay compared with ERCP and LC. There were no significant differences between groups in terms of mortality, morbidity, treatment cost or recurrent/retained stones. (47)

A meta-analysis included 8 RCTs (n=1,130) assessing single-stage (LC and LCBDE) versus two-stage management (preoperative ERCP and LC) in patients with gallstones and

concomitant CBD stones. The results found the rate of CBD stone clearance was significantly higher and duration of hospital stay was significantly shorter in the single-stage group compared with the two-stage group. There were no significant differences between management strategies in terms of postoperative morbidity, mortality, and conversion to other procedures. (48)

An RCT with patients (n=104) with CBD stones undergoing emergency laparoscopic cholecystectomy were randomised to either intraoperative ERCP or LCBDE. The results found that clearance rates for intraoperative ERCP was higher at 87% compared to LCBDE at 69%, although this was not significant. The rate of retained stones was significantly less in ERCP patients at 15% compared to 42% in LCBDE and median postoperative length of stay was significantly shorter in ERCP patients at 2 days compared to 3 days for LCBDE patients. (49)

An RCT in people with concomitant gallbladder and CBD stones (n= 168) were randomised to either single-stage LCBDE and LC or two-stage ERCP followed by LC. The results found the success rate of CBD clearance for LCBDE was 91.7% and ERCP was 88.1%. There were no significant differences between overall success rate for both groups (88.1% in single-stage group and 79.8% in two-stage group). Direct choledochotomy was performed in 83 patients. The overall duration of hospital stay was significantly less in the single-stage group compared with the two-stage group (4.6 +/- 2.4 versus 5.3 +/- 6.2 days respectively). The two-stage group had a significantly greater number of procedures per patient and higher cost. There were no significant differences between both management strategies regarding postoperative wound infection rates or major complications. (50)

An RCT in patients (n=221) with gallstones and concomitant CBD stones compared single-stage LC and LCBDE (within the same operation) or two-stage preoperative

endoscopic CBD clearance followed by LC 2-5 days later. The results found no significant differences in the rates of successful CBD clearance or complications between both management strategies. During longer term follow-up (time not specified), reoccurrence of CBD stones were significantly more frequent in the two-stage group (9.5%) compared with the single-stage group (2.1%). (51)

Other management strategies

A Cochrane review included 5 RCTs (n=517) comparing endoscopic sphincterotomy and stone removal followed by LC (single-stage rendezvous technique) versus preoperative endoscopic sphincterotomy followed by LC (two stages) in people with gallbladder and CBD stones. The results found that overall morbidity may be lower with a laparoscopic-endoscopic rendezvous procedure (RR 0.59, 95% CI 0.29 to 1.20), although this was reported as low quality evidence. Length of hospital stay was around 3 days shorter in the laparoscopic-endoscopic rendezvous group (95% CI 3.51 to 2.50 days shorter) compared with the group undergoing preoperative endoscopic sphincterotomy followed by LC, however this was also reported as low quality evidence. Length of operative time was found to be longer with laparoscopic-endoscopic rendezvous procedure (MD 34.07 minutes, 95% CI 11.41 to 56.74), however this was based on very low quality evidence. (52)

Timing of interventions in the management of CBD stones

A systematic review included 14 studies (n=1,930) evaluating the optimal time interval between ERCP and LC in the management of CBD stones. The pooled estimate for conversion to open surgery increased from 4.2% when LC occurred within 24 hours of ERCP to 7.6% when delayed LC occurred (24-72 hours) post ERCP, to 12.3% when delayed LC either occurred within 2 weeks or between 2- 6 weeks and 14% when LC occurred after 6 weeks (significance not reported). (53)

An RCT in patients with concomitant gallbladder and CBD stones (n=NR) compared ELC versus DLC following ERCP. Patients were randomised to receive either ELC within 72 hours after ERCP or DLC 1 month after ERCP. The results found no significant differences in terms of conversion rate to open surgery, degree of adhesion, cystic duct diameter, and intraoperative CBD injury or bleeding between both groups, whereas recurrent biliary symptoms were significantly higher in the DLC group compared to ELC group (7 versus 1 patient respectively). (54)

Intelligence gathering

NICE has produced a medtech innovation briefing; [The SpyGlass direct visualisation system for diagnostic and therapeutic procedures during endoscopy of the biliary system](#) (February 2015) MIB21. The SpyGlass system is used for diagnostic and therapeutic management of large stones of the biliary system when standard ERCP is unsuccessful or considered inappropriate.

One topic expert felt there should be a “recommendation allowing for postoperative ERCP”. The evidence did not clearly demonstrate that postoperative ERCP was superior to other procedures, therefore it is not anticipated that this new evidence will impact current recommendations

Regarding specific subgroups of the population, a topic expert asked whether the recommendations apply to pregnant women. No evidence on management of common bile duct stones relating to this subgroup was identified.

Impact statement

Pre/intra/postoperative ERCP +LC compared with bile duct exploration + LC

Evidence was identified (7 studies consisting of 1 Cochrane review, 2 systematic reviews, 1 meta-analysis, 3 RCTs) on laparoscopic common bile duct exploration (LCBDE) and

laparoscopic cholecystectomy (LC) compared with LC and pre/intra/postoperative endoscopic retrograde cholangiopancreatography (ERCP) for endoscopic extraction of common bile duct (CBD) stones.

One identified Cochrane review found no significant differences in terms of mortality and morbidity between laparoscopic bile duct clearance and endoscopic procedures. The evidence indicated that single-stage management (LC and LCBDE) may be superior compared to the two-stage management (pre/postoperative ERCP and LC) of CBD stones in terms of duration of hospital stay and cost. Several studies noted no significant differences between both strategies in terms of morbidity, mortality, overall success rate and complications. As such, it is not anticipated that this new evidence will impact current recommendations to offer both treatments for clearing the bile duct.

Other management strategies

One Cochrane review was identified that assessed endoscopic sphincterotomy and stone removal followed by LC (the single-stage rendezvous technique) versus preoperative endoscopic sphincterotomy followed by LC

(two stages) in people with gallbladder and CBD stones. The review reported that whilst the laparoscopic-endoscopic rendezvous procedure may be associated with a longer operating time, it may result in a lower length of hospital stay when compared with preoperative endoscopic sphincterotomy followed by LC. However, further evidence synthesis is required before considering this as an area for update.

Timing of interventions in the management of CBD stones

Two studies (1 systematic review, 1 RCT) were identified that assessed the timing of interventions used in the management of CBD stones. Both studies reported different time intervals for early LC either within 24 or 72 hours of ERCP. There was mixed evidence on the benefit of early LC in reducing the conversion rate to open surgery compared with delayed LC. Early surgery may be associated with a reduction in recurrent biliary symptoms, based on the findings of one study. However, at present the evidence base is too small to recommend this as an area for update.

New evidence is unlikely to change guideline recommendations.

1.4 Patient, family member and carer information

Recommendations in this section of the guideline

- 1.4.1 Advise people to avoid food and drink that triggers their symptoms until they have their gallbladder or gallstones removed.
- 1.4.2 Advise people that they should not need to avoid food and drink that triggered their symptoms after they have their gallbladder or gallstones removed.
- 1.4.3 Advise people to seek further advice from their GP if eating or drinking triggers existing symptoms or causes new symptoms to develop after they have recovered from having their gallbladder or gallstones removed.

Surveillance decision

This section of the guideline should not be updated.

2018 surveillance summary

Patient, family member and carer information

A Cochrane review included 4 RCTs (n=431) comparing the benefits and harms of formal preoperative patient education for patients undergoing LC. Patients were either randomised to receive formal patient education (included verbal education, multimedia DVD programme, computer-based multimedia program, and a Power Point presentation) or standard care. There was no clear evidence of effect on patient satisfaction, knowledge or anxiety between both groups.(55)

A qualitative study with a phenomenological approach involved patients (n=NR) diagnosed with acute cholecystitis and who underwent cholecystectomy to gain further insight into the experience of hospitalised patients. Face to face interviews were conducted prior to scheduled surgery. Interviews were also completed post-surgery in patients who experienced an uneventful cholecystectomy. There were 5 themes: "(a) consumed by discomfort and pain, (b) restless discomfort interrupting sleep, (c) living in uncertainty, (d) impatience to return to normalcy, and (e) feelings of vulnerability". Patients described distressing pain both before and after cholecystectomy which affected daily activities including sleep and family responsibilities. The

authors concluded that "increased awareness is needed to prevent the disruption to daily life that can result from the cholecystitis and resulting cholecystectomy surgery. Also, nurses can help ease the unpredictability of the experience by providing relevant patient education, prompt pain relief, and an attentive approach to the nursing care". (56)

Intelligence gathering

Regarding specific subgroups of the population, a topic expert asked whether the recommendations apply to pregnant women. No evidence for this group was identified.

Impact statement

Limited evidence was identified on the information and education needs of patients and carers of people with gallstone disease and the type of information people would find useful. Although one study indicated increased awareness of gallstones and cholecystectomy is important.

The current recommendations focus on dietary advice prior and post removal of gallstones and no evidence was identified through the surveillance review to indicate those recommendations would be impacted.

New evidence is unlikely to change guideline recommendations.

Research recommendations

2.1 Diagnosing gallstone disease

What are the long-term benefits and harms, and cost effectiveness of endoscopic ultrasound (EUS) compared with magnetic resonance cholangiopancreatography (MRCP) in adults with suspected common bile duct stones?

Summary of findings

One study relevant to the research recommendation was found (see [Endoscopic ultrasound \(EUS\) and MRCP/ERCP](#)).

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

2.2 Managing gallbladder stones

What are the benefits and harms, and cost effectiveness of routine intraoperative cholangiography in people with low to intermediate risk of common bile duct stones?

Summary of findings

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

2.3 Managing common bile duct stones

What models of service delivery enable intraoperative endoscopic retrograde cholangiopancreatography (ERCP) for bile duct clearance to be delivered within the NHS? What are the costs and benefits of different models of service delivery?

Summary of findings

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

2.4 Timing of laparoscopic cholecystectomy

In adults with common bile duct stones, should laparoscopic cholecystectomy be performed early (within 2 weeks of bile duct clearance), or should it be delayed (until 6 weeks after bile duct clearance)?

Summary of findings

One study was identified relevant to this research recommendation (see [Timing of interventions in the management of CBD stones](#)).

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

2.5 Information for patients and carers

What is the long-term effect of laparoscopic cholecystectomy on outcomes that are important to patients?

Summary of findings

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

References

1. Gurusamy KS, Giljaca V, Takwoingi Y, Higgie D, Poropat G, Stimac D, et al. (2015) Ultrasound versus liver function tests for diagnosis of common bile duct stones. *Cochrane Database of Systematic Reviews* (2):CD011548
2. Stogryn S, Metcalfe J, Vergis A, Hardy K (2016) Does ultrasonography predict intraoperative findings at cholecystectomy? An institutional review. *Canadian Journal of Surgery* 59(1):12–8
3. Chen W, Mo JJ, Lin L, Li CQ, Zhang JF (2015) Diagnostic value of magnetic resonance cholangiopancreatography in choledocholithiasis. *World Journal of Gastroenterology* 21(11):3351–60
4. Toppi JT, Johnson MA, Page P, Fox A (2016) Magnetic resonance cholangiopancreatography: utilization and usefulness in suspected choledocholithiasis. *ANZ Journal of Surgery* 86(12):1028–32
5. Su-Lim L, Hyung-Keun K, Hyun-Ho C, Bu-Seok J, Tae-Hyung K, Jong-Min C, et al. (2018) Diagnostic value of magnetic resonance cholangiopancreatography to detect bile duct stones in acute biliary pancreatitis. *Pancreatology* 18(1):22–8
6. Giljaca V, Gurusamy KS, Takwoingi Y, Higgie D, Poropat G, Stimac D, et al. (2015) Endoscopic ultrasound versus magnetic resonance cholangiopancreatography for common bile duct stones. *Cochrane Database of Systematic Reviews* (2):CD011549
7. Yaser M, Khalil A-S, Mohammad Y (2017) Diagnostic accuracy of EUS compared with MRCP in detecting choledocholithiasis: a meta-analysis of diagnostic test accuracy in head-to-head studies. *Gastrointestinal Endoscopy* 86(6):986–93
8. Morris S, Gurusamy KS, Sheringham J, Davidson BR (2015) Cost-effectiveness analysis of endoscopic ultrasound versus magnetic resonance cholangiopancreatography in patients with suspected common bile duct stones. *PLoS ONE [Electronic Resource]* 10(3):e0121699
9. Anderloni A, Galeazzi M, Ballare M, Pagliarulo M, Orsello M, Piano D, et al. (2015) Early endoscopic ultrasonography in acute biliary pancreatitis: A prospective pilot study. *World Journal of Gastroenterology* 21(36):10427–34
10. Ruchir P, Meghraj I, Dhaval C, Prateik P, Vikas P, Prabha S (2017) Endoscopic Ultrasonography Can Prevent Unnecessary Diagnostic Endoscopic Retrograde Cholangiopancreatography Even in Patients with High Likelihood of Choledocholithiasis and Inconclusive Ultrasonography: Results of a Prospective Study. *Clinical Endoscopy* 50(6):592–7
11. Netinatsunton N, Attasaranya S, Sottisuporn J, Witeerungrot T, Jongboonyanuparp T, Piratvisuth T, et al. (2016) Comparing cost-effectiveness between endoscopic ultrasound and endoscopic retrograde cholangiopancreatography in diagnosis of common bile duct stone in patients with predefined risks: A study from a developing country. *Endoscopic Ultrasound* 5(3):165–72
12. Bansal NK, Panda N, Alagammai PL, Narsimhan M, Ardhanari R (2017) Benefits of endoscopic ultrasonography. First strategy in patients with intermediate and high risk for choledocholithiasis. *Acta Gastroenterologica Latinoamericana* 47(4):252–8
13. Jeon TJ, Cho JH, Kim YS, Song SY, Park JY (2017) Diagnostic Value of Endoscopic

- Ultrasonography in Symptomatic Patients with High and Intermediate Probabilities of Common Bile Duct Stones and a Negative Computed Tomography Scan. *Gut & Liver* 11(2):290–7
14. Min W, Xu H, Chuan T, Jian L, Feng M, Hong-Yan L (2016) The Diagnostic Accuracy of Linear Endoscopic Ultrasound for Evaluating Symptoms Suggestive of Common Bile Duct Stones. *Gastroenterology research & practice* 2016:6957235
 15. Zhang J, Li NP, Huang BC, Zhang YY, Li J, Dong JN, et al. (2016) The Value of Performing Early Non-enhanced CT in Developing Strategies for Treating Acute Gallstone Pancreatitis. *Journal of Gastrointestinal Surgery* 20(3):604–10
 16. Ajlan AM, Mesurole B, Stein L, Kao E, Artho G, Al-Rujaib M, et al. (2015) Detectability of choledocholithiasis on CT: The effect of positive intraduodenal enteric contrast on portovenous contrast-enhanced studies. *Saudi Journal of Gastroenterology* 21(5):306–12
 17. Gurusamy KS, Giljaca V, Takwoingi Y, Higgie D, Poropat G, Stimac D, et al. (2015) Endoscopic retrograde cholangiopancreatography versus intraoperative cholangiography for diagnosis of common bile duct stones. *Cochrane Database of Systematic Reviews* (2):CD010339
 18. Fagenholz PJ, Fuentes E, Kaafarani H, Cropano C, King D, Moya de, et al. (2015) Computed Tomography Is More Sensitive than Ultrasound for the Diagnosis of Acute Cholecystitis. *Surgical Infections* 16(5):509–12
 19. Changphaisarnkul P, Saengruang-Orn S, Boonya-Asadorn T (2015) The Diagnosis of Acute Cholecystitis: Sensitivity of Sonography, Cholescintigraphy and Computed Tomography. *Journal of the Medical Association of Thailand* 98(8):812–9
 20. Kaoutzanis C, Davies E, Leichtle SW, Welch KB, Winter S, Lampman RM, et al. (2014) Abdominal ultrasound versus hepato-imino diacetic acid scan in diagnosing acute cholecystitis--what is the real benefit? *Journal of Surgical Research* 188(1):44–52
 21. Brazzelli M, Cruickshank M, Kilonzo M, Ahmed I, Stewart F, McNamee P, et al. (2015) Systematic review of the clinical and cost effectiveness of cholecystectomy versus observation/conservative management for uncomplicated symptomatic gallstones or cholecystitis. *Surgical Endoscopy* 29(3):637–47
 22. Brazzelli M, Cruickshank M, Kilonzo M, Ahmed I, Stewart F, McNamee P, et al. (2014) Clinical effectiveness and cost-effectiveness of cholecystectomy compared with observation/conservative management for preventing recurrent symptoms and complications in adults presenting with uncomplicated symptomatic gallstones or cholecystitis: a syste. *Health Technology Assessment (Winchester, England)* 18(55):1–101, v
 23. Ding GQ, Cai W, Qin MF (2015) Is intraoperative cholangiography necessary during laparoscopic cholecystectomy for cholelithiasis? *World Journal of Gastroenterology* 21(7):2147–51
 24. Ambe PC, Kaptanis S, Papadakis M, Weber SA, Jansen S, Zirngibl H (2016) The Treatment of Critically Ill Patients With Acute Cholecystitis. *Deutsches Arzteblatt International* 113(33–34):545–51
 25. Tang H, Dong A, Yan L (2015) Day surgery versus overnight stay laparoscopic cholecystectomy: A systematic review and meta-analysis. *Digestive & Liver Disease* 47(7):556–61

26. Sanjay K, Shadan A, Shabi A, Kusum M, Chandola HC (2015) Randomised Controlled Trial of Day-Case Laparoscopic Cholecystectomy vs Routine Laparoscopic Cholecystectomy. *Indian Journal of Surgery* 77(Suppl 2):520–4
27. Jochen S, Matthias G (2015) Acute Cholecystitis. *Viszeralmedizin* 31(3):163–5
28. Cao AM, Eslick GD, Cox MR (2015) Early Cholecystectomy Is Superior to Delayed Cholecystectomy for Acute Cholecystitis: a Meta-analysis. *Journal of Gastrointestinal Surgery* 19(5):848–57
29. Wu XD, Tian X, Liu MM, Wu L, Zhao S, Zhao L (2015) Meta-analysis comparing early versus delayed laparoscopic cholecystectomy for acute cholecystitis. *British Journal of Surgery* 102(11):1302–13
30. Menahem B, Mulliri A, Fohlen A, Guittet L, Alves A, Lubrano J (2015) Delayed laparoscopic cholecystectomy increases the total hospital stay compared to an early laparoscopic cholecystectomy after acute cholecystitis: an updated meta-analysis of randomized controlled trials. *HPB* 17(10):857–62
31. Zhou MW, Gu XD, Xiang JB, Chen ZY (2014) Comparison of clinical safety and outcomes of early versus delayed laparoscopic cholecystectomy for acute cholecystitis: a meta-analysis. *TheScientificWorldJournal* 2014:274516
32. Rajcok M, Bak V, Danihel L, Kukucka M, Schnorrer M (2016) Early versus delayed laparoscopic cholecystectomy in treatment of acute cholecystitis. *Bratislavske Lekarske Listy* 117(6):328–31
33. Roulin D, Saadi A, Mare D, L, Demartines N, Halkic N (2016) Early Versus Delayed Cholecystectomy for Acute Cholecystitis, Are the 72 hours Still the Rule?: A Randomized Trial. *Annals of Surgery* 264(5):717–22
34. Rati A, Sood KC, Bhupender A (2015) Evaluation of Early versus Delayed Laparoscopic Cholecystectomy in Acute Cholecystitis. *Surgery Research & Practice Print* 2015:349801
35. Ozkardes AB, Tokac M, Dumlu EG, Bozkurt B, Ciftci AB, Yetisir F, et al. (2014) Early versus delayed laparoscopic cholecystectomy for acute cholecystitis: a prospective, randomized study. *International Surgery* 99(1):56–61
36. Mestral de, C, Hoch JS, Laupacis A, Wijeyesundera HC, Rotstein OD, et al. (2016) Early Cholecystectomy for Acute Cholecystitis Offers the Best Outcomes at the Least Cost: A Model-Based Cost-Utility Analysis. *Journal of the American College of Surgeons* 222(2):185–94
37. Sutton AJ, Vohra RS, Hollyman M, Marriott PJ, Buja A, Alderson D, et al. (2017) Cost-effectiveness of emergency versus delayed laparoscopic cholecystectomy for acute gallbladder pathology. *British Journal of Surgery* 104(1):98–107
38. Doa'a K, Alexander Z, Reshma B, Nadia A, Grace B, Bharat S, et al. (2018) Early laparoscopic cholecystectomy is more cost-effective than delayed laparoscopic cholecystectomy in the treatment of acute cholecystitis. *Clinicoeconomics & Outcomes Research* 10:119–25
39. Schwartz DA, Shah AA, Zogg CK, Nicholas LH, Velopulos CG, Efron DT, et al. (2015) Operative delay to laparoscopic cholecystectomy: Racking up the cost of health care. *The Journal of Trauma and Acute Care Surgery* 79(1):15–21
40. Du-Jiang Y, Hui-Min L, Qiang G, Shan L, Ling Z, Wei-Ming H (2017) Timing of

Laparoscopic Cholecystectomy After Mild Biliary Pancreatitis: A Systematic Review and Meta-Analysis. *Journal of Laparoendoscopic & Advanced Surgical Techniques Part A* 22:22

41. Costa da, W D, Bouwense SA, Schepers NJ, Besselink MG, Santvoort van, et al. (2015) Same-admission versus interval cholecystectomy for mild gallstone pancreatitis (PONCHO): a multicentre randomised controlled trial. *Lancet* 386(10000):1261–8
42. Costa da, W D, Dijkman LM, Bouwense SA, Schepers NJ, Besselink MG, et al. (2016) Cost-effectiveness of same-admission versus interval cholecystectomy after mild gallstone pancreatitis in the PONCHO trial. *British Journal of Surgery* 103(12):1695–703
43. Li JS, Razman J, Foong LK, Krishnan R (2018) Outcomes of early versus delayed cholecystectomy in patients with mild to moderate acute biliary pancreatitis: A randomized prospective study. *Asian Journal of Surgery* 41(1):47–54
44. Morris S, Gurusamy KS, Patel N, Davidson BR (2014) Cost-effectiveness of early laparoscopic cholecystectomy for mild acute gallstone pancreatitis. *British Journal of Surgery* 101(7):828–35
45. Dasari BV, Tan CJ, Gurusamy KS, Martin DJ, Kirk G, McKie L, et al. (2013 [cited 2018 Aug 13]) Surgical versus endoscopic treatment of bile duct stones. Chichester, UK: John Wiley & Sons, Ltd
46. Kenny R, Richardson J, McGlone ER, Reddy M, Khan OA (2014) Laparoscopic common bile duct exploration versus pre or post-operative ERCP for common bile duct stones in patients undergoing cholecystectomy: is there any difference? *International Journal Of Surgery* 12(9):989–93
47. Narayan SA, Ragini K (2018) Single-stage laparoscopic common bile duct exploration and cholecystectomy versus two-stage endoscopic stone extraction followed by laparoscopic cholecystectomy for patients with gallbladder stones with common bile duct stones: systematic review and meta-. *Surgical Endoscopy* 30:30
48. Zhu HY, Xu M, Shen HJ, Yang C, Li F, Li KW, et al. (2015) A meta-analysis of single-stage versus two-stage management for concomitant gallstones and common bile duct stones. *Clinics & Research in Hepatology & Gastroenterology* 39(5):584–93
49. Poh BR, Ho SP, Sritharan M, Yeong CC, Swan MP, Devonshire DA, et al. (2016) Randomized clinical trial of intraoperative endoscopic retrograde cholangiopancreatography versus laparoscopic bile duct exploration in patients with choledocholithiasis. *British Journal of Surgery* 103(9):1117–24
50. Bansal VK, Misra MC, Rajan K, Kilambi R, Kumar S, Krishna A, et al. (2014) Single-stage laparoscopic common bile duct exploration and cholecystectomy versus two-stage endoscopic stone extraction followed by laparoscopic cholecystectomy for patients with concomitant gallbladder stones and common bile duct stones: a randomized con. *Surgical Endoscopy* 28(3):875–85
51. Ding G, Cai W, Qin M (2014) Single-stage vs. two-stage management for concomitant gallstones and common bile duct stones: a prospective randomized trial with long-term follow-up. *Journal of Gastrointestinal Surgery* 18(5):947–51
52. Vettoretto N, Arezzo A, Famiglietti F, Cirocchi R, Moja L, Morino M (2018 [cited 2018 Aug 13]) Laparoscopic-endoscopic rendezvous versus preoperative endoscopic sphincterotomy in people undergoing laparoscopic cholecystectomy for stones in the

- gallbladder and bile duct. Cochrane Database of Systematic Reviews (4)
53. Friis C, Rothman JP, Burcharth J, Rosenberg J (2017) Optimal Timing For Laparoscopic Cholecystectomy After Endoscopic Retrograde Cholangiopancreatography: A Systematic Review. *Scandinavian Journal of Surgery: SJS* :1457496917748224
 54. Nakeeb E, A, Ezzet H, Askar W, Hanafy E, E, et al. (2016) Early Versus Late Cholecystectomy After Clearance of Common Bile Duct Stones by Endoscopic Retrograde Cholangiopancreatography: A Prospective Randomized Study. *Surgical Laparoscopy, Endoscopy & Percutaneous Techniques* 26(3):202–7
 55. Gurusamy KS, Vaughan J, Davidson BR (2014) Formal education of patients about to undergo laparoscopic cholecystectomy. *Cochrane Database of Systematic Reviews* (2):CD009933
 56. Lindseth GN, Denny DL (2014) Patients' experiences with cholecystitis and a cholecystectomy. *Gastroenterology Nursing* 37(6):407–14

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