Gallstones
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Abstract
Gallstones are extremely common in the UK and have a major effect on healthcare resources. Presentation depends on whether the stones occlude the cystic duct or the common bile duct. Treatment for symptomatic gallstones is laparoscopic cholecystectomy as a day case. Conversion rates to open surgery should be <10% overall; many series report much lower rates. Stones in the common bile duct should be suspected and diagnosed preoperatively and may be removed by preoperative endoscopic retrograde cholangiopancreatography (ERCP). In the young, an attempt should be made to preserve the biliary sphincter, and stones diagnosed preoperatively may be managed by ERCP and stenting followed by laparoscopic exploration, or directly by laparoscopic exploration. Laparoscopic cholecystectomy may be accompanied by selective or routine cholangiography. Stones discovered at elective laparoscopic cholecystectomy during on-table cholangiography may be managed by laparoscopic transcystic exploration or laparoscopic choledochotomy with bile duct exploration. On-table combined perioperative ERCP is another option and this technique may be enhanced by combined procedures to carry out a sphincterotomy or to place a biliary stent. Failure of these options may be followed by open exploration of the bile duct or postoperative ERCP. The treatment of acute gallstone disease is conservative, with subsequent elective laparoscopic cholecystectomy or urgent laparoscopic cholecystectomy. Urgent surgery is more economical, with a low conversion rate to open surgery in specialist hands.

Keywords gallstones; laparoscopic cholecystectomy; common bile duct; ERCP

Prevalence
Gallstone disease is extremely common in the UK; gallstones are found in 10–20% of patients at post mortem; they are responsible for 1–2% of deaths. Every year, an estimated 50,000 cholecystectomies are done in England and Wales, with about 11% of patients undergoing emergency surgery. It is estimated that 1.5% of men and 6.1% of women will have gallstone disease by the age of 40 years; the prevalence in older patients has increased over the last 25 years.

Classification
Gallstones are classified into cholesterol and pigment; the former account for 70% of stones and the latter the remainder. Cholesterol is poorly soluble in water and is held in solution in bile in the form of mixed micelles comprising:

- cholesterol
- phospholipids (mainly lecithin)
- bile salts (primary bile salts (cholic and chenodeoxycholic acids) and secondary bile acids (deoxycholic acid and lithocholic acid)).

Individuals with cholesterol gallstones secrete bile that is supersaturated with cholesterol, and this is related to reduced secretion of bile salts (with a reduction in the total bile salt pool) and increased cholesterol secretion. Most patients with gallstones have gallbladders that empty more slowly and less completely than those without gallstones. Pigment stones are formed mainly of calcium salts of unconjugated bilirubin deposited in a matrix of glycoprotein.

Risk factors
Geographical – certain Native American communities have an extremely high prevalence due to the production of supersaturated bile. Pima Indian women have an overall prevalence of gallstones of 48.6%.

Familial – there is a familial tendency to gallstone disease: there is a twofold increase in gallstones in first-degree relatives compared with controls.

Age – the prevalence of gallstones increases with age.

Sex – gallstones are more common in females at all ages, and may be an effect of female sex hormones.

Oral contraceptive therapy is associated with increased cholesterol saturation, and these drugs increase the incidence of gallstones.

Obesity increases supersaturated bile and thus the risk of gallstones increases.

Diabetes mellitus may be associated with an increase in the prevalence of gallstones related to cholesterol metabolism and gallbladder dysfunction.

Gastric surgery (in particular fundoplication) may be associated with an increase in gallstone disease due to damage to the hepatic branches of the vagus nerve.

Inflammatory bowel disease (e.g. Crohn’s disease) is associated with a much higher incidence of gallstone disease due to disease of the terminal ileum, leading to abnormalities in the enterohepatic circulation of bile salts. Failure to absorb bile salts and bile acids effectively alters the balance of bile acids, leading to a smaller total bile acid pool. Stones are often asymptomatic in this condition.

Haemolytic anaemia is associated with increased formation of pigment stones.

Total parental nutrition over long periods is associated with pigment gallstone disease.

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**Clinical presentations of cholelithiasis**

It is estimated that patients with gallstones found during screening examinations have a 2% chance per year of developing symptoms. In most patients, the first presentation is biliary colic, but occasionally patients present with severe acute pancreatitis.

Presentation depends on the site of obstruction of the biliary tree by gallstones. The commonest site of obstruction is Hartmann’s pouch of the gallbladder or the cystic duct, and leads to episodes of biliary colic.

**Biliary colic** is associated with constant, severe pain in the right upper quadrant and epigastrium lasting between 20 minutes and several hours, with pain often radiating through to the back or the right scapula. The pain may be very intense and may be relieved by spontaneous disimpaction of the gallstone from Hartmann’s pouch or migration of the stone into the common bile duct.

**Acute cholecystitis** is also initiated by a stone becoming impacted in the cystic duct or Hartmann’s pouch, leading to intense pain in the right upper quadrant and epigastrum. With time, a sterile inflammation develops and the pain progresses to constant, severe pain in the right upper quadrant lasting for hours to days. With secondary bacterial infection, signs of right upper quadrant peritonism associated with a leukocytosis (and often derangement of liver function due to swelling and oedema of Hartmann’s pouch affecting the bile duct) may develop.

**Complications of cholecystitis** – between 5% and 10% of patients may develop one of the complications of cholecystitis (e.g. an empyema followed by gangrene and perforation of the gallbladder; Figure 1). Perforation may lead to biliary peritonitis or the gallbladder may be walled off by the colon or duodenum; perforation of such a walled-off gallbladder leads to a cholecystocholedochal fistula or a cholecystoduodenal fistula. In patients with infected cholecystitis, the commonest organism cultured from gallbladder bile is *Escherichia coli*, but other enteric bacteria are also found. Chemical cholecystitis may resolve with the development of a mucocoele of the gallbladder, presenting with pain in the right upper quadrant and a distended and palpable gallbladder.

**Obstructive jaundice:** a large stone impacted in Hartmann’s pouch may press on the common bile duct, leading to obstructive jaundice (Mirizzi syndrome type 1). In the chronic setting, such a stone may erode through the gallbladder wall and through the wall of the common bile duct, with the development of a cholecystocholedochal fistula (Mirizzi type 2). Obstructive jaundice may also be caused by stones that enter the common bile duct via the cystic duct.

**Clinical presentations of choledocholithiasis**

**Cholangitis:** stones migrating from the gallbladder into the common bile duct may be asymptomatic but, as they grow in size, they can cause obstruction of the bile duct which, combined with secondary infection, leads to cholangitis. These patients characteristically present with epigastric pain radiating through to the back which is associated with severe nausea and persistent vomiting. Obstructive jaundice develops, but it is usually mild to moderate. Extremely high concentrations of bilirubin are uncommon and may represent complete obstruction of the bile duct as seen in malignant disease or stricture of the bile duct rather than obstruction due to gallstones. Organisms usually found in the infected bile ducts are Gram-negative bacteria, but occasionally Gram-positive aerobes and anaerobes are also cultured. The commonest bacteria are *Escherichia coli*, *Klebsiella pneumoniae*, *Streptococcus faecalis* and enterococci. Acute ascending cholangitis is easily diagnosed by the combination of symptoms and signs of epigastric pain, jaundice and fever—Charcot’s triad. Confusion and hypotension may develop in elderly patients due to systemic

**Figure 1**

Resection specimens showing a empyema of the gallbladder with b mural necrosis.
sepsis and dehydration; in some patients, the presentation may be insidious with features of septicaemic shock associated with deranged liver function tests.

**Acute gallstone pancreatitis**: impaction of bile duct stones in the terminal common bile duct can lead to compression of the pancreatic duct where it enters the duodenum at the ampulla of Vater, leading to acute gallstone pancreatitis.

**Investigations**

**Ultrasound** of the biliary tree provides information on stones or sludge in the gallbladder. It may show thickening of the gallbladder wall, suggesting inflammation. It should show biliary dilation and it may show stones in the common bile duct.

**Magnetic resonance cholangiopancreatography** (MRCP, Figure 2) is the best way to see the bile ducts.

**Endoscopic retrograde cholangiopancreatography** (ERCP, Figure 3) was previously used for diagnostic imaging, but is now exclusively reserved for therapeutic procedures in jaundiced patients.

**Endoscopic ultrasound** detects small ductal calculi and may be particularly useful in the assessment of idiopathic pancreatitis.

**Management of gallstones**

**Elective surgery**

First-line treatment is laparoscopic cholecystectomy. Patients who are American Surgical Association (ASA) grade 1 or 2 with a body mass index of <30 and aged <70 years may be offered a laparoscopic cholecystectomy as a day case provided that they have uncomplicated gallstone disease without a history of jaundice, dilated ducts or acute pancreatitis. Previous upper abdominal surgery is not a contraindication to day-case surgery (see Gandhimani, CROSS REFERENCES).

At least 90% of procedures are completed laparoscopically in most institutions that have an interest in laparoscopic cholecystectomy. The overall conversion rate varies from 2% to 10% depending on the series, and patients should be warned of the risk. The prevalence of injury to the bile duct is about 0.3% and patients should be warned of this complication. Laparoscopic cholecystectomy as a day case should account for at least 50% of elective cholecystectomies and discharge within eight hours of surgery should be the aim. The complication rate within day-surgery group should be <10%.

**Surgery in the acute setting**

The management of acute gallstone disease is controversial. Options include:

- treating the acute episode and returning the patient for elective surgery
- carrying out an urgent laparoscopic cholecystectomy.

Supporters of conservative management with later elective gallbladder surgery cite a low conversion rate as the reason for this approach; those who support urgent laparoscopic cholecystectomy cite repeat admissions to hospital while patients wait for surgery, with the attendant morbidity, expense and lost time this involves. Urgent laparoscopic cholecystectomy for patients...
presenting with acute gallstone disease requiring hospital admission should be carried out within 3–4 days of admission; there is a higher risk of complications in terms of conversion to open surgery if delayed beyond this time. Early surgery is associated with:

- a shorter stay in hospital
- a reduction in recuperation time
- avoidance of the problems of failed conservative management. Early surgery was previously associated with conversion rates of up to 30%, but recent studies have reported conversion rates of 11–15% in specialist hands.

**Routine versus selective cholangiography**

Operative cholangiography reveals undetected stones in the biliary tree; laparoscopic ultrasound is as sensitive as operative cholangiography in skilled hands. Debate continues as to whether cholangiography should be routinely carried out as part of every laparoscopic cholecystectomy or done selectively in those who have a higher risk of having stones in the common bile duct. Large series of routine intraoperative cholangiography show that this is possible and successful in >99% of patients and that asymptomatic bile duct stones will be found in up to 10% of patients. Proponents of selective intraoperative cholangiography maintain that it does not predispose patients to a higher rate of injury to the biliary tree and it helps avoid unwarranted exploration of the common bile duct in 20–30% of false-positive studies. It also saves time and the lowers the cost of the procedure. Proponents of routine intraoperative cholangiography acknowledge that most intraoperative cholangiography results are negative studies, but argue that added cost and the time of the procedure are minimal. Despite a strong case for selective cholangiography, routine operative cholangiography reduces the extent of injury to the bile duct and its sequelae should such an injury occur. Surgeons who practice selective operative cholangiography should be doing cholangiograms in at least 10–15% of their patients who undergo laparoscopic cholecystectomy.

**Management of stones in the common bile duct**

Patients with symptomatic stones in the common bile duct may have them extracted at ERCP before laparoscopic cholecystectomy; this is particularly important in older patients. ERCP and duct clearance may be the definitive treatment in elderly patients who are not troubled by gallbladder stones, and if laparoscopic cholecystectomy is better avoided. Young jaundiced patients with stone disease should have the jaundice managed (by ERCP and sphincterotomy, or ampullary balloon dilation with stone clearance) before surgery. The ampullary sphincter should be preserved (particularly in a very young patient) and a biliary stent may be placed before laparoscopic cholecystectomy. In younger non-jaundiced patients, laparoscopic cholecystectomy with on-table cholangiography is the best treatment and stones found in the common bile duct are dealt with appropriately.

**Options if operative cholangiography reveals stones in the common bile duct**

Several procedures can be done acutely or electively if operative cholangiography reveals stones in the common bile duct.

- Exploration of the bile duct by conversion to open exploration of the common bile duct or a laparoscopic exploration. The latter may be done by a laparoscopic transcytic exploration or a laparoscopic choledochotomy with choledochoscopy and exploration of the common bile duct.
- On-table ERCP, after completing the laparoscopic cholecystectomy.
- Complete the laparoscopic procedure and refer the patient postoperatively for an ERCP 1–2 weeks later if the surgeon does not possess the requisite skills to carry out laparoscopic exploration of the bile duct, or a skilled ERCP specialist is unavailable.

If the cholangiogram shows a stone in the common bile duct but contrast flows into the duodenum, the cystic duct may be clipped, ‘endo-looped’ and the procedure completed. If contrast does not enter the duodenum on cholangiography, the biliary tree may be completely obstructed and a transcystic drain should be tied in to the biliary tree to function as a vent before the procedure is completed and the gallbladder removed.

**Laparoscopic exploration**

*Laparoscopic transcytic exploration* is useful if one or two small stones are shown within the common bile duct. It involves balloon dilation of the cystic duct, followed by choledochoscopy (if possible) through the cystic duct. If this is not possible, a Dormia basket may be introduced through the opening of the cystic duct and the stone seen and grasped with the basket under fluoroscopy. A small stone may be successfully extracted through the cystic duct, which can then be clipped shut.

*Laparoscopic choledochotomy* is the procedure of choice if one or two large stones are in the common bile duct. The two approaches for opening the common bile duct are by a transverse or longitudinal choledochotomy. The arteries that supply the bile duct are longitudinal and it is conventional at open exploration of the bile duct to carry out a longitudinal choledochotomy. In the era of laparoscopic exploration, transverse choledochotomy has been done because it is easier and is safe (although long-term follow-up data are not available and the risk of biliary stricturing over many years is unknown). Once the duct is opened, operative choledochoscopy then stone removal under direct vision with a Dormia basket should be possible.

Immediate conversion to open exploration of the bile duct is the safest option if:

- appropriate laparoscopic skills are unavailable
- an inflamed bile duct with difficult distorted anatomy is present
- very large impacted stones are present.

In patients who have not had a preoperative sphincterotomy, closure of the choledochotomy should be accompanied by placement of a T-tube within the biliary tree. A T-tube cholangiogram (Figure 4) is done seven days later to confirm that the duct is clear of stones, and the tube may be ligated and the patient discharged. The T-tube may be removed in the Outpatients Clinic three weeks later.

**Options if there is sufficient experience of ERCP:** if the operator has sufficient ERCP experience and is not an advocate of laparoscopic choledochotomy, then the laparoscopic
cholecystectomy may be completed and the patient turned on to his front or left side for perioperative ERCP. The option is to proceed to open exploration of the bile duct if ERCP fails in this setting. Intraoperative ERCP to extract common bile duct stones is advantageous because the patient is not subjected to the possibility of failure of postoperative ERCP. If intraoperative ERCP is unsuccessful, open exploration of the common bile duct may be done under the same anaesthesia. One very useful option is a transcystic drain, through which a wire may be passed through the bile duct and out into the duodenum, where it may be snared via the duodenoscope ('Tuteur transcystique-transpapillaire’ technique). This combined procedure allows for guaranteed cannulation of the biliary tree, after which a sphincterotome may be passed down the duodenoscope and an endoscopic sphincterotomy can be done. Also, by using the wire, a biliary stent may be deployed across the ampulla if all the stones cannot be extracted endoscopically at ERCP initially. Another variation is to confirm a laparoscopically placed wire through the cystic duct and ampulla into the duodenum using a side-viewing duodenoscope. This may be followed by placing an endoscopic biliary stent over the wire laparoscopically; this stent can be used to facilitate a pre-cut papillotomy or sphincterotomy at a later date with successful stone extraction. It is common for many patients with stones identified on operative cholangiography to be referred for postoperative ERCP but, if the latter fails, the patient is committed to a second anaesthetic and surgery for stone removal.

**ERCP**

**Failure of ERCP:** the following are predictors of failure of ERCP:
- stones >25 mm in diameter or a stone diameter larger than the bile duct
- intrahepatic stones and multiple tightly-packed stones in the common bile duct and impacted stones
- a stricture in the common bile duct
- previous Bilroth II gastrectomy or Roux-en-Y anastomosis; diverticula in the duodenum rendering cannulation difficult.

**Stone size and retained stones:** small stones (<3 mm in size) may pass spontaneously. Cotton found that the perceived risk of developing symptoms from a retained stone over ten years is 35% if a stone is <5 mm and 70% for stones >5 mm in diameter. The perceived risk of developing severe symptoms from a retained stone over ten years was 11% for stones <5 mm and 28% for stones >5 mm in diameter.

**Complications:** ERCP is associated with significant morbidity (about 5%) and a mortality of 0.1–0.5%. Post-ERCP acute pancreatitis may be severe. Bleeding after endoscopic sphincterotomy may require transfusion, re-endoscopy and injection (or even angiography and embolization). Duodenal perforation is a serious complication requiring surgery.

**Long-term effects of endoscopic sphincterotomy**

The long-term effects of endoscopic sphincterotomy are not fully established, but chronic duodenogastric reflux up the bile ducts may have long-term effects. Some studies have shown that nausea and pale stools are reported by one-quarter of patients and that nearly one-fifth of patients have symptoms suggestive of recurrent cholangitis. A minority of patients suffer occasional symptoms suggesting biliary dysfunction.

**Comparison of approaches**

A recent prospective, randomized multicentre clinical trial promoted by the European Association of Endoscopic Surgeons compared combined ERCP and endoscopic sphincterotomy with laparoscopic cholecystectomy versus single-staged laparoscopic treatment of bile duct stones.

Identical efficacy for stone removal was shown in both approaches and the morbidity and mortality rates were very similar. The clear advantage for the laparoscopic approach was a shorter stay in hospital because the long periods between ERCP and laparoscopic cholecystectomy prolonged hospitalization in the combined treatment group. The single-staged laparoscopic approach was the more cost effective of the two options. Some patients are suitable for an open approach when neither ERCP nor laparoscopy is feasible. Patients who have undergone a Bilroth II partial gastrectomy, or those with multiple stones and Mirizzi’s syndrome, are probably best managed by an open approach to bile duct stones.
CROSS REFERENCE

FURTHER READING