Gallstones

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Abstract

Gallstone disease is one of the most common medical problems and presents to physicians and surgeons in many forms. This article discusses the cause of gallstones, their presentation and their management.

Keywords Bile duct stones; cholecystitis; ERCP; gallstones; laparoscopic cholecystectomy; MRCP

Key points

- Asymptomatic gallstones in the gallbladder do not require further investigation or management
- Patients with symptomatic gallstones should be offered laparoscopic cholecystectomy unless medically unfit for surgery
- Laparoscopic cholecystectomy is the only recommended treatment for symptomatic gallbladder stones
- Patients with acute presentation of cholecystitis or gallstone pancreatitis should undergo early cholecystectomy, preferably during the same admission unless there are contraindications to surgery
- Bile duct stones should be removed either by simultaneous bile duct exploration or perioperative endoscopic retrograde cholangiopancreatography depending on local resources and skills

Introduction

The gallbladder serves as a reservoir to hold bile and release it in a bolus when fat is ingested (Figure 1). Fat in the stomach results in the release of cholecystokinin, which causes contraction and emptying of the gallbladder as food enters the duodenum. Bile helps to emulsify fat within the small bowel and aid its absorption. While in the gallbladder, bile is concentrated by the absorption of up to 70% of its water content.

Pathogenesis of gallstones

Bile is composed of a complex solution of bilirubin (the byproduct of effete red blood cells), cholesterol, fatty acids and various minerals. If one or more of the major components is present in excess, the solution becomes supersaturated and cholesterol crystals form within the bile (Figure 2). These eventually coalesce to form cholesterol or 'mixed' (cholesterol −bilirubin) gallstones.

Loss of gallbladder motility leads to prolonged bile stasis (delayed gallbladder emptying) and decreased reservoir function with the formation of biliary sludge and subsequently stones. Diminished gallbladder motility is commonly seen during pregnancy, with a 10−15 times higher incidence of cholelithiasis in women who have had children (Table 1).

Black pigment stones account for approximately 10% of gallstones and are most frequently seen in patients with chronic haemolytic anaemias (e.g. hereditary spherocytosis, sickle cell disease, β-thalassemia) where there is an excess of unconjugated bile.

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Presentation

Gallstones are very common, with an incidence of 10−15% of the adult population. Most people with gallstones are asymptomatic and do not require prophylactic cholecystectomy. In post mortem studies, approximately 90% of individuals with gallstones had no attributable symptoms during their lifetime.

Biliary pain

Gallstones cause symptoms when the cystic duct is occluded during the attempted expulsion of bile from the gallbladder. The resulting contraction of the gallbladder smooth muscle results in referred pain over the associated dermatome (T9) in the epigastrium and radiation round or through to the back. Viscerally innervated pain is often poorly localized and can be accompanied by nausea or vomiting.

Local cytokine release can cause irritation of the adjacent parietal peritoneum resulting in pain in the right upper quadrant (RUQ). The pain lasts for a significant period of time (typically 20 minutes to several hours) and the severity is sufficient to interfere with performance of daily activities. It is frequently very severe, often described by women as 'worse than childbirth', or misdiagnosed as a 'heart attack'. The popular term 'biliary colic' is a misnomer as the pain is constant and unrelenting and not colicky in nature; it should more accurately be referred to as biliary pain. The number of stones, their size and the thickness of the gallbladder wall do not correlate well with the presence, absence or severity of biliary symptoms. In many patients with significant biliary pain the gallbladder looks quite normal at the time of surgery.

It is important to clarify what constitutes true biliary pain in order to better predict relief after surgery. Cholecystectomy fails to relieve symptoms in 10−30% of patients with documented gallstones. Results for cholecystectomy in patients with 'biliary dyspepsia' alone are worse than in those who have more classic bouts of biliary pain (Table 2); the procedure should only be

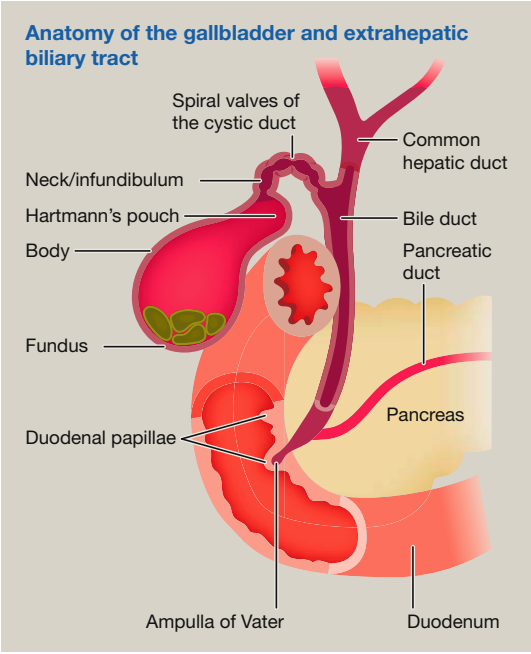

Figure 1

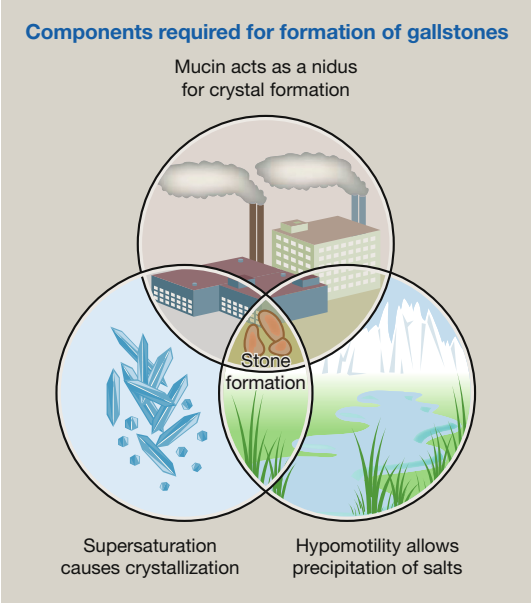

Figure 2

undertaken after appropriate exclusion of other causes where possible and with clear counselling that benefits are less likely.

Acute cholecystitis

When biliary pain persists for more than a few hours and is accompanied by localized RUQ discomfort, it is termed 'acute cholecystitis'. The inflammatory process results in irritation of the parietal peritoneum causing RUQ tenderness, and inspiration with the examiner's hand in this region results in pain as the inflamed gallbladder pushes against it (Murphy's sign).

Inflammatory markers (white cell count, erythrocyte sedimentation rate, C-reactive protein) may be elevated. Liver function tests (LFTs) are often deranged because of localized inflammation within the adjacent liver parenchyma or from compression of the common bile duct (CBD) by the inflamed gallbladder. Secondary infection can develop in this setting but is rarely the primary event. The condition can, however, evolve and result in a variety of complications (Figure 3).

Common bile duct stones

Approximately 8–16% of patients with symptomatic gallbladder stones have simultaneous CBD stones. The natural history of these stones is unknown, but there is evidence that many do not cause symptoms. However, because of the uncertainty in their natural history, most clinicians advise patients to have them removed once they have been discovered, even if asymptomatic.

The presence of a dilated CBD or intrahepatic ducts with elevated LFT results raises the suspicion of CBD stones. Classically, obstructive jaundice is accompanied by pale stools because of the lack of the brown pigment stercobilin (which requires the presence of bilirubin in the gut) and dark urine (because of increased bilirubin in the urine). Obstructive jaundice resulting from CBD stones is often associated with a history of biliary pain.

Typical features of biliary pain

Location	**Epigastric/RUQ**
Duration	From around 20 minutes up to hours
Radiation	Round or through to back (band-like)
Severity	Severe (inhibits daily activity)
Periodicity	Intermittent/pain-free between episodes
Less strongly associated	Nocturnal onset
	After a fatty meal

Table 2

Risk factors for cholelithiasis

- Female
- Fair (Caucasian)
- Fat (high cholesterol excretors, rapid weight loss, obesity)
- Fertile (after pregnancy and gallbladder stasis)
- Forties (requires several years to develop from crystals to stones)

This old adage acts as a good mnemonic and still holds more than a modicum of truth

Table 1

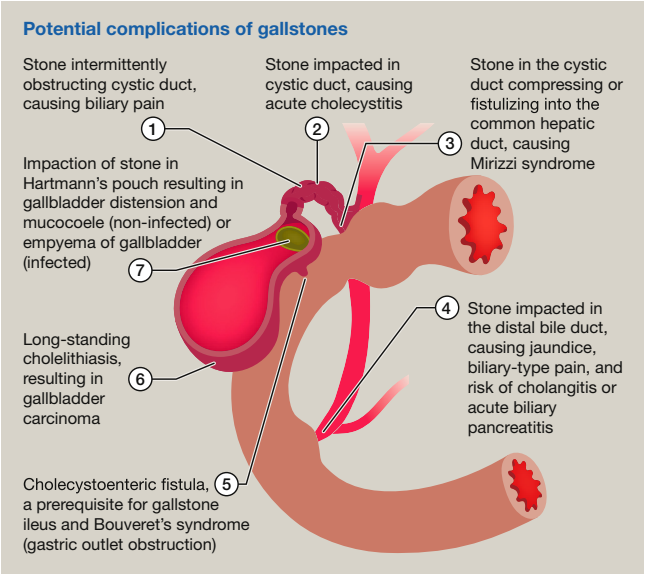

Figure 3

This contrasts with jaundice associated with malignant obstruction, which is usually painless, but the distinction is not absolute. CBD stones are best identified by magnetic resonance cholangiopancreatography or endoscopic ultrasound; these techniques have replaced endoscopic retrograde cholangiopancreatography (ERCP) (with its attendant risks) as a diagnostic tool.

If infection develops in an obstructed bile duct, jaundice is invariably accompanied by high temperatures and RUQ pain (Charcot's triad) and is termed 'cholangitis'. Fevers are typically fluctuating, with high temperatures of 39–40°C punctuated by chills and bouts of shaking (rigors). Cholangitis results from secondary infection within the biliary tract, usually caused by enteric bacteria from the duodenum, most commonly Gram-negative species. Early management with intravenous antibiotics (broad-spectrum cephalosporin or ciprofloxacin) followed by early decompression of the ducts by stone removal or stenting is essential. Failure to treat this condition frequently results in septicaemia, which can be fatal.

Acute pancreatitis

CBD stones (usually small) can pass out of the papilla at the bottom of the bile duct and in some cases result in acute pancreatitis. The most popular theory for the pathogenesis of gallstone pancreatitis is that a gallstone impacted in the distal bile duct obstructs the pancreatic duct, increasing pancreatic pressure, thereby damaging ductal and acinar cells. Patients should be offered early cholecystectomy to prevent further, potentially life-threatening, attacks.

Mirizzi's syndrome

First described by Argentinian surgeon Pablo Mirizzi in 1948, the term is used to describe the situation where a stone impacted in Hartmann's pouch produces an inflammatory process that results in adherence of Hartmann's pouch to the CBD with loss of the space between the two (i.e. obliteration of Calot's triangle). The result is a partial obstruction of the common hepatic duct with deranged LFTs. The most useful subclassification is into type I, with no fistula, and type II, where the stone has eroded into the bile duct, resulting in a cholecysto-choledochal fistula.

Management of gallstones

Non-operative management

During the 1970s and 1980s there were many attempts to develop strategies for non-surgical management of gallstones by oral dissolution, injection of solvents into the biliary tract and extracorporeal shock wave lithotripsy. However, none achieved significant reliable dissolution of the stones, even in highly selected study groups, and all required long-term bile salt therapy (with a high incidence of abdominal cramps and diarrhoea) to prevent recurrent stone formation.

Alternative treatments such as the 'gallbladder flush' (essentially consisting of giving purgative agents such as Epsom salts, olive oil and lemon juice) have been popularized by the internet. However, there is no evidence of efficacy, although they do result in the production of small pellet-like faeces that can be mistaken for stones by enthusiasts for the procedures!

Cholecystectomy

Patients with biliary pain should be offered cholecystectomy as definitive treatment for their disease. Currently, 99% of procedures are performed laparoscopically ('keyhole') and 70% as day-case surgery in the UK.

Acute cholecystitis

Patients with acute cholecystitis generally require admission for analgesia and intravenous fluid rehydration. Non-steroidal anti-inflammatory agents reduce inflammation and speed recovery, and broad-spectrum antibiotics, such as a second-generation cephalosporin, are recommended to prevent secondary bacterial infection. Patients should undergo emergency laparoscopic surgery, ideally within the first 72 hours of admission.

Bile duct stones

There are two main approaches to the removal of CBD stones: ERCP and surgical bile duct exploration.

Endoscopic retrograde pancreatography: this is the most common approach to the management of CBD stones. It involves insertion of a side-viewing endoscope (a duodenoscope) through the mouth into the duodenum. The papilla is cannulated with a fine cannula to enter the bile duct. The papilla can be cut using a sphincterotome, which employs diathermy to divide the sphincter of Oddi, and stones can be extracted with baskets or balloons (Figure 4). Larger stones can be crushed with a mechanical lithotripter. ERCP is performed with the patient under sedation and carries a risk of acute pancreatitis from manipulation of the papilla (approximately 5%), bleeding or perforation (approximately 1%), and death (0.1%).

Surgical bile duct exploration: bile duct exploration was originally performed via laparotomy but is increasingly performed laparoscopically. The trans-cystic approach is limited to stones small enough to be retrieved through the cystic duct (typically stones <5 mm). Larger stones can be managed by a direct

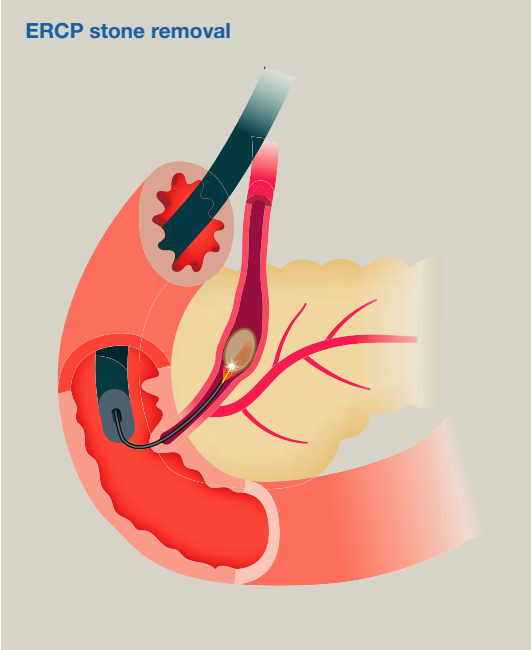

Figure 4

transductal approach through an incision in the CBD. Impacted stones can be removed by shattering under direct vision with contact lithotripsy.

Postoperative problems (chronic)

Postoperative pain resolution after cholecystectomy depends on case selection. Post-cholecystectomy pain is invariably the result of pre-cholecystectomy symptoms or other diagnoses, and there is no evidence that the procedure of laparoscopic cholecystectomy (LC) in itself results in the development of abdominal pain. Patients can return to a normal diet with no restrictions on fat or other specific food intake.

Around 5% of patients develop looser bowel habit or urgency of defaecation after LC, although this is often patients who already had some degree of symptoms (e.g. irritable bowel syndrome). It is thought to be caused by a more constant flow of bile entering a relatively empty bowel. It resolves within 3–6 months in half of those affected as a degree of adaptation occurs. Patients who continue to be troubled by diarrhoea may benefit from loperamide to control urgency and/or a bile-binding agent such as colestyramine. ◆

FURTHER READING

Davidoff AM, Pappas TN, Murray EA, et al. Mechanisms of major biliary injury during laparoscopic cholecystectomy. *Ann Surg* 1992; **215:** 196–202.

Kalloo AN, Kantsevoy SV. Gallstones and biliary disease. *Prim Care* 2001; **28:** 591–606.

Rhodes M, Sussman L, Cohen L, et al. Randomised trial of laparoscopic exploration of common bile duct versus postoperative endoscopic retrograde cholangiography for common bile duct stones. *Lancet* 1998; **351:** 159–61.

Reynolds W. The first laparoscopic cholecystectomy. *J Soc Laparoend Surg* 2001; **5:** 8–94.

Williams EJ, Beckingham I, El Sayad G, et al. Updated guidelines on the management of common bile duct stones (CBDS). *Gut* 2017; **66:** 765–82.

