Gallstones: Prevalence, Diagnosis and Treatment

Simon Bar-Meir MD

Department of Gastroenterology, Sheba Medical Center, Tel-Hashomer, and Sackler Faculty of Medicine, Tel Aviv University, Israel

Key words: gallstones, cholecystectomy, endoscopic retrograde cholangiopancreatography, percutaneous transhepatic cholangiography, magnetic resonance cholangiopancreatography, cholelithiasis, common bile duct

IMAJ 2001;3:111-113

Gallstone disease is the most common and costly of all digestive diseases in the United States, resulting in 700,000 cholecystectomies and as many as 1 million hospitalizations annually. In recent years, the development of laparoscopic cholecystectomy has significantly reduced hospital inpatient costs and recovery time, but this cost saving has been offset by an increase in the number of cholecystectomies [1].

The prevalence of gallstones varies between different ethnic populations. Specific ethnic groups have a higher prevalence, like the Pima Indians whose prevalence reaches 70% by the age of 25 years. Large ultrasound-based studies from Europe have characterized both the prevalence and incidence of gallstones. In the Multicenter Italian Study of Cholelithiasis (MICOL), which examined nearly 33,000 subjects aged 30–69 years, the overall prevalence of gallstone disease was 18.8% in women and 9.5% in men [2]. Similar results were noted in the Simione study. In addition, in the Simione study, ultrasounds were repeated on the same patients at 5 year intervals, and the 10 year cumulative incidence of new gallstones was found to be 4.6% [3].

Risk factors for cholelithiasis include age, female gender, parity, obesity, rapid weight loss, hypertriglyceridemia, genetics, various medications (such as estrogens, clofibrate and ceftriaxone), terminal ileal resection, and gallbladder hypomotility as seen in post-vagotomy and total parenteral nutrition.

Diagnosis

Imaging of the gallbladder and biliary tree has undergone major changes in the last decade, mainly due to advances in ultrasound, computed tomography and magnetic resonance imaging. These techniques are now capable of imaging the entire biliary tract non-invasively, with accuracy rates approaching those of invasive techniques such as endoscopic retrograde cholangiopancreatography and percutaneous transhepatic cholangiography.

Ultrasound remains the primary modality for imaging the biliary system and is particularly successful for examining the gallbladder. A gallstone appears as an echogenic structure within the gallbladder lumen that casts a distal acoustic shadow. Sonography is accurate in the diagnosis of gallstones in the gallbladder in up to 96% of patients. Sensitivity for sonographic detection of common bile duct stones is close to 75%. It is easier to demonstrate stones in a dilated CBD, but in about one-third of cases with duct stones no duct dilatation is seen due to the intermittent nature of stone obstruction. Intraoperative ultrasound was found to be an effective procedure for biliary exploration during laparoscopic cholecystectomy, and compares favorably with intraoperative cholangiography in terms of detecting bile duct stones.

The introduction of helical CT has improved the ability to image the biliary tract by allowing the rapid acquisition of a volume of data capable of imaging all portions of the ductal system. CT detects approximately 75% of gallstones; approximately 25% of gallstones are not detected as they are either isodense to bile or too small to be visualized adequately.

MRI of the biliary system has undergone a major change due to the recent introduction of non-invasive methods that provide projectional images of the biliary tree, simulating those obtained at ERCP. This technique has been termed magnetic resonance cholangiopancreatography. It uses the inherent tissue contrast between fluid-filled structures and the surrounding solid organ to generate images of fluid-containing structures only. No exogenous contrast is necessary and the technique is completely non-invasive. MRCP has become the primary diagnostic imaging modality, surpassing CT and ultrasound in stone detection. Recent experience with MRCP has demonstrated a sensitivity that approaches 98% [4].

Endoscopic ultrasound is a relatively new technique that is highly accurate for the diagnosis of gallstones. In addition, EUS may be valuable in detecting microlithiasis, a known cause of pancreatitis and abdominal pain of obscure origin. In one study, more than 90% of patients with preoperative EUS findings had resolution of biliary pain following cholecystectomy. EUS appears to be a more sensitive means of detecting choledocholithiasis (sensitivity of 96%) and may be comparable to ERCP without the risk of pancreatitis. In experienced centers, EUS may be the only pre-cholecystectomy procedure necessary in patients with a low to medium risk of choledocholithiasis, thus

CBD = common bile duct
ERCP = endoscopic retrograde cholangiopancreatography
MRCP = magnetic resonance cholangiopancreatography
EUS = endoscopic ultrasound

avoiding the risk of ERCP. However, in patients with CBD stones detected by other modalities, EUS is unnecessary and such patients are best managed by ERCP.

Treatment

The vast majority of patients with gallstones have no symptoms. In large Italian studies of gallstone patients, approximately 85% of screened volunteers had no biliary symptoms and the prevalence of silent stones was 6.5% for men and 10.5% for women [2]. The annual incidence of stone formation in southern Italy was found to be 9.7 per 1,000. While the presence of gallstones may be associated with billiary-type pain, there is a dispute whether an association exists with vague symptoms such as dyspepsia, bloating nausea and fat intolerance. Exercise may decrease the rate of symptoms related to gallstones, probably by either decreasing lithogenicity of bile or altering the motility of the gallbladder.

The natural history of gallstones was studied prospectively in two Italian studies [5,6]. In the Simione study, 22% of the 132 subjects found during a screening examination to have gallstones had biliary symptoms. During a 10 year follow-up of the remaining asymptomatic subjects 16% developed biliary symptoms. The development of symptoms leveled off after 5 years. Similar studies were also performed by GREPCO (Rome Group for Epidemiology and Prevalence of Cholelithiasis). Following 118 asymptomatic subjects with gallstones to determine the rate of biliary colic, complications, cholecystectomy, and death at 2 year intervals, they found a 2–3% annual incidence of biliary colic and a 3% complication rate at 10 years.

The progression of symptom development from asymptomatic to non-specific symptoms to biliary colic usually occurs in a stepwise progression prior to complications such as acute cholecystitis. It is rare for acute cholecystitis to develop without antecedent symptoms. The stepwise progression of symptoms allows physicians to prevent complications of gallstones by performing cholecystectomy in symptomatic patients. The role of prophylactic cholecystectomy in asymptomatic patients is therefore doubtful. Life expectancy of gallstone patients after various interventions at various ages did not increase when a prophylactic cholecystectomy was performed.

Biliary sludge is a reversible condition. Upon withdrawal of the noxious agent or condition, sludge dissolves or is discharged in most cases. However, a minority of patients develop gallstones that may become symptomatic. By far the most serious complication of biliary sludge is the development of biliary pancreatitis. Occult microlithiasis should be strongly suspected in cases of acute pancreatitis of unknown origin, especially when there are frequent relapses [7]. In such patients, therapy with ursodeoxycholic acid, laparoscopic cholecystectomy or endoscopic sphincterotomy should be considered.

Some patients present initially with a complication of their gallstones, such as acute cholecystitis, gallstone pancreatitis or obstructive jaundice. However, three-quarters of patients with gallstones present with attacks of pain, usually in the right upper quadrant or epigastrium, before a complication of gallstone disease occurs. Symptomatic patients should be advised to undergo cholecystectomy because of the high rate of recurrent billiard-type pain and development of complications. Patients who develop acute cholecystitis should undergo early rather than delayed cholecystectomy. High risk patients may be treated safely and effectively by percutaneous transhepatic drainage of the gallbladder.

Bile duct stones should be removed by endoscopic sphincterotomy with the help of a Dormia basket or balloon catheter. However, if there is a disproportion between the stone's size and the diameter of the bile ducts through which the stone must pass, techniques to crush the stone should be applied. Available techniques include mechanical, electrohydraulic, contact, laser and extracorporeal shock wave lithotripsy. Occasionally, topical application of solutions such as mono-octain and methyl tert-buthyl ether can be applied to dissolve gallstones. CBD stones are classified according to their site of formation. Primary bile duct stones arise *de novo* in the bile ducts, and secondary bile duct stones form in the gallbladder and subsequently migrate into the bile duct. In the western world, secondary bile duct stones predominate, 80–95% of patients with common duct stones having concomitant gallbladder stones. The composition of secondary bile duct stones reflects the composition of gallbladder stones, with about 80% being of cholesterol origin. Primary bile duct stones are composed primarily of calcium bilirubinate. The discovery of CBD stones, even when incidental, warrants active intervention to remove the stones. More than 50% of patients with retained bile duct stones will develop symptoms and 25% will develop resultant serious complications [8]. Recent studies, however, suggest a more indolent course of symptomatic CBD stones. Biliary colic is a misnomer because the pain is constant in nature. It is usually accompanied by nausea and vomiting, and typically lasts for 30 minutes to several hours. Food ingestion may precipitate an attack of pain, but the composition of a meal is not a proven factor. Stone impaction in the distal CBD may lead to jaundice, cholangitis, or gallstone pancreatitis. The serum bilirubin is usually elevated to less than 15 mg/dl and the alkaline phosphatase level may be normal or elevated to several times normal. ERCP and sphincterotomy are the treatment of choice, with a more than 90% success rate of stone retrieval. In difficult cases, where there is a therapeutic purpose, the success rate of sphincterotomy can be enhanced by the performance of precut papillotomy. Precut carries a modestly higher rate of complications and should be reserved for therapeutic procedures only. In 5% of situations where the stone extraction is incomplete, a nasobiliary tube or a stent should be inserted to maintain biliary drainage and prevent stone impaction in the distal CBD. Repeat ERCPs should be performed at a later time and are successful in two-thirds of patients. Endobiliary stent placement should not be considered as a long-term solution in patients with cholelithiasis because of the high rate of complications [9].

Early complications of endoscopic sphincterotomy occur in approximately 5% of patients and the procedure-related mortality ranges from 0.2 to 0.4%. Complications include pancreatitis (3%), hemorrhage (1–2%), cholangitis (1–2%) and retroduodenal perforation (0.3%). Sphincter of Oddi dysfunction increases the rate of complications. Early ERCP and sphincterotomy can be safely and effectively performed after stone detection on T-tube cholangiography. The endoscopic success rate is over 90%, with 7% morbidity and 0.6% mortality. The long-term complication rate ranges between 10 and 25% and includes recurrent CBD stones and biliary sphincter stenosis with cholangitis. Balloon dilatation of the sphincter of Oddi is an alternative to sphincterotomy in patients with a stone less than 1 cm in size. However, a recent study found both morbidity and mortality to be higher in patients who underwent sphincter dilatation for stone extraction [10].

Laparoscopic common bile duct exploration can be performed at the time of cholecystectomy, both through the cystic duct and through a supra-duodenal route. In a randomized control trial this procedure was as effective as ERCP and had similar morbidity. About 1% of patients who underwent cholecystectomy have sphincter of Oddi dysfunction [11]. The prevalence increases to above 10% in patients with post-cholecystectomy syndrome.

Percutaneous transhepatic techniques are preferred when endoscopic therapy fails and for intrahepatic biliary calculi such as seen in oriental cholangiohepatitis. When endoscopic failure is the result of inability to gain deep cannulation of the bile duct, a combined percutaneous-endoscopic "rendezvous" technique is often performed. The principal advantage of the intrahepatic approach to biliary intervention is the control that can be achieved for manipulation within the ductal system. The major disadvantage of the transhepatic approach is the morbidity associated with the capsular puncture and the transparenchymal tract.

Patients with severe gallstone pancreatitis should undergo urgent endoscopic sphincterotomy. If the pancreatitis is mild and moderate, supportive therapy alone is advised. In elderly patients with intact gallbladder who have recovered from gallstone pancreatits, endoscopic sphincterotomy should be considered. The rationale for endoscopic sphincterotomy in the absence of ductal stone is to eliminate the common channel, so that gallstones that migrate from the gallbladder can pass unimpeded through the bile duct into the duodenum without obstructing the pancreatic duct and causing pancreatitis. Studies [12] have substantiated the efficacy of the endoscopic approach in reducing the incidence of recurrent pancreatitis to less than 5% during a mean follow-up of 4 years.

The diagnosis and treatment of gallstone disease is shifting to less invasive procedures. Ultrasonography (transabdominal amd endoscopic) and MCRP rather than ERCP and percutaneous transhepatic cholangiography for diagnosis, and laparoscopy rather than open cholecystectomy contribute to the decrease in morbidity related to gallstones.

References

1. Steiner CA, Bass EB, Talamini MA, Pitt HA, Steinberg EP. Surgical rates and operative mortality for open and laparoscopic cholecystectomy in Maryland. *N Engl J Med* 1994;330:403–8.
2. Attili AF, Carulli N, Roda E. Barbara B, Capocaccia L, Menotti A, Okoliksanyi L, Rioci G, Capocaccia R, Festi D, Lalloni L, Mariotti S, Sama C, Scarfeto E. Epidemiology of gallstone disease in Italy; prevalence data of the multicenter Italian study on cholelithiasis (MICOL). *Am J Epidemiol* 1995;141:158–65.
3. Barbara L, Sama C, Morselli-Labate AM. A ten year incidence of gallstone disease: the Si rmione study. *J Hepatol* 1993;18:43–8.
4. Soto JA, Barish MA, Yucel EK, Seigenberg D, Ferruci JT, Chuttani R. Magnetic resonance cholangigraphy: comparison with endoscopic retrograde cholangiopancreatography. *Gastroenterology* 1996;110:589–97.
5. Barbara L, Sama C, Morselli Labate AM. A population study on the prevalence of gallstone disease: the Sirmione study. *Hepatology* 1987;7:913–17.
6. Attili AF, De Santis A, Repice AM, Maselli S, the GREPCO Group. The natural history of gallstones: the GREPCO experience. *Hepatology* 1995;21:656–60.
7. Paricio PP, Olmo DG, Franco EP, Gonzalez AP, Gonzalez LC, Lopez JB. Gallbladder cholesterolosis: an aetiological factor in acute pancreatitis of uncertain origin. *Br J Surg* 1990;77:735–6.
8. Johnson A, Hosking S. Appraisal of the management of bile duct stones. *Br J Surg* 1987;74:555–60.
9. Bergman JJ, Rauws EAJ, Tijssen JGP, Tytgat GN, Huibregtse K. Biliary endoprosthesis in elderly patients with endoscopically irretrievable common bile duct stones: report on 117 patients. *Gastrointest Endosc* 1995;42:195–201.
10. DiSario JA, Freeman ML, Bjorkman DJ, MacMathuna P, Petersen B, Sherman S, Lehman G, Hixson L, Jaffe P, Al-Kawas F, Moore J, Khandelwal M. Endoscopic balloon dilatation compared to sphincterotomy (EDES) for extraction of bile duct stones: preliminary results. *Gastrointest Endosc* 1997;45:A129.
11. Bar Meir S, Halpern Z, Bardan E, Gilat T. Frequency of papillany dysfunction among cholecystectomized patients. *Hepatology* 1984;4:328–30.
12. Welbourn CRB, Beckly DE, Eyre-Brook IA. Endoscopic sphincterotomy without cholecystectomy for gallstone pancreatitis. *Gut* 1995;37:119–20.

Correspondence: Dr. S. Bar-Meir, Dept. of Gastroenterology, Sheba Medical Center, Tel-Hashomer 52621, Israel. Phone: (972-3) 530-2679, Fax: (972-3) 530-2913, email: barmeir@netvision.net.il

To hurt innocent people whom I knew many years ago in order to save myself is, to me, inhuman and indecent and dishonorable. I cannot and will not cut my conscience to fit this year's fashions

Lillian Hellman, American playwright and writer (1905–84), in a letter to the Chairman of the House Committee during the wave of anticommunist hysteria, wild accusations and blacklists initiated by Republican politician Joe McCarthy.