

Choledocholithiasis Without Cholelithiasis: Should the Gallbladder Stay or Should It Go?

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Cholelithiasis (gallstones) is common, with an estimated prevalence of ~12 % of adult population in the USA. The prevalence, increasing with age, approaches 33 % in elderly women [1]. Approximately 15 % of patients with cholelithiasis have concurrent choledocholithiasis (bile duct stones), and conversely, 95 % of patients with choledocholithiasis have cholelithiasis [2, 3]. Although the natural history of asymptomatic common bile duct (CBD) stones is not well defined, they are thought to be less benign than asymptomatic gallbladder gallstones. Although CBD stones may pass uneventfully through the ampulla of Vater into the duodenum, their passage can induce acute pancreatitis and stone impaction at the distal bile duct, causing biliary colic and cholangitis. Because adverse events may be serious and life-threatening, it is generally recommended that CBD stones be removed.

Over the last several decades, endoscopic retrograde cholangiopancreatography (ERCP) with sphincterotomy has emerged as the procedure of choice to remove CBD stones. Sphincterotomy may be performed with or without balloon dilation. After removal of CBD stones, cholecystectomy is typically performed, unless the patient has significant comorbid conditions. The rationale for this approach is that (1) cholesterol CBD stones, which represent >75 % of bile duct stones in the USA and Europe, originate in the gallbladder and (2) gallbladder function is impaired in patients with cholesterol gallstones and persists

after the removal of stones [4]. Thus, unless expected lifespan is short, cholelithiasis and subsequent choledocholithiasis are predicted to recur. Indeed, a meta-analysis of five randomized controlled trials comparing cholecystectomy after endoscopic sphincterotomy to a wait-and-see approach reported a significantly higher risk of biliary complications and death in the latter group in the five studies [5].

Unlike cholesterol stones that originate in the gallbladder, brown pigment stones, common in Asia (e.g., Korea, Japan, China, Vietnam, Taiwan, and Southeast Asia), may arise de novo within the bile duct, including the intrahepatic ducts. These stones, composed of calcium bilirubinate, may account for up to 30 % of ductal stones in these regions and are associated with recurrent cholangitis, biliary cirrhosis, and cholangiocarcinoma [6]. The precise etiology is unknown, but infection of the bile ducts by parasites such as liver flukes (e.g., *Clonorchis sinensis*) and parasitic worms is thought to be contributory. Bile stasis, induced by the parasites and their ova, is postulated to lead to bacterial colonization. Bacterial enzymes, in turn, hydrolyze bilirubin conjugates and phospholipids in bile, releasing free bilirubin and fatty acids that form insoluble precipitates with biliary calcium. The resulting concretions are termed brown pigment stones [7]. The necessity of cholecystectomy after ERCP extraction of isolated brown bile duct stones is less clear. In fact, none of the individual studies in the meta-analysis described earlier specifically reports the outcomes of patients with isolated bile duct stones in the absence of cholelithiasis [5].

In the current issue of *Digestive Diseases and Sciences*, Kim et al. [8] retrospectively describe the natural history of 453 South Korean patients with bile duct stones who underwent ERCP with sphincterotomy and/or balloon dilation for stone removal between 1998 and 2000, but did

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not undergo cholecystectomy. Concurrent cholelithiasis was present in 256 (57 %) patients and absent in 197 (43 %). As is typical for this population, the majority of stones in both groups were brown pigment; only 5–11 % of patients had cholesterol stones. Patients with cholelithiasis who did not undergo cholecystectomy had either declined surgery or had comorbidities that portended a prohibitive operative risk. The investigators followed these patients for a mean duration of 785 days. Gallbladder complications (biliary colic, acute cholecystitis, and gallbladder cancer) occurred in 29 (11.3 %) patients in the calculous gallbladder group compared to 5 (2.5 %) patients in the acalculous gallbladder group ($p = 0.001$). The incidence of recurrent bile duct stones, with or without cholangitis, did not differ significantly in patients with or without gallbladder stones (11.3 and 10.2 %, respectively). No gallbladder- or bile duct stone-related mortality occurred in any of the patients. The authors conclude that prophylactic cholecystectomy may not be necessary after clearing pigment stones from the bile duct if the patient does not have concurrent cholelithiasis.

Should physicians recommend cholecystectomy after endoscopic removal of isolated CBD stones or adopt a wait-and-see approach? The results of the study are certainly consistent with that of several other non-randomized retrospective publications from Asia [9]. To place in perspective the 2.5 % risk of gallbladder-related complications reported in the present study, the overall perioperative morbidity for elective cholecystectomy is ~10 % [3]. Despite the retrospective nature of these studies, it does appear that a wait-and-see approach is reasonable in patients with isolated CBD pigment stones.

Nevertheless, Can we extrapolate these conclusions to a Western population? Cholesterol stones account for the vast majority of stones in Western countries (either pure cholesterol or mixed stones that contain at least 50 % cholesterol by weight). In this population, stones originate almost exclusively in the gallbladder; choledocholithiasis results when gallbladder stones pass through the cystic duct. Consequently, isolated bile duct cholesterol stones may indeed be a misnomer as patients may have unrecognized gallbladder sludge or microlithiasis that by itself can induce cholecystitis, cholangitis, and pancreatitis as well as develop into larger stones that may pass into the CBD. Although ursodeoxycholic acid (UDCA) treatment can reduce the amount of biliary sludge and its

complications [10], once it is discontinued, sludge and stones return in >50 % of patients over 5–12 years [11].

Pending a well-designed prospective trial, we recommend, at least in Western populations, elective cholecystectomy in patients with an acalculous gallbladder following removal of CBD stones. In high-risk patients and in older adults, individualized management (i.e., a wait-and-see approach) is reasonable. In those with sludge or small stones, UDCA therapy may be considered.

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