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## Asymptomatic bile duct stones: The devil is in the details

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### Abstract

Common bile duct (CBD) stones are a common biliary tract disease. For asymptomatic CBD stones, stone removal by endoscopic retrograde cholangiopancreatography (ERCP) is recommended in available guidelines. Because asymptomatic CBD stones is a benign disease with no noticeable symptoms, the risk *vs* benefit strategy should be thoroughly considered before performing ERCP in these patients. Clinical care review, technical aspects of the procedure, and patient preferences should also be considered.

**Key Words:** Asymptomatic; Common bile duct stones; Endoscopic retrograde cholangiopancreatography; Outcome; Guidelines

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**Core Tip:** The ongoing debate surrounding the management of asymptomatic common bile duct stones presents a critical decision-making challenge for gastroenterologists. While conservative approaches emphasize watchful waiting and monitoring, endoscopic interventions offer potential benefits in terms of preventing future complications. However, both approaches carry a risk of complications. This review delves into the current evidence, weighing the pros and cons of both conservative and endoscopic strategies, aiming to guide practitioners in making informed decisions tailored to individual patient profiles.

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## INTRODUCTION

Bile duct stones (choledocholithiasis) most frequently result from the migration of gallstones from the gallbladder into the bile duct. Gallstones are the consequence of cholesterol supersaturation in bile, inadequate bile salt levels or function, and diminished contractility of the biliary epithelium due to the multifactorial effects of diet, hormones, and genetic predisposition[1]. Choledocholithiasis results in biliary obstruction, cholangitis, and pancreatitis in a significant number of patients. The primary treatment, endoscopic retrograde cholangiopancreatography (ERCP), is minimally invasive but associated with adverse events in 6% to 15% of patients. Removal of asymptomatic CBD stones is a common practice as they can cause obstructive jaundice, acute cholangitis, and biliary pancreatitis. However, other issues and aspects should be considered[2].

## NATURAL HISTORY OF ASYMPTOMATIC BILE DUCT STONES

CBD stones usually cause symptoms such as abdominal pain, fever, or jaundice and complications including cholangitis and pancreatitis, warranting evaluation and treatment. In some cases, CBD stones are found incidentally during routine health screening or evaluations for non-relevant disease without noticeable symptoms. The prevalence of CBD stones detected incidentally in patients who underwent cholecystectomy is reportedly as high as 12% [3]. Due to the advances and availability of abdominal imaging modalities, asymptomatic bile duct stones are increasingly identified in clinical practice[4].

Primary ductal stones form *de novo* within the intrahepatic and extrahepatic ducts. They are most prevalent in Asian populations and give rise to the distinct clinical entity of recurrent pyogenic cholangitis. Secondary CBD stones originate in the gall bladder and migrate into the bile duct *via* the cystic duct. They account for the majority of CBDs that occur in European patients[5].

## APPROACH FOR ASYMPTOMATIC BILE DUCT STONES

Removal of bile duct stones has been recommended by many guidelines; the European Society of Gastrointestinal Endoscopy (ESGE), British Society of Gastroenterology (BSG), American Society for Gastrointestinal Endoscopy (ASGE), and Japanese Society of Gastroenterology. The ESGE recommends offering stone extraction to patients with symptomatic and asymptomatic bile duct stones who are fit enough to tolerate the procedure[6]. The GallRiks study suggested that when CBD stones are detected they should be removed to reduce the risk of complications over time. Of the 3969 patients with CBD stones, during follow-up ranging from 0 to 4 years, 25.3% of patients with CBD stones *in situ* developed complications (pancreatitis, cholangitis, or obstruction of the bile duct) *vs* 12.7% of patients who had undergone CBD stones removal [odds ratio (OR): 0.44, 95% confidence interval (CI): 0.35–0.55]. The likelihood of an unfavorable outcome increased with the size of the CBDs, but the incidence of complications even for CBDs less than 4 mm was 5.9% *vs* 8.9% for larger CBD stones (OR: 0.52, 95% CI: 0.34–0.79)[7].

Some studies have suggested that small unsuspected stones can pass spontaneously without the need for intervention [8]. The spontaneous passage of small CBD stones without serious complications was demonstrated by Collins *et al*[9] in 24 of 46 patients with a filling defect observed on intraoperative cholangiography in whom a cystic duct catheter was left in place after laparoscopic cholecystectomy. The asymptomatic migration of small (< 8 mm) stones has also been noted in the interval between diagnosis at endoscopic ultrasonography (EUS) and ERCP[10].

## ENDOSCOPIC TREATMENT OF ASYMPTOMATIC BILE DUCT STONES

### Outcomes of endoscopic treatment

Many recent published reports showed that the risk of ERCP-related complications has been identified to be higher with asymptomatic CBD stones than symptomatic patients.

A multicenter retrospective study included a cohort of patients with CBD stones and compared 164 asymptomatic versus 949 symptomatic patients. The study revealed that the rate of ERCP-related complications was higher in asymptomatic patients than patients with symptomatic disease (19.5% *vs* 6.2%). The study highlighted that post-ERCP pancreatitis (PEP) was significantly higher in asymptomatic individuals than symptomatic patients (14.6% *vs* 3.0%)[11].

Similar results have been obtained by a prospective study that compared 53 asymptomatic patients versus 274 symptomatic patients. Both the rate of ERCP-related complications and rates of PEP were higher in asymptomatic patients than symptomatic group (26.4% *vs* 11.7% and 20.8% *vs* 6.9%, respectively)[12].

A number of explanations can attribute the higher incidence of PEP in asymptomatic patients. Asymptomatic patients had normal serum bilirubin, nondilated CBD, and difficult cannulation, which are considered as patient- and procedure-related risk factors of PEP. Additionally, an asymptomatic CBD stone itself may be an important clinical risk factor for PEP[11].

### Technical tips for the endoscopic treatment of asymptomatic CBD stones

The goal of endoscopic treatment of asymptomatic CBD stones beyond stone extraction is to try to reduce ERCP-related complications.

Precut sphincterotomy, biliary sphincter dilation, and involvement of trainee endoscopists were found to be significant risk factors for PEP in asymptomatic CBD stones in a previous study[13]. Another study compared safety of ERCP performed by experienced endoscopists for asymptomatic CBD stones versus symptomatic patients and reported that safety was comparable in both groups[14].

Asymptomatic patients with risk factors for PEP such as precut sphincterotomy and biliary sphincter dilatation should undergo prophylactic procedures such as placement of prophylactic pancreatic stent[13].

Revised Tokyo guidelines for the management of acute cholangitis and cholecystitis, accepted single-stage CBD stones removal following endoscopic sphincterotomy at the first ERCP session in patients with mild-to-moderate cholangitis, making patients with asymptomatic CBD stones candidates for single-stage CBD stones removal[14].

In a retrospective study, single-stage CBD stones removal with challenging biliary cannulation requiring > 15 min was found to be a significant risk factor for PEP. In those asymptomatic patients requiring > 15 min for biliary cannulation, it may be better to remove the CBD stones at the 2<sup>nd</sup> ERCP session to reduce the risk of PEP[11].

### Endoscopic treatment vs conservative management outcomes

Some factors may support the approach of stone extraction in asymptomatic CBD stones; the occurrence of unfavorable outcomes is not different in patients classified as asymptomatic or symptomatic[4]. The lifetime risk of untreated CBD is unknown and may be higher than that reported, and severe complications such as cholangitis, pancreatitis, or obstructive jaundice can occur without being preceded by any warning symptoms[15]. A conservative approach may only be considered in patients in whom the risks of surgical or endoscopic CBD stone extraction outweigh the risks of leaving stones *in situ*, especially in elderly patients, patients who experience difficulties performing activities of daily living, and those with serious underlying diseases. When offering stone extraction to asymptomatic patients with CBD stones, patients should be made aware of the limited evidence regarding this recommendation and the risks associated with ERCP, which may be elevated in asymptomatic patients[16].

Spontaneous passage of CBD stones has been observed in many cases. A retrospective cohort study reported that CBD stone < 5 mm in diameter, single CBD stone and symptomatic improvement before ERCP procedure are considered key predictors of spontaneous CBD stone passage in cholangitis[17]. In such clinical scenarios, a conservative strategy should be more widely considered.

### Other considerations

EUS is replacing diagnostic ERCP to avoid subjecting patients to unnecessary invasive procedures. Among asymptomatic individuals, biliary dilation may not be clinically significant; however, EUS is often relied on for the exclusion of coincidentally benign, malignant pathology or anatomical variation that might require further intervention or may add technical difficulty and risks to the ERCP procedure. Simultaneous EUS and ERCP can also be used to diagnose and treat CBD stones if needed[18].

CBD stones encountered in patients with intestinal reconstruction is an added challenge to the underlying anatomical variation after intestinal reconstruction and should be managed in referral centers. The presence of anatomical variations hinders the success of intubation and cannulation by using a conventional endoscope. Hence, the use of a newly designed enteroscope with dedicated accessories is efficient[19].

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## CONCLUSION

Patients with CBD stones should be offered stone extraction, assuming that they are fit enough to undergo treatment. It should be noted that there are no controlled studies examining the natural history of CBD stones that are found incidentally in asymptomatic patients being investigated for other medical problems. Patients should be made aware that advice to undergo stone extraction in this setting is based on evidence from symptomatic patients and expert opinion. A wait-and-see strategy is an option, considering the incidence of procedure-related complications of endoscopic intervention for asymptomatic patients. The benefits and disadvantages of endoscopic treatment should be carefully evaluated. The decision for considering either approach should be case-by-case and may need discussion in a multidisciplinary team setting. Patient engagement in decision making and face-to-face assessment are also recommended.

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## FOOTNOTES

**Author contributions:** Talkhan MG conducted the extensive literature review and research on management strategies for asymptomatic bile duct stones, and provided critical insights into the clinical implications and practical considerations of the discussed management plans; Elsayed MOK conceptualized the editorial, contributed to the overall design and structure, and contributed to the manuscript by offering expert opinions and perspectives based upon experience in the field; Both authors contributed to the writing, review, and editing of the editorial and approved the final version for submission.

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## REFERENCES

- 1 **Paumgartner G**, Sauerbruch T. Gallstones: pathogenesis. *Lancet* 1991; **338**: 1117-1121 [PMID: 1682550 DOI: 10.1016/0140-6736(91)91972-w]
- 2 **Figueiredo JC**, Haiman C, Porcel J, Buxbaum J, Stram D, Tambe N, Cozen W, Wilkens L, Le Marchand L, Setiawan VW. Sex and ethnic/racial-specific risk factors for gallbladder disease. *BMC Gastroenterol* 2017; **17**: 153 [PMID: 29221432 DOI: 10.1186/s12876-017-0678-6]
- 3 **Murison MS**, Gartell PC, McGinn FP. Does selective peroperative cholangiography result in missed common bile duct stones? *J R Coll Surg Edinb* 1993; **38**: 220-224 [PMID: 7693932]
- 4 **Kondo S**, Isayama H, Akahane M, Toda N, Sasahira N, Nakai Y, Yamamoto N, Hirano K, Komatsu Y, Tada M, Yoshida H, Kawabe T, Ohtomo K, Omata M. Detection of common bile duct stones: comparison between endoscopic ultrasonography, magnetic resonance cholangiography, and helical-computed-tomographic cholangiography. *Eur J Radiol* 2005; **54**: 271-275 [PMID: 15837409 DOI: 10.1016/j.ejrad.2004.07.007]
- 5 **Williams EJ**, Green J, Beckingham I, Parks R, Martin D, Lombard M; British Society of Gastroenterology. Guidelines on the management of common bile duct stones (CBDs). *Gut* 2008; **57**: 1004-1021 [PMID: 18321943 DOI: 10.1136/gut.2007.121657]
- 6 **Manes G**, Paspatis G, Aabakken L, Anderloni A, Arvanitakis M, Ah-Soune P, Barthet M, Domagk D, Dumonceau JM, Gigot JF, Hritz I, Karamanolis G, Laghi A, Mariani A, Paraskeva K, Pohl J, Ponchon T, Swahn F, Ter Steege RWF, Tringali A, Vezakis A, Williams EJ, van Hooft JE. Endoscopic management of common bile duct stones: European Society of Gastrointestinal Endoscopy (ESGE) guideline. *Endoscopy* 2019; **51**: 472-491 [PMID: 30943551 DOI: 10.1055/a-0862-0346]
- 7 **Möller M**, Gustafsson U, Rasmussen F, Persson G, Thorell A. Natural course vs interventions to clear common bile duct stones: data from the Swedish Registry for Gallstone Surgery and Endoscopic Retrograde Cholangiopancreatography (GallRiks). *JAMA Surg* 2014; **149**: 1008-1013 [PMID: 25133326 DOI: 10.1001/jamasurg.2014.249]
- 8 **Khan OA**, Balaji S, Branagan G, Bennett DH, Davies N. Randomized clinical trial of routine on-table cholangiography during laparoscopic cholecystectomy. *Br J Surg* 2011; **98**: 362-367 [PMID: 21254008 DOI: 10.1002/bjs.7356]
- 9 **Collins C**, Maguire D, Ireland A, Fitzgerald E, O'Sullivan GC. A prospective study of common bile duct calculi in patients undergoing laparoscopic cholecystectomy: natural history of choledocholithiasis revisited. *Ann Surg* 2004; **239**: 28-33 [PMID: 14685097 DOI: 10.1097/01.sla.0000103069.00170.9c]
- 10 **Frossard JL**, Hadengue A, Amouyal G, Choury A, Marty O, Giostra E, Sivignon F, Sosa L, Amouyal P. Choledocholithiasis: a prospective study of spontaneous common bile duct stone migration. *Gastrointest Endosc* 2000; **51**: 175-179 [PMID: 10650260 DOI: 10.1016/s0016-5107(00)70414-7]
- 11 **Saito H**, Koga T, Sakaguchi M, Kadono Y, Kamikawa K, Urata A, Imamura H, Tada S, Kakuma T, Matsushita I. Post-endoscopic retrograde cholangiopancreatography pancreatitis in patients with asymptomatic common bile duct stones. *J Gastroenterol Hepatol* 2019; **34**: 1153-1159 [PMID: 30650203 DOI: 10.1111/jgh.14604]
- 12 **Xu XD**, Qian JQ, Dai JJ, Sun ZX. Endoscopic treatment for choledocholithiasis in asymptomatic patients. *J Gastroenterol Hepatol* 2020; **35**: 165-169 [PMID: 31334888 DOI: 10.1111/jgh.14790]
- 13 **Saito H**, Kakuma T, Matsushita I. Risk factors for the development of post-endoscopic retrograde cholangiopancreatography pancreatitis in patients with asymptomatic common bile duct stones. *World J Gastrointest Endosc* 2019; **11**: 515-522 [PMID: 31798772 DOI: 10.4253/wjge.v11.i10.515]
- 14 **Miura F**, Okamoto K, Takada T, Strasberg SM, Asbun HJ, Pitt HA, Gomi H, Solomkin JS, Schlossberg D, Han HS, Kim MH, Hwang TL, Chen MF, Huang WS, Kiriya S, Itoi T, Garden OJ, Liau KH, Horiguchi A, Liu KH, Su CH, Gouma DJ, Belli G, Dervenis C, Jagannath P, Chan ACW, Lau WY, Endo I, Suzuki K, Yoon YS, de Santibañes E, Giménez ME, Jonas E, Singh H, Honda G, Asai K, Mori Y, Wada K, Higuchi R, Watanabe M, Rikiyama T, Sata N, Kano N, Umezawa A, Mukai S, Tokumura H, Hata J, Kozaka K, Iwashita Y, Hibi T, Yokoe M, Kimura T, Kitano S, Inomata M, Hirata K, Sumiyama Y, Inui K, Yamamoto M. Tokyo Guidelines 2018: initial management of acute biliary infection and flowchart for acute cholangitis. *J Hepatobiliary Pancreat Sci* 2018; **25**: 31-40 [PMID: 28941329 DOI: 10.1002/jhbp.509]
- 15 **Cox MR**, Budge JP, Eslick GD. Timing and nature of presentation of unsuspected retained common bile duct stones after laparoscopic cholecystectomy: a retrospective study. *Surg Endosc* 2015; **29**: 2033-2038 [PMID: 25398193 DOI: 10.1007/s00464-014-3907-x]
- 16 **Kim SB**, Kim KH, Kim TN. Comparison of Outcomes and Complications of Endoscopic Common Bile Duct Stone Removal Between Asymptomatic and Symptomatic Patients. *Dig Dis Sci* 2016; **61**: 1172-1177 [PMID: 26589817 DOI: 10.1007/s10620-015-3965-5]
- 17 **Sanguanlois S**, Viriyaraj V, Yodying H, Rookkachart T, Sathornviriyapong S, Boonsinsukh T. The influence of stone size on spontaneous passage of common bile duct stones in patients with acute cholangitis: A retrospective cohort study. *Ann Med Surg (Lond)* 2020; **60**: 72-75 [PMID: 33133588 DOI: 10.1016/j.amsu.2020.10.040]
- 18 **Rocca R**, De Angelis C, Castellino F, Masoero G, Daperno M, Sostegni R, Rigazio C, Crocellà L, Lavagna A, Ercole E, Pera A. EUS diagnosis and simultaneous endoscopic retrograde cholangiography treatment of common bile duct stones by using an oblique-viewing echoendoscope. *Gastrointest Endosc* 2006; **63**: 479-484 [PMID: 16500400 DOI: 10.1016/j.gie.2005.11.042]

- 19 **Park ET.** Endoscopic Retrograde Cholangiopancreatography in Bilioenteric Anastomosis. *Clin Endosc* 2016; **49**: 510-514 [PMID: [27838918](#) DOI: [10.5946/ce.2016.138](#)]





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