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**Role and timing of endoscopy in acute** **biliary pancreatitis**

Anderloni A *et al*. Endoscopy used in ABP

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**Abstract**

The role and timing of endoscopy in the setting of acute biliary pancreatitis (ABP) is still being debated. Despite numerous randomized trials have been published, there is an obvious lack of consensus on the indications and timing of endoscopic retrograde cholangiopancreatography (ERCP) in ABP in meta-analyses and nationwide guidelines. The present editorial has been written to clarify the role of endoscopy in ABP. In clinical practice the decision to perform an ERCP is often based on biochemical and radiological criteria despite they already have been shown to be unreliable predictors of common bile duct stone presence. Endoscopic ultrasonography (EUS) is not currently a worldwide standard diagnostic procedure early in the course of acute biliary pancreatitis, but it has been shown to be accurate, safe and cost effective in diagnosing biliary obstructions compared with magnetic resonance cholangiopancreatography and ERCP and therefore in preventing unnecessary ERCP and its related complications. Early EUS in ABP allows, if appropriate, immediate endoscopic treatment and significant spare of unnecessary operative procedures thus reducing possible related complications.

**Key words:** Acute biliary pancreatitis; Choledocolithiasis; Common bile duct stone; Endoscopic retrograde cholangiography; Endoscopic ultrasonography; Endoscopic ultrasonography

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**Core tip:** Although several reports have been published on role and timing of endoscopy in the treatment of acute biliary pancreatitis (ABP), there are still some controversial in this subject. In clinical practice the decision to perform an endoscopic retrograde cholangiopancreatography is often based on biochemical and radiological criteria despite they already have been shown to be unreliable predictors of common bile duct (CBD) stone presence. Both magnetic resonance cholangiopancreatography and endoscopic ultrasonography (EUS) are now indicated as the best noninvasive imaging methods for CBD stone detection. Early EUS in ABP allows, if appropriate, immediate endoscopic treatment and significant spare of unnecessary operative procedures thus reducing possible related complications.

Anderloni A, Repici A. Role and timing of endoscopy in acute biliary pancreatitis. *World J Gastroenterol* 2015; In press

The role and timing of endoscopy in the setting of acute biliary pancreatitis (ABP) is still being debated. A recent systematic review by van Geenen *et al*[1] clearly demonstrated that, despite numerous randomized trials, there is an obvious lack of consensus on the indications and timing of endoscopic retrograde cholangiopancreatography (ERCP) in ABP in meta-analyses and nationwide guidelines. Although the indication of early (within 24-48 h) ERCP with papillosphincterotomy for patients with ABP and related cholangitis is well established[2,3], its role in cases of either mild or severe ABP, without signs of cholangitis, remains controversial.

Biliary pancreatitis results from the migration of a gallstone to the common bile duct (CBD) with impaction or temporary obstruction of the major duodenal papilla[2]. Most ABP attacks are not severe, are self-limiting, and improve with conservative management[4]. Spontaneous passage of CBD stones in the duodenum has been described in up to 50% of cases of ABP[5,6]. However, conservative management of these patients is associated with a biliary complication rate of up to 20%. In such cases, ERCP is delayed and must be performed under possibly more difficult conditions, thus increasing the failure rate[7,8]. Moreover, without definitive treatment, the risk of a recurrent attack within the next several months is about 30–50%[9,10]. Even after a mild attack, cholecystectomy and/or biliary sphincterotomy should be considered within weeks[11]. In a large retrospective study, Nguyen *et al*[12] demonstrated that hospital readmission rates for ABP within 12 months were significantly reduced with cholecystectomy (14.0% *vs* 5.6%) or ERCP (13.1% *vs* 5.1%).

In clinical practice, the decision to perform early ERCP is often based on biochemical and radiological criteria, such as the presence of cholestatic liver biochemistry and a dilated CBD. Nevertheless, studies have shown that commonly used biochemical and radiological predictors of the presence of CBD stones in patients with ABP are unreliable[13]. Even with the application of various clinical predictors, only 37%–42% of patients undergoing ERCP were found to have CBD stones[14,15].

The rate of complications after therapeutic ERCP ranges from 7% to 10% and the mortality rate from 0.2% to 2.2%[16,17]. Therefore, accurate prediction of CBD stones is warranted to select patients for early therapeutic ERCP. Other noninvasive (or minimally invasive) imaging techniques such as endoscopic ultrasonography (EUS) and magnetic resonance cholangiopancreatography (MRCP) have been used to select patients for therapeutic ERCP to minimize the risk of complications associated with unnecessary diagnostic ERCPs. Both EUS and MRCP have been conﬁrmed in meta-analyses to be highly accurate for the diagnosis of CBD stones[18,19], with similar sensibility, specificity, accuracy, negative predictive value, and positive predictive value for detection of CBD stone[20].

In case of ABP without signs of cholangitis, the American guidelines[21] suggest performing EUS or MRCP prior to ERCP depending on the local expertise and facilities. Although MRCP also provides excellent imaging of the biliary tree, EUS is more accurate in the detection of small stones (< 5 mm), which are responsible for at least half of all cases of acute pancreatitis, and is better for visualizing microlithiasis of the gallbladder[21]. Indeed, despite the fact that most stones pass spontaneously, establishing a biliary etiology is extremely important because there is a high risk of recurrent pancreatitis (33%–60%) if the gallstone disease is not treated[22–24].

The relative sensitivity of MRCP and EUS for the detection of CBD stones use as a reference standard the extraction of CBD stones after endoscopic sphincterotomy during ERCP[25]. However, it is well known that small stones can be missed even during therapeutic ERCP. Therefore, EUS has recently been proposed as the new gold standard in the diagnosis of choledocholithiasis[26].

In 2001, Scheiman *et al*[27] prospectively compared the clinical efficacies of EUS and MRCP when performed within 24 h before ERCP in patients with biliary disease. They reported that although MRCP had the lowest procedural reimbursement, the initial EUS strategy had the greatest cost utility by avoiding unnecessary ERCP examinations. Thus, the selection of endoscopic treatment based on EUS may eventually impact the treatment of ABP and provide greater safety for the patients, as well as more rational use of healthcare resources[28]. A preliminary EUS may help in decision-making: if a stone is present, ERCP with extraction can be performed in the same endoscopic session, whereas if no stone is found, the patient can be spared the added risk. This stepwise strategy has been shown to help avoid unnecessary ERCP in most patients[29].

Certainly, either EUS or MRCP can be chosen based on local availability[30]. Postponing treatment for symptomatic CBD stones exposes the patient to biliary complication, especially cholangitis[31]. Moreover, in a 2008 editorial on gastrointestinal endoscopy, Savides noted that even if MRCP reveals a CBD stone, it is still worth considering an EUS immediately before the ERCP because approximately 21% of CBD stones (especially those < 8 mm) can pass spontaneously, which could occur in the interval between MRCP and ERCP[5,32]. In many centers and in real-life practice, timing and availability of MRCP precludes its acceptability as a method for determining the need for prompt ERCP, whereas EUS is more readily accessible.

EUS is not currently a worldwide standard diagnostic procedure early in the course of ABP, but because of its accuracy, safety, and cost effectiveness in diagnosing biliary obstructions compared with MRCP and ERCP, we think it should be considered as the first choice in approaching ABP. EUS is also a preferable diagnostic choice because it can be performed at the bed of the patient, which is especially relevant for patients in an ICU. An early (within 24-48 h) EUS can easily and quickly categorize those patients who do not require subsequent therapeutic ERCP, thus allowing even an early discharge in select cases, which is important in terms of cost effectiveness.

EUS and MRCP are now considered alternative noninvasive methods for evaluating biliary obstruction, and guidelines suggest performing one or the other prior to therapeutic ERCP depending on local availability. However, we think it is important to have a more rational use of healthcare resources while trying to follow the best clinical practice, rather than mainly adapting our practice to the resources available locally. Ideally, we should aim to have an integrated gastroenterology unit that can manage CBD stones by a combined, simultaneous two-step approach, and gastroenterologists responsible for ERCP should be trained in EUS and *vice versa*[33].

**REFERENCES**

1 **van Geenen EJ**, van Santvoort HC, Besselink MG, van der Peet DL, van Erpecum KJ, Fockens P, Mulder CJ, Bruno MJ. Lack of consensus on the role of endoscopic retrograde cholangiography in acute biliary pancreatitis in published meta-analyses and guidelines: a systematic review. *Pancreas* 2013; **42**: 774-780 [PMID: 23774699 DOI: 10.1097/MPA.0b013e318287d208]

2 **Forsmark CE**, Baillie J. AGA Institute technical review on acute pancreatitis. *Gastroenterology* 2007; **132**: 2022-2044 [PMID: 17484894 DOI: 10.1053/j.gastro.2007.03.065]

3 **van Santvoort HC**, Besselink MG, de Vries AC, Boermeester MA, Fischer K, Bollen TL, Cirkel GA, Schaapherder AF, Nieuwenhuijs VB, van Goor H, Dejong CH, van Eijck CH, Witteman BJ, Weusten BL, van Laarhoven CJ, Wahab PJ, Tan AC, Schwartz MP, van der Harst E, Cuesta MA, Siersema PD, Gooszen HG, van Erpecum KJ. Early endoscopic retrograde cholangiopancreatography in predicted severe acute biliary pancreatitis: a prospective multicenter study. *Ann Surg* 2009; **250**: 68-75 [PMID: 19561460 DOI: 10.1097/SLA.0b013e3181a77bb4]

4 **Frey CF**, Zhou H, Harvey DJ, White RH. The incidence and case-fatality rates of acute biliary, alcoholic, and idiopathic pancreatitis in California, 1994-2001. *Pancreas* 2006; **33**: 336-344 [PMID: 17079936]

5 **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]

6 **Cavdar F**, Yildar M, Tellioğlu G, Kara M, Tilki M, Titiz Mİ. Controversial issues in biliary pancreatitis: when should we perform MRCP and ERCP? *Pancreatology* 2014; **14**: 411-414 [PMID: 25200693 DOI: 10.1016/j.pan.2014.08.002]

7 **Neoptolemos JP**, Carr-Locke DL, London NJ, Bailey IA, James D, Fossard DP. Controlled trial of urgent endoscopic retrograde cholangiopancreatography and endoscopic sphincterotomy versus conservative treatment for acute pancreatitis due to gallstones. *Lancet* 1988; **2**: 979-983 [PMID: 2902491]

8 **Fölsch UR**, Nitsche R, Lüdtke R, Hilgers RA, Creutzfeldt W. Early ERCP and papillotomy compared with conservative treatment for acute biliary pancreatitis. The German Study Group on Acute Biliary Pancreatitis. *N Engl J Med* 1997; **336**: 237-242 [PMID: 8995085 DOI: 10.1056/NEJM199701233360401]

9 **DeIorio AV** Jr, Vitale GC, Reynolds M, Larson GM. Acute biliary pancreatitis: The roles of laparoscopic cholecystectomy and endoscopic retrograde cholangiopancreatography. *Surg Endosc* 1995; **9**: 392-396 [PMID: 7660260]

10 **Kuo VC**, Tarnasky PR. Endoscopic management of acute biliary pancreatitis. *Gastrointest Endosc Clin N Am* 2013; **23**: 749-768 [PMID: 24079788 DOI: 10.1016/j.giec.2013.06.002]

11**Johnson CD**, Charnley R, Rowlands B et UK Working Party on Acute Pancreatitis. UK guidelines for the management of acute pancreatitis. *Gut* 2005; 54 Suppl 3: iii1-iii9 [PMID: 15831893 DOI: 10.1136/gut.2004.057026]

12 **Nguyen GC**, Rosenberg M, Chong RY, Chong CA. Early cholecystectomy and ERCP are associated with reduced readmissions for acute biliary pancreatitis: a nationwide, population-based study. *Gastrointest Endosc* 2012; **75**: 47-55 [PMID: 22100300 DOI: 10.1016/j.gie.2011.08.028]

13 **van Santvoort HC**, Bakker OJ, Besselink MG, Bollen TL, Fischer K, Nieuwenhuijs VB, Gooszen HG, Erpecum KJ. Prediction of common bile duct stones in the earliest stages of acute biliary pancreatitis. *Endoscopy* 2011; **43**: 8-13 [PMID: 20972954 DOI: 10.1055/s-0030-1255866]

14 **Chang L**, Lo SK, Stabile BE, Lewis RJ, de Virgilio C. Gallstone pancreatitis: a prospective study on the incidence of cholangitis and clinical predictors of retained common bile duct stones. *Am J Gastroenterol* 1998; **93**: 527-531 [PMID: 9576442]

15 **Cohen ME**, Slezak L, Wells CK, Andersen DK, Topazian M. Prediction of bile duct stones and complications in gallstone pancreatitis using early laboratory trends. *Am J Gastroenterol* 2001; **96**: 3305-3311 [PMID: 11774941 DOI: 10.1111/j.1572-0241.2001.05330.x]

16 **Cotton PB**, Lehman G, Vennes J, Geenen JE, Russell RC, Meyers WC, Liguory C, Nickl N. Endoscopic sphincterotomy complications and their management: an attempt at consensus. *Gastrointest Endosc* 1991; **37**: 383-393 [PMID: 2070995]

17 **Loperfido S**, Angelini G, Benedetti G, Chilovi F, Costan F, De Berardinis F, De Bernardin M, Ederle A, Fina P, Fratton A. Major early complications from diagnostic and therapeutic ERCP: a prospective multicenter study. *Gastrointest Endosc* 1998; **48**: 1-10 [PMID: 9684657]

18 **Romagnuolo J**, Bardou M, Rahme E, Joseph L, Reinhold C, Barkun AN. Magnetic resonance cholangiopancreatography: a meta-analysis of test performance in suspected biliary disease. *Ann Intern Med* 2003; **139**: 547-557 [PMID: 14530225]

19 **Tse F**, Liu L, Barkun AN, Armstrong D, Moayyedi P. EUS: a meta-analysis of test performance in suspected choledocholithiasis. *Gastrointest Endosc* 2008; **67**: 235-244 [PMID: 18226685 DOI: 10.1016/j.gie.2007.09.047]

20 **Kikinzon L**, Modai I, Valevski A. [Chronic pain in psychiatry]. *Harefuah* 1991; **121**: 259-262 [PMID: 1686007]

21 **Maple JT**, Ben-Menachem T, Anderson MA, Appalaneni V, Banerjee S, Cash BD, Fisher L, Harrison ME, Fanelli RD, Fukami N, Ikenberry SO, Jain R, Khan K, Krinsky ML, Strohmeyer L, Dominitz JA. The role of endoscopy in the evaluation of suspected choledocholithiasis. *Gastrointest Endosc* 2010; **71**: 1-9 [PMID: 20105473 DOI: 10.1016/j.gie.2009.09.041]

22 **Frei GJ**, Frei VT, Thirlby RC, McClelland RN. Biliary pancreatitis: clinical presentation and surgical management. *Am J Surg* 1986; **151**: 170-175 [PMID: 2418700]

23 **Paloyan D**, Simonowitz D, Skinner DB. The timing of biliary tract operations in patients with pancreatitis associated with gallstones. *Surg Gynecol Obstet* 1975; **141**: 737-739 [PMID: 1198310]

24 **Wilcox CM**, Varadarajulu S, Eloubeidi M. Role of endoscopic evaluation in idiopathic pancreatitis: a systematic review. *Gastrointest Endosc* 2006; **63**: 1037-1045 [PMID: 16733122]

25 **Moon JH**, Cho YD, Cha SW, Cheon YK, Ahn HC, Kim YS, Kim YS, Lee JS, Lee MS, Lee HK, Shim CS, Kim BS. The detection of bile duct stones in suspected biliary pancreatitis: comparison of MRCP, ERCP, and intraductal US. *Am J Gastroenterol* 2005; **100**: 1051-1057 [PMID: 15842578]

26 **Gabbrielli A**, Pezzilli R, Uomo G, Zerbi A, Frulloni L, Rai PD, Castoldi L, Costamagna G, Bassi C, Carlo VD. ERCP in acute pancreatitis: What takes place in routine clinical practice? *World J Gastrointest Endosc* 2010; **2**: 308-313 [PMID: 21160762 DOI: 10.4253/wjge.v2.i9.308]

27 **Scheiman JM**, Carlos RC, Barnett JL, Elta GH, Nostrant TT, Chey WD, Francis IR, Nandi PS. Can endoscopic ultrasound or magnetic resonance cholangiopancreatography replace ERCP in patients with suspected biliary disease? A prospective trial and cost analysis. *Am J Gastroenterol* 2001; **96**: 2900-2904 [PMID: 11693324]

28 **Santos JS**, Kemp R, Ardengh JC, Jr JE. Conservative management of cholestasis with and without fever in acute biliary pancreatitis. *World J Gastrointest Surg* 2012; **4**: 55-61 [PMID: 22530079 DOI: 10.4240/wjgs.v4.i3.55]

29 **De Lisi S**, Leandro G, Buscarini E. Endoscopic ultrasonography versus endoscopic retrograde cholangiopancreatography in acute biliary pancreatitis: a systematic review. *Eur J Gastroenterol Hepatol* 2011; **23**: 367-374 [PMID: 21487299 DOI: 10.1097/MEG.0b013e3283460129]

30 **Ainsworth AP**, Rafaelsen SR, Wamberg PA, Durup J, Pless TK, Mortensen MB. Is there a difference in diagnostic accuracy and clinical impact between endoscopic ultrasonography and magnetic resonance cholangiopancreatography? *Endoscopy* 2003; **35**: 1029-1032 [PMID: 14648416]

31 **Benjaminov F**, Stein A, Lichtman G, Pomeranz I, Konikoff FM. Consecutive versus separate sessions of endoscopic ultrasound (EUS) and endoscopic retrograde cholangiopancreatography (ERCP) for symptomatic choledocholithiasis. *Surg Endosc* 2013; **27**: 2117-2121 [PMID: 23389062 DOI: 10.1007/s00464-012-2720-7]

32 **Savides TJ**. EUS-guided ERCP for patients with intermediate probability for choledocholithiasis: is it time for all of us to start doing this? *Gastrointest Endosc* 2008; **67**: 669-672 [PMID: 18374026 DOI: 10.1016/j.gie.2007.09.015]

**33 Anderloni A,** Ballarè M, Pagliarulo M, [Conte D](http://www.ncbi.nlm.nih.gov/pubmed/?term=Conte%20D%5BAuthor%5D&cauthor=true&cauthor_uid=24380748), [Galeazzi M](http://www.ncbi.nlm.nih.gov/pubmed/?term=Galeazzi%20M%5BAuthor%5D&cauthor=true&cauthor_uid=24380748), [Orsello M](http://www.ncbi.nlm.nih.gov/pubmed/?term=Orsello%20M%5BAuthor%5D&cauthor=true&cauthor_uid=24380748), [Andorno S](http://www.ncbi.nlm.nih.gov/pubmed/?term=Andorno%20S%5BAuthor%5D&cauthor=true&cauthor_uid=24380748), [Del Piano M](http://www.ncbi.nlm.nih.gov/pubmed/?term=Del%20Piano%20M%5BAuthor%5D&cauthor=true&cauthor_uid=24380748). [Prospective evaluation of early endoscopic ultrasonography for triage in suspected choledocholithiasis: Results from a large single centre series.](http://www.ncbi.nlm.nih.gov/pubmed/24380748) *Dig Liver Dis* 2014; **46**: 335-339 [PMID: 24380748 DOI: 10.1016/j.dld.2013.11.007]

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