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Endoscopic Papillary Balloon Dilation Can Be Safely Performed in Patients on Dual Antiplatelet Therapy: A Pilot Study

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ABSTRACT

Background & Aims: Endoscopic papillary balloon dilation (EPBD), a low-risk procedure for bleeding, has been suggested as an alternative to endoscopic sphincterotomy for papillary dilatation in patients undergoing endoscopic stone removal who are at a higher risk of bleeding. Several guidelines recommend that combination of two antiplatelet agents should be reduced to single antiplatelet therapy when endoscopic sphincterotomy is performed. However, there is no evidence that EPBD affects the risk of bleeding in patients receiving a combination of two antiplatelet agents; thus, we aimed to explore this problem.
Methods: We included 31 patients who underwent EPBD for common bile duct stones at our hospital from May 2014 to August 2022 and received either a combination of two antiplatelet agents or single antiplatelet therapy prior to the procedure. The group receiving a combination of two antiplatelet agents included patients who underwent EPBT without antiplatelet therapy withdrawal or with a shorter withdrawal period than those recommended by the guidelines**.**
Results: In the group that received a combination of two antiplatelet agents, one of the two antiplatelet agents used was thienopyridine. No bleeding was observed after EPBD in this study. We did not find any significant between-group differences in hemoglobin levels and rate of post-endoscopic retrograde cholangiopancreatography pancreatitis.
Conclusions: In patients treated with a combination of two antiplatelet agents, EPBD could be safely performed without bleeding. Therefore, future prospective studies are warranted.

Key words: antiplatelet therapy – common bile duct stones – combination of two antiplatelet agents – dual antiplatelet therapy – endoscopic papillary balloon dilation – endoscopic retrograde cholangiopancreatography – thienopyridine.

Abbreviations: APA: antiplatelet agents; ASGE: American Society of Gastrointestinal Endoscopy; CTAA: combination of two antiplatelet agents; EPBD: endoscopic papillary balloon dilation; ERCP: endoscopic retrograde cholangiopancreatography; ESGE: European Society of Gastrointestinal Endoscopy; EST: endoscopic sphincterotomy; JGES: Japan Gastroenterological Endoscopy Society; PEP: Post-ERCP pancreatitis; SAPT: single antiplatelet therapy.

INTRODUCTION

It is well documented that aspirin and antiplatelet agents (APAs) increase the risk of gastrointestinal bleeding [1, 2]. Antiplatelet agents, such as thienopyridines, bind to the P2Y12 component of the ADP receptor on platelets and irreversibly inhibit platelet function for 7–10 days. Thienopyridines have been reported to increase bleeding rates in endoscopic procedures with a high risk of bleeding, especially endoscopic submucosal dissection and endoscopic mucosal resection [3]. The European Society of Gastrointestinal Endoscopy (ESGE), American Society of Gastrointestinal Endoscopy (ASGE), and Japan Gastroenterological Endoscopy Society (JGES) guidelines recommend that the combination of two antiplatelet agents (CTAA) should be reduced to single antiplatelet therapy (SAPT) when endoscopic sphincterotomy (EST) is performed (5–7 days of thienopyridine drug cessation, while aspirin or cilostazol is continued) [6–8]. In cases of cholangitis with choledocholithiasis, the number of endoscopic retrograde cholangiopancreatography (ERCP) sessions increases

considering the two-stage treatment, in which a bile duct stent is placed first, and stones are retrieved with EST after the CTAA is reduced to SAPT. If patients spend their withdrawal period in the hospital, they will have a prolonged hospital stay and will be at risk of several well-known complications, such as pneumonia, venous thromboembolism, and muscle weakness (especially in the elderly) [9, 10].

In endoscopic stone removal for common bile duct (CBD) stones, endoscopic papillary balloon dilation (EPBD), a low-bleeding risk procedure, is described in the JGES, ASGE, and ESGE guidelines as a papillary dilatation procedure in patients at high risk of bleeding and an alternative to EST [11–13]. A systematic review of retrospective studies analyzed EST, a high-bleeding risk procedure, and EPBD, a low-bleeding risk procedure, and noted that they may not increase bleeding in patients receiving CTAA [14]. However, only a small number of patients who have undergone EPBD with CTAA were included in the study, and the withdrawal duration of CTAA and breakdown of the antiplatelet agents used were not described [15]. Generally, EPBD has a reported bleeding rate of less than 1% and a lower risk of bleeding than EST, and EPBD may be performed in patients receiving CTAA with low-bleeding risk [14, 16, 17].

Thus, there is no evidence that EPBD increases the risk of bleeding in patients with CTAA, and the benefits of reducing it to SAPT are not clear. Moreover, no reports have focused on EPBD in patients receiving CTAA. Therefore, we propose the hypothesis that EPBD does not increase bleeding risk in patients receiving CTAA and treating these cases with EPBD without CTAA withdrawal leads to a reduction in the number of ERCPs, shorter hospital stay, and avoidance of an increased risk of embolism during the CTAA reduction period.

METHODS

The study was reviewed and approved by our Institutional Review Board. All procedures were performed in accordance with the ethical standards of the 1964 Declaration of Helsinki and its later amendments. The protocol was registered in the UMIN Clinical Trials Registry (UMIN-CTR) on October 13, 2022 (UMIN-CTR; No.: UMIN000049209; URL: https://www.umin.ac.jp/ctr/index.htm).

Study Population

This retrospective study was conducted at our institution. Study enrollment commenced in May 2014 and ended in August 2022. This study included patients who underwent EPBD for CBD stones and received CTAA or SAPT prior to EPBD. Patients receiving warfarin or other anticoagulant therapies or those with hepatolithiasis or cholecystitis were excluded (Fig. 1). We investigated patient characteristics, ERCP findings, incidence of EPBD bleeding, and complications associated with EPBD.

Of the 78 patients enrolled, 47 were excluded based on the exclusion criteria. 31 patients were included in the final analysis. Moreover, the number of patients who underwent EPBD with CTAA therapy (CTAA group) was 9, while 22 underwent EPBD with SAPT (SAPT group) (Fig. 1).

Endoscopic Procedure

Endoscopic papillary balloon dilatation was performed using biliary balloon dilation catheters, REN (Kaneka medics, Osaka, Japan), Hurricane (Boston Scientific Japan, Tokyo, Japan), and ZARA (Kaneka medics, Osaka, Japan) through a side-viewing endoscope (JF-260V, TJF-290V; Olympus, Tokyo, Japan). The procedures were performed by experts who had performed >1,000 ERCP procedures. After EPBD balloon insertion into the papilla, the balloon was gradually pressurized until the waist disappeared. In principle, a balloon diameter of 8 mm was selected for the EPBD procedure and dilated until the waist disappeared; however, in cases with a distal bile duct diameter <6 mm, the bile duct was dilated at low pressure regardless of the disappearance of the waist. Although during the second half of the study the balloon dilation procedure was performed for 1 to 2 minutes, during the first half of the study the duration of the procedure was at the discretion of the endoscopists, often ranging from 30 seconds to 1 minute.

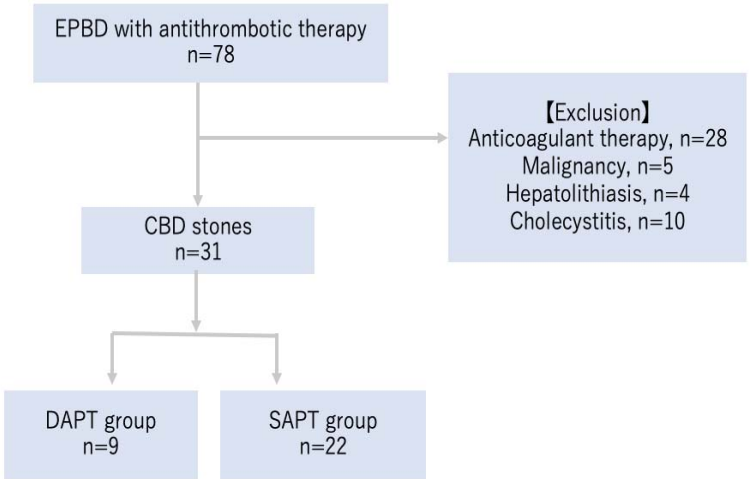

Fig. 1. Study population. CBD: common bile duct; CTAA: combination of two antiplatelet agents; SAPT: single antiplatelet therapy; EPBD: endoscopic papillary balloon dilation.

Antiplatelet Agents

The ESGE and ASGE guidelines do not state APAs other than aspirin and thienopyridine [6, 7], whereas other APAs have been stated in the JGES guidelines. Although the evidence level is low, according to this guideline, in patients receiving CTAA (including antiplatelet agents other than aspirin and thienopyridines), a high-risk endoscopic procedure may increase the rate of post procedural bleeding [8]. Therefore, the JGES guideline recommends that CTAA should be changed to SAPT, with a reduction to aspirin or cilostazol alone and with a 5- to 7-day break for thienopyridines following high-bleeding risk procedures. In principle, EPBD was performed as a low-risk bleeding procedure with continued CTAA, and in patients receiving CTAA who were not at a higher risk of thromboembolism due to the discontinuation of APAs according to the JGES guideline [8], EPBD was performed as a high-risk bleeding procedure with a dose reduction from CTAA to SAPT.

Definitions

The CTAA included antiplatelet agents other than aspirin and thienopyridines, such as sarpogrelate hydrochloride and ethyl icosapentate. The CTAA group included patients who underwent EPBD without antiplatelet therapy withdrawal or with a shorter withdrawal period than those recommended by the guidelines. In the patients with a shorter withdrawal period, EPBD was performed early to reduce the length of hospital stay due to the onset of delirium or the patient's desire.

Endoscopic papillary balloon dilatation bleeding was defined as bleeding occurring after EPBD, which was subsequently defined as bleeding with clinical (i.e., not just endoscopic) evidence of bleeding or a drop in hemoglobin of <3 g/dL [5]. Post-ERCP pancreatitis (PEP) was defined based on the revised Atlanta classification [5].

Statistical Analysis

We compared bleeding after EPBD, hemoglobin change within one week after EPBD, and post-ERCP pancreatitis outcomes between the CTAA and SAPT groups. The primary study outcome was bleeding after EPBD. The Mann-Whitney U test was used to compare continuous variables that were non-normally distributed, and the $\chi 2$-test or Fisher's exact test was used to compare categorical variables. Multivariate analysis was performed using a logistic regression analysis. Differences were considered statistically significant at two-tailed p-values <0.05. All statistical analyses were performed using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan) and a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria), which is a modified version of the R commander designed to allow additional statistical functions that are frequently used in biostatistics [18].

RESULTS

Table I summarizes patients' characteristics. We retrospectively analyzed the data of 31 patients who received antiplatelet therapy and underwent EPBD. Of these, 9 patients (29%) received CTAA, and 22 (71%) received SAPT. Among patients who receiving CTAA, seven had myocardial infarction, two had cerebral infarction, and one had diabetes. This study included no patients with severe cholangitis, such as those who were hemodynamically unstable or had coagulopathy. There were no significant between-group differences in age, gender, complicated cholangitis, underlying disease, platelet count, prothrombin time, or prothrombin time-international normalized ratio. In the present study, most of the cases were complicated by cholangitis. Table II shows the breakdown of antiplatelet agents; all patients in the CTAA group received thienopyridine. Table III summarizes the duration of incomplete thienopyridine withdrawal in patients treated with CTAA; five patients did not withdraw from CTAA, while four patients withdrew incompletely.

All patients in this study had naïve papilla. Table IV summarizes the ERCP findings in the study population. There were no significant between-group differences in difficult endoscopic biliary cannulation, peri-ampullary diverticulum, endoscopic nasobiliary drainage, endoscopic stone removal, pancreatography, plastic stents in the bile or pancreatic duct, self-expandable metallic stents, CBD diameter, CBD stone diameter, ERCP procedure time, or number of cases that required two ERCPs for bile duct procedures. In each group, only one patient required two ERCPs for bile duct procedures. This was because the patient had difficulty with bile duct cannulation or had low platelet counts due to a complication of acute cholangitis and, therefore, only a stent was placed during the first ERCP. All the patients in the study had clinical success regarding stone removal.

Table I. Patient characteristics

	CTAA group, n=9	SAPT group, n=22	p-value
Age (years) (IQR)	85 (76–90)	82 (70–87)	0.56
Gender (male), n (%)	8 (88.9)	11 (50.0)	0.1
Cardiovascular, n (%)	6 (66.7)	13 (59.1)	>0.99
Cerebral bleeding, n (%)	0 (0)	0 (0)	1
Stroke, n (%)	3 (33.3)	10 (45.5)	0.7
Cholangitis, n (%)	9 (100)	19 (86.4)	0.54
Diabetes mellitus, n (%)	4 (44.4)	5 (22.7)	0.39
Hemodialysis patients, n (%)	1 (11.1)	1 (4.5)	0.5
Liver cirrhosis, n (%)	0 (0)	1 (4.5)	>0.99
PT-INR; median (IQR)	1.1 (1.0–1.2)	1.1 (1.0–1.2)	0.61
PT, %; mean (SD)	86.5 (14.7)	88.3 (16.1)	0.78
Platelet, 104/uL; mean (SD)	17.6 (4.3)	20.1 (7.1)	0.34

IQR: interquartile range; SD: standard deviation; PT: prothrombin time; PT-INR: prothrombin time-international normalized ratio; CTAA: combination of two antiplatelet agents; SAPT: single antiplatelet therapy; EPBD: endoscopic papillary balloon dilation.

Table II. Breakdown of antiplatelet agents

	CTAA group, n=9	SAPT group, n=22
Aspirin	7	4
Thienopyridine	9	18
Sarpogrelate hydrochloride	1	0
Ethyl icosapentate	1	0

All patients in the CTAA group used thienopyridine. For abbreviations see Table I.

Table III. Duration of incomplete thienopyridine withdrawal in patients receiving CTAA

Thienopyridine withdrawal in patients receiving CTAA (days)	CTAA group, n=9
No interruption	5
1	2
2	1
3	1
4	0
5	0
6	0
7	0

Five patients did not withdraw from the CTAA, and four patients withdrew incompletely. For abbreviations see Table I.

Table IV. ERCP findings

	CTAA group, n=9	SAPT group, n=22	p-value
Diverticulum, n (%)	3 (33.3)	9 (40.9)	>0.99
Difficulty biliary cannulation, n (%)	2 (22.2)	5 (22.7)	>0.99
Cases of a guidewire inserted into the pancreatic duct, n (%)	2 (22.2)	5 (22.7)	>0.99
Cases with pancreatography, n (%)	3 (37.5)	8 (36.4)	>0.99
Diameter of CBD, mm (IQR)	10 (7.0–10.0)	8.5 (7.3–9.9)	0.73
Diameter of CBD stone, mm (IQR)	5.0 (3.0–8.0)	5.0 (3.0–7.0)	0.74
Passed stone, n (%)	0 (0)	5 (22.7)	0.29
Stone extraction, n (%)	8 (88.9)	22 (100)	0.29
ENBD, n (%)	2 (22.2)	2 (9.1)	0.56
Cases in which CBD plastic stents were implanted, n (%)	1 (11.1)	1 (4.5)	0.5
Cases in which CBD SEMS were implanted, n (%)	0 (0)	0 (0)	1
Cases in which pancreatic duct plastic stents were implanted, n (%)	1 (11.1)	1 (4.5)	0.5
ERCP time, min (IQR)	25 (20–30)	20 (17–25)	0.39
Cases who required two ERCPs for bile duct procedures, n (%)	1 (11.1)	1 (4.5)	0.5

CBD: common bile duct; ENBD: endoscopic nasobiliary drainage; SEMS: self-expandable metallic stent; ERCP: endoscopic retrograde cholangiopancreatography; For the rest of abbreviation see Table I.

Table V summarizes the clinical outcomes of the study. No bleeding occurred after EPBD in the 31 patients in this study. We did not find any significant between-group differences in the changes in hemoglobin levels and PEP. All the PEP cases were mild, and no other complications other than PEP occurred in this study.

DISCUSSION

In the JGES and ASGE guidelines, EPBD is a low-risk procedure in terms of bleeding; however, the evidence for EPBD in patients receiving CTAA is lacking [6, 13].

Table V. EPBD bleeding and outcomes

	CTAA group, n=9	SAPT group, n=22	p-value
Bleeding after EPBD, n (%)	0 (0)	0 (0)	1
Hemoglobin change within 1 week after EPBD, g/dl (IQR)	-1.3 (-2.1 to -1.2)	-1.25 (-1.7 to -0.6)	0.29
Post-ERCP pancreatitis, n (%)	2 (22.2%)	3 (13.6%)	0.61

For abbreviations see Table I.

Nevertheless, since EST may be safely performed in patients treated with CTAA [14], EPBD, which has a lower bleeding rate than EST, may be safer [19]. Therefore, we conducted this study to propose the hypothesis that EPBD can be safely performed in patients receiving CTAA without APA withdrawal.

In this study, post-EPBD bleeding was not observed in any patient. There is a question of whether patients receiving CTAA might have minor bleeding that would stop spontaneously, but there was also no significant difference in hemoglobin change in the CTAA group compared with the SAPT group to suggest this.

Furthermore, thienopyridines have been reported to increase bleeding rates in endoscopic procedures with a high risk of bleeding [3]. It is noteworthy that all CTAA regimens in this study included thienopyridines, but there were no bleeding complications.

For mild or moderate cholangitis due to choledocholithiasis, it is also acceptable in the 2018 Tokyo Guidelines to perform endoscopic stone removal simultaneously with drainage depending on the patient's situation [20]. However, in patients receiving CTAA, stenting is performed at the first ERCP, APAs are withdrawn, and endoscopic stone removal is performed with EST at the second ERCP; if EPBD can be performed without APA withdrawal, the number of sessions of ERCPs, length of hospital stay, and risk of thrombosis owing to the required withdrawal period can be reduced [3]. Furthermore, previous reports have indicated that the incidence of pneumonia increases in the length of hospital stay [9, 10], but it is unclear whether EPBD without APA withdrawal would have any preventive effect on pneumonia, even with a reduction in the length of hospital stay by 5 to 7 days. Instead, the benefit of EPBD without APA withdrawal may be to reduce the number of ERCP sessions from two to one, thereby reducing aspiration pneumonia. However, further studies are needed to clarify this point.

Moreover, EPBD has been suspected to increase the risk of PEP [21], but several studies have disproven this [22, 23]; furthermore, there are studies based on race that show no increase in risk among Asian populations [19]. In addition, the efficacy of prophylactic drugs for PEP, such as nonsteroidal anti-inflammatory drugs (NSAIDs), has been demonstrated in recent years [24], and the efficacy of the combination of NSAIDs and nitrates has also been studied [25]. Therefore, reduction in the incidence of PEP has been successful.

This study had a few important limitations. First, it was a retrospective, single-center study with a small number of cases. Therefore, this study only suggests a hypothesis, and it cannot be confirmed that the rate of bleeding complications is not increased in patients receiving CTAA who undergo

EPBD. We would perform prospective multicenter studies in the future to verify the risk of bleeding due to EPBD in patients receiving CTAA. Second, we considered aligning background factors by performing propensity score matching, but it was difficult to do so homogeneously; therefore, we analyzed all cases (Supplementary file).

CONCLUSIONS

Endoscopic sphincterotomy or EPBD is a necessary papillary dilatation technique for CBD stone extraction. In patients treated with CTAA, guidelines require CTAA reduction prior to EST. Although no reports have focused on EPBD in patients receiving CTAA, EPBD may be safe to perform on these patients, as there was no bleeding after EPBD in this study. If the hypothesis of this study is validated, it would lead to reduction in the number of ERCPs, shorter hospital stays, and avoidance of an increased risk of embolism during the CTAA reduction period in patients with CBD stones receiving CTAA. Prospective studies are required to confirm our results and ensure evidence-based recommendations for EPBD in patients receiving CTAA.

Conflicts of interest: None to declare.

Authors' contribution: S.M. and K. Koizumi were the major contributors in writing the manuscript. S.M., R.J., and A.S. analyzed and interpreted the patient data regarding bleeding risk after endoscopic sphincterotomy. S.M., R.J., K. Koizumi, M.M., T.N., K.S., K. Kimura, C.S., J.K., C.I., A.S., M. Kobayashi, M. Kako, H.U., and A.S. designed and initiated the study, enrolled patients, edited the paper, and approved the final version.

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REFERENCES

1. Kimchi NA, Broide E, Scapa E, Birkenfeld S. Antiplatelet therapy and the risk of bleeding induced by gastrointestinal endoscopic procedures. A systematic review of the literature and recommendations. Digestion 2007;75:36–45. doi:10.1159/000101565
2. Hussain N, Alsulaiman R, Burtin P, et al. The safety of endoscopic sphincterotomy in patients receiving antiplatelet agents: A case-control study. Aliment Pharmacol Ther 2007;25:579–584. doi:10.1111/j.1365-2036.2006.03225.x
3. Ono S, Fujishiro M, Yoshida N, et al. Thienopyridine derivatives as risk factors for bleeding following high risk endoscopic treatments: Safe Treatment on Antiplatelets (STRAP) study. Endoscopy 2015;47:632–637. doi:10.1055/s-0034-1391354
4. Dumonceau JM, Kapral C, Aabakken L, et al. ERCP-related adverse events: European Society of Gastrointestinal Endoscopy (ESGE) guideline. Endoscopy 2020;52:127–149. doi:10.1055/a-1075-4080
5. ASGE Standards of Practice Committee; Chandrasekhara V, Khashab MA, Muthusamy VR, et al. Adverse events associated with ERCP. Gastrointest Endosc 2017;85:32–47. doi:10.1016/j.gie.2016.06.051
6. ASGE Standards of Practice Committee; Acosta RD, Abraham NS, Chandrasekhara V, et al. The management of antithrombotic agents for patients undergoing GI endoscopy. Gastrointest Endosc 2016;83:3–16. doi:10.1016/j.gie.2015.09.035
7. Veitch AM, Radaelli F, Alikhan R, et al. Endoscopy in patients on antiplatelet or anticoagulant therapy: British Society of Gastroenterology (BSG) and European Society of Gastrointestinal Endoscopy (ESGE) guideline update. Gut 2021;70:1611–1628. doi:10.1136/gutjnl-2021-325184
8. Fujimoto K, Fujishiro M, Kato M, et al. Guidelines for gastroenterological endoscopy in patients undergoing antithrombotic treatment. Dig Endosc 2014;26:1–14. doi:10.1111/den.12183
9. Welch C, Hassan-Smith ZK, Greig CA, Lord J , Jackson TA. Acute sarcopenia secondary to hospitalisation– an emerging condition affecting older adults. Aging Dis 2018;9:151–164. doi:10.14336/AD.2017.0315
10. Heit JA, Melton LJ 3rd, Lohse CM, et al. Incidence of venous thromboembolism in hospitalized patients vs community residents. Mayo Clin Proc 2001;76:1102–1110. doi:10.4065/76.11.1102
11. Buxbaum JL, Abbas Fehmi SM, Sultan S, et al. ASGE guideline on the role of endoscopy in the evaluation and management of choledocholithiasis. Gastrointest Endosc 2019;89:1075–1105.e15. doi:10.1016/j.gie.2018.10.001
12. Manes G, Paspatis G, Aabakken L, , et al. Endoscopic management of common bile duct stones: European Society of Gastrointestinal Endoscopy (ESGE) guideline. Endoscopy 2019;51:472–491. doi:10.1055/a-0862-0346
13. Tazuma S, Unno M, Igarashi Y, et al. Evidence-based clinical practice guidelines for cholelithiasis 2016. J Gastroenterol 2017;52:276–300. doi:10.1007/s00535-016-1289-7
14. Bhurwal A, Mutneja H, Goel A, et al. No significant difference in post-ERCP bleeding rates between dual antiplatelet agents and aspirin alone: A systematic review and meta-analysis. J Clin Gastroenterol 2022;56:546–551. doi:10.1097/MCG.0000000000001559
15. Hamada T, Yasunaga H, Nakai Y, et al. Bleeding after endoscopic sphincterotomy or papillary balloon dilation among users of antithrombotic agents. Endoscopy 2015;47:997–1004. doi:10.1055/s-0034-1392408
16. Tsujino T, Kawabe T, Komatsu Y, et al. Endoscopic papillary balloon dilation for bile duct stone: Immediate and long-term outcomes in 1000 patients. Clin Gastroenterol Hepatol 2007;5:130–137. doi:10.1016/j.cgh.2006.10.013
17. Fujita N, Maguchi H, Komatsu Y, et al. Endoscopic sphincterotomy and endoscopic papillary balloon dilatation for bile duct stones: A prospective randomized controlled multicenter trial. Gastrointest Endosc 2003;57:151–155. doi:10.1067/mge.2003.56
18. Kanda Y. Investigation of the freely available easy-to-use software 'EZR' for medical statistics. Bone Marrow Transplant 2013;48:452–458. doi:10.1038/bmt.2012.244
19. Zhao HC, He L, Zhou DC, Geng XP, Pan FM. Meta-analysis comparison of endoscopic papillary balloon dilatation and endoscopic sphincteropapillotomy. World J Gastroenterol 2013;19:3883–3891. doi:10.3748/wjg.v19.i24.3883
20. Miura F, Okamoto K, Takada T, et al. Tokyo Guidelines 2018: Initial management of acute biliary infection and flowchart for acute

cholangitis. J Hepatobiliary Pancreat Sci 2018;25:31–40. doi:10.1002/jhbp.509

21. Weinberg BM, Shindy W, Lo S. Endoscopic balloon sphincter dilation (sphincteroplasty) versus sphincterotomy for common bile duct stones. Cochrane Database Syst Rev 2006;2006(4):CD004890. doi:10.1002/14651858.CD004890.pub2
22. Bergman JJ, Rauws EA, Fockens P, et al. Endoscopic balloon dilation (sphincteroplasty) versus endoscopic sphincterotomy for removal of bile duct stones. Lancet 1997;349:1124–1129. doi:10.1016/S0140-6736(96)11026-6
23. Park CH, Jung JH, Nam E, et al. Comparative efficacy of various endoscopic techniques for the treatment of common bile duct stones: A network meta-analysis. Gastrointest Endosc 2018;87:43–57.e10. doi:10.1016/j.gie.2017.07.038
24. Luo H, Zhao L, Leung J, et al. Routine pre-procedural rectal indometacin versus selective post-procedural rectal indometacin to prevent pancreatitis in patients undergoing endoscopic retrograde cholangiopancreatography: A multicentre, single-blinded, randomized controlled trial. Lancet 2016;387:2293–2301. doi:10.1016/S0140-6736(16)30310-5
25. Tomoda T, Kato H, Ueki T, et al. Combination of diclofenac and sublingual nitrates is superior to diclofenac alone in preventing pancreatitis after endoscopic retrograde cholangiopancreatography. Gastroenterology 2019;156:1753–1760.e1. doi:10.1053/j.gastro.2019.01.267