Tohoku J. Exp. Med., 2020, **250**, 173-179

Saline Solution Irrigation of the Bile Duct after Stone Removal Reduces the Recurrence of Common Bile Duct Stones

Ryoma Endo,[1] Akihiko Satoh,[1] Yu Tanaka,[1] Fumiko Shimoda,[1] Kaoru Suzuki,[1] Kiichi Takahashi,[1] Hideki Okata,[1] Keiichiro Hiramoto,[1] Osamu Kimura,[1] Sho Asonuma,[1] Ken Umemura[1] and Tooru Shimosegawa[1]

[1]Department of Gastroenterology, South Miyagi Medical Center, Shibata-gun, Miyagi, Japan

Common bile duct (CBD) stone is a relatively common but potentially life-threatening disease. Endoscopic sphincterotomy (EST) has been performed as standard therapy for CBD stones, but the rate of recurrence of CBD stones is high. Risk factors have been poorly defined, and no effective means for the prevention of the recurrence of CBD stones have been established so far. We aimed to identify significant risk factors for the recurrence of bile duct stones. This study included 477 patients (231 women; mean age, 80.5 years) who underwent EST and cleared CBD stones on cholangiography. A retrospective analysis was performed for the consecutively collected data. During the follow-up period of 6-75 months, the recurrence of CBD stones was observed in 99 patients (20.8%). The median time to the recurrence was 19.0 months (range 4-72 months). Multivariate analysis identified the need for mechanical lithotripsy, which was used for stone fragmentation, as a risk factor. Mechanical lithotripsy caused cholangiography-negative small residua. Notably, saline solution irrigation of the bile duct reduced the recurrence of CBD stones. These results demonstrate that subsequent biliary irrigation after stone removal may prevent the recurrence of CBD stones by clearing small residual fragments.

Keywords: biliary stone; endoscopic sphincterotomy; irrigation; lithotripsy; recurrence
Tohoku J. Exp. Med., 2020 March, **250** (3), 173-179.

Introduction

Cholelithiasis is one of the most prevalent in gastrointestinal diseases. On the national survey in Japan (Tazuma et al. 2015), 25.6% of the patients with cholelithiasis had common bile duct (CBD) stones that often cause serious complications, including acute cholangitis, obstructive jaundice, and acute pancreatitis.

Endoscopic sphincterotomy (EST) has been accepted as a standard therapy for CBD stones, but the rate of recurrence of CBD stones is high, reaching to 20% of cases (Prat et al. 1996; Pereira-Lima et al. 1998; Kim et al. 2001; Sugiyama and Atomi 2002; Doi et al. 2013). Various trials to prevent the recurrence of CBD stones have been performed; however, no effective means for the prevention of the recurrence of CBD stones has been established so far. Risk factors for the recurrence of CBD stones such as the elderly patients (Keizman et al. 2006a), history of prior cholecystectomy (Ando et al. 2003; Keizman et al. 2006b), dilated CBD (Pereira-Lima et al. 1998; Ohashi et al. 1999; Kim et al. 2001; Keizman et al. 2006b; Konstantakis et al. 2017), acute CBD angulation (Keizman et al. 2006b), and the presence of periampullary diverticulum (Ueno et al. 2003; Keizman et al. 2006b) have been identified. In addition to these patients' factors, incomplete stone clearance is demonstrated as a probable risk factor (Tsuchiya et al. 2008; Konstantakis et al. 2017). It has been reported that cholangiography-negative small stones persisted in 23-40% of the patients after EST and stone extraction (Ohashi et al. 1999; Ang et al. 2009; Endo et al. 2011; Ahn et al. 2018). So residual small stones or sludge after EST may be a therapeutic target for the prevention of the recurrence of CBD stones. There is a clue to approach this task. Ang et al. (2009) reported that saline solution irrigation through a catheter inserted to the CBD was useful in clearing small residual stones. Furthermore, additional preventive saline

Received December 9, 2019; revised and accepted February 26, 2020. Published online March 12, 2020; doi: 10.1620/tjem.250.173.
Correspondence: Akihiko Satoh, M.D., Ph.D., Department of Gastroenterology, South Miyagi Medical Center, 38-1 Aza-Nishi, Ohgawara-machi, Shibata-gun, Miyagi 989-1253, Japan.
e-mail: asato@bf7.so-net.ne.jp
Part of this work was presented at the Digestive Disease Week in San Diego, 21-24 May 2016, and published in abstract form in Gastrointestinal Endoscopy 2016;83: AB621.

irrigation of the bile duct after stone extraction has been reported to decrease residual CBD stones (Jang et al. 2013; Ahn et al. 2018).

In the present study, we investigated the risk factors of the recurrence of CBD stones. We also evaluated the efficacy of biliary irrigation balloon catheter in cleansing remaining CBD stones and assessed the usefulness of saline solution irrigation for the prevention of stone recurrence.

Methods

Study design

The patients who were hospitalized for CBD stones at South Miyagi Medical Center between September 2012 and June 2018 were consecutively enrolled in the study. The presence of CBD stones had been confirmed before endoscopic retrograde cholangiopancreatography (ERCP) by each of the following imaging modalities: transabdominal ultrasonography (US), endoscopic ultrasonography (EUS), computed tomography (CT) scan, and magnetic resonance cholangiopancreatography (MRCP).

Patients who could not achieve complete clearance of CBD stones on the examination of cholangiography, who had concomitant pancreaticobiliary malignancy, and who underwent endoscopic papillary balloon dilation because of technical difficulties or enhanced risk of EST, were excluded.

The patients were followed in the outpatient clinic after the endoscopic removal of CBD stones, and special attention was directed to episodes of fever and abdominal pain. They were advised to consult us if any symptom occurred. When symptoms occurred or abnormal blood test was noted, an imaging study such as abdominal US, EUS, CT scan or MRCP was carried out. If the recurrence of CBD stone was suspected on the imaging, they were readmitted, and ERCP was performed. The recurrence of stones was defined as those occurring after three months of the initial removal of the stones and confirmed by ERCP. The patients who received the second ERCP for recurrent CBD stones during the observation period were also included in this study and the day of the second ERCP was defined as the start of the follow-up.

Age, sex, CBD diameter, CBD angulation, the presence of periampullary diverticulum, history of cholecystectomy and the need for mechanical lithotripsy (Ohashi et al. 1999; Ando et al. 2003) were evaluated as risk factors for the recurrence of CBD stones. The CBD diameter was measured at its widest point, and the CBD angulation was measured as the sharpest angle using a method of Keizman et al. (2006b).

The study was approved by the Institutional Review Board (No. 30-3), and the research was conducted following the Declaration of Helsinki. Written informed consent to undergo endoscopy and to participate in the study was obtained from each participant.

EST and removal of the stones

ERCP was performed by experienced endoscopists with a duodenoscope (JF260V; Olympus, Tokyo, Japan) under appropriate sedation with midazolam and continuous cardiopulmonary monitoring. Standard sphincterotomy and a subsequent stone extraction with a basket and/or a retrieval balloon with or without mechanical lithotripsy

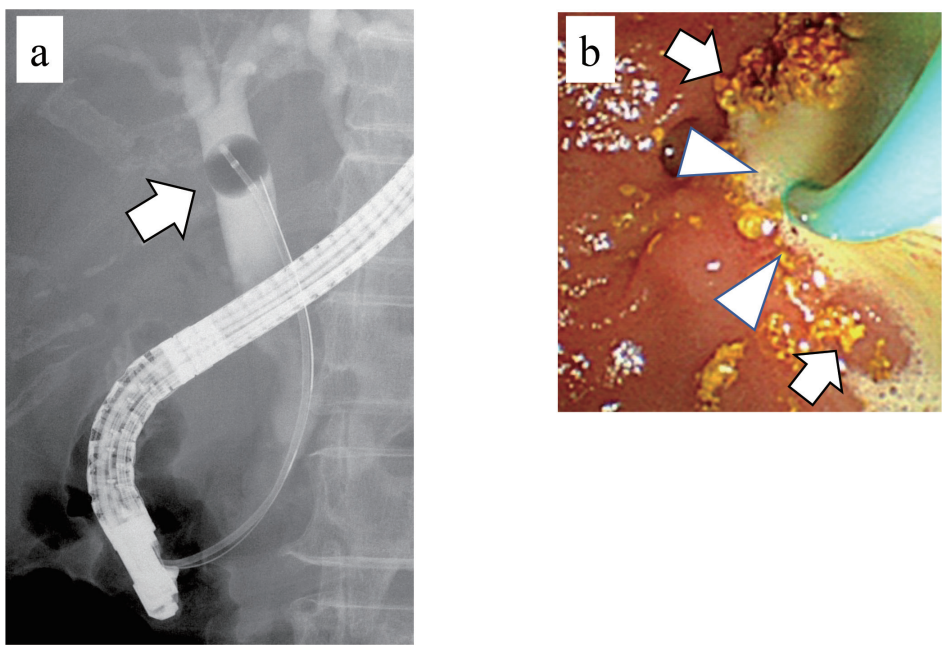

Fig. 1. Saline solution irrigation with the EXT71820F.
(a) The catheter was inserted and the balloon was positioned in the proximal common bile duct (arrow), and the bile duct was washed with 20 ml saline solution five times. (b) The irrigation streamed down out of the papilla (arrowheads) and flushed out brown fragments from the bile duct (arrows).

were performed.

The CBD was considered to be cleared when both the endoscopist and the attending radiologist agreed that no stone was detected on the cholangiogram.

Saline solution irrigation

From April 2014, we performed biliary irrigation after endoscopic removal of CBD stones in some patients with soft brown stones; namely, these stones were more likely to be broken into pieces and cause residua (Fig. 1). We washed out the CBD using the irrigation balloon catheter (EXT71820F, ZEON MEDICAL INC, Tokyo, Japan) that is specially designed to facilitate effective and efficient biliary irrigation (Balloon size 18 mm in diameter, proximal injection). The EXT71820F was inserted and the balloon was positioned in the proximal CBD (Fig. 1a). The bile duct was flushed out with 20 ml saline solution five times (Fig. 1b).

Intraductal ultrasonography (IDUS) for identification of CBD residua

In a small series, IDUS was carried out before and after the irrigation of CBD with a probe (UM-G20-29R, OLYMPUS, Tokyo, Japan; diameter 2.0 mm, frequency 20 MHz) via the transpapillary route. Residuum (stone or sludge) was defined as a hyperechoic material, distinguishable from air bubbles as hyperechoic defects with strong reverberation (Ohashi et al. 1999; Tsuchiya et al. 2008; Ang et al. 2009). The image was traced, and the number of spots in the CBD was counted (Fig. 2). The clearance rate of stone fragments was calculated using IDUS imaging before and after the irrigation of CBD.

Statistical analysis

Continuous variables were analyzed using the Student's t-test or by the Mann-Whitney U test. Categorical variables were compared using Pearson's Chi-square test and Fisher's exact test. The cumulative stone recurrence rate was calculated by the Kaplan-Meier method. The Cox proportional hazards model was used to determine the significant factors related to the recurrence. Variables that were found to have a potential significant association with p value < 0.1 by univariate analysis were selected for the entry into a multiple logistic regression model. Differences were considered statistically significant with a p value < 0.05. Statistical analysis was performed using the statisti-

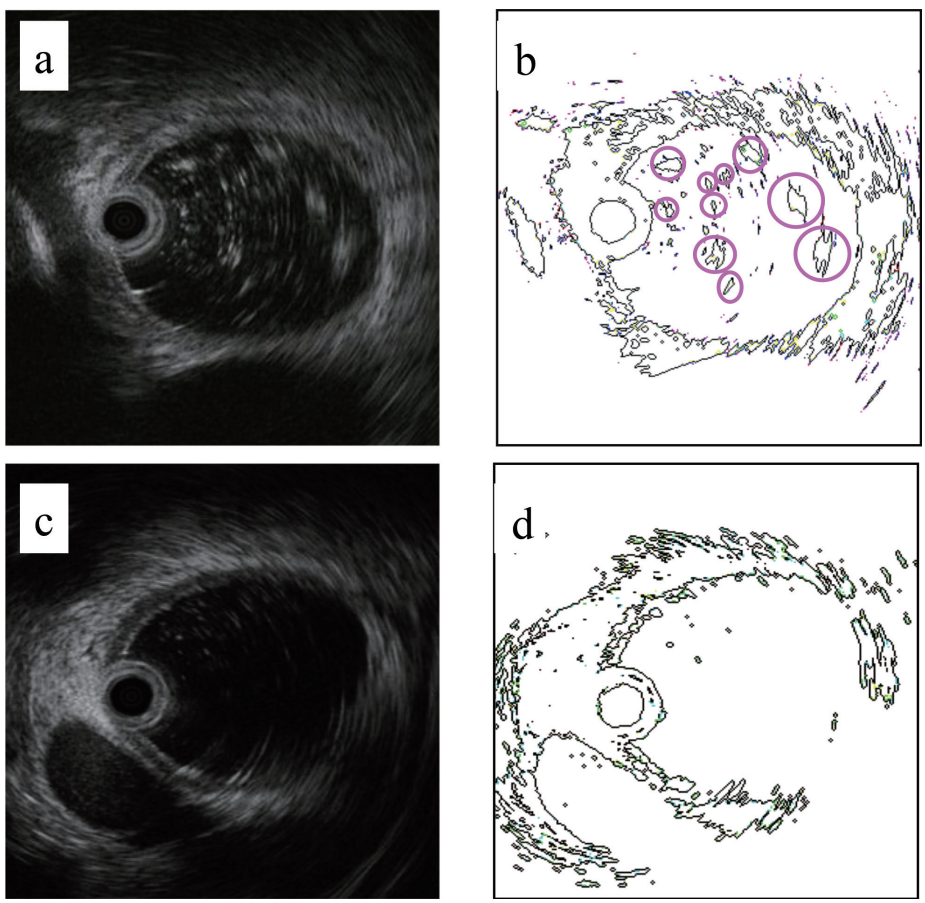

Fig. 2. Intraductal ultrasonography for identification of common bile duct residua.
Shown are representative intraductal ultrasonography images before (a) and after (c) the irrigation. Residuum was identified as a hyperechoic material. The images were traced (b, d), and the number of spots (circles) in the common bile duct was counted.

cal software (ESUMI Co., Ltd., Tokyo, Japan).

Results

During the study period, 609 patients with CBD stones were treated, and 520 patients underwent endoscopic removal of CBD stones. Of them, 43 patients were excluded for the following reasons: 18 by incomplete removal of stones, 17 by use of endoscopic papillary balloon dilation, and eight by concomitant pancreaticobiliary malignancy. Finally, a total of 477 patients were included in this study. Two hundred forty-six were male and 231 were female. Their ages were 80.5 ± 10.8 years.

During the observation period of 6-75 months, the recurrence of CBD stones was observed in 99 patients (20.8%). Among them, eight patients were lost due to causes unrelated to biliary stone, and 14 patients were dropped out of the follow-up. Fig. 3 shows the cumulative non-recurrence of CBD stones. The median time to recurrence of CBD stones was 19.0 months (range 4-72 months), and most of the recurrent stones (96.0%) were soft brown stones.

At the time of CBD stone recurrence, fever and abdominal pain were the two common presenting symptoms (Table 1), but 14 patients were asymptomatic, and five patients were normal in the blood tests. Table 2 provides a summary of the background information of the patients with recurrence and non-recurrence patients. There was no significant difference between the two groups concerning sex, age, or history of prior cholecystectomy.

The results of univariate analysis for the recurrence of CBD stones with each factor are shown in Table 3. The dilated CBD, acute CBD angulation and the need for lithotripsy were associated with significant increases in the recurrence rates. A multivariate analysis identified two independent risk factors: acute CBD angulation (< 135 degrees; Hazard risk [HR] 1.879; 95% confidence interval [CI], 1.014-3.482; $p = 0.045$) and the need for lithotripsy (HR, 3.500; 95% CI, 2.004-6.117; $p < 0.001$). Saline solution irrigation was found to be the factor for the decrease in the CBD stone recurrence (HR, 0.207; 95% CI, 0.070-0.612; $p = 0.004$) (Table 4).

Table 1. Clinical presentation in 99 patients at the time of common bile duct stone recurrence.

	% (n)
Clinical symptoms	86 (85)
Fever	73 (72)
Abdominal pain	71 (70)
Nausea/vomiting	28 (28)
Jaundice	16 (16)
Abnormal data in the blood tests	95 (94)
Liver function	87 (86)
CRP	64 (63)
WBC	76 (75)
Amylase	3 (3)

CRP, C-reactive protein; WBC, white blood cell.

In a small series of patients (n = 24) from the 36 patients, who needed mechanical lithotripsy and were treated by subsequent saline solution irrigation, IDUS was carried out. Although CBD was considered to be cleared on the cholangiography, IDUS detected residual stones or sludge in all cases. As expected, saline solution irrigation (20 ml × five times) with the EXT71820F catheter effectively flushed out residual stones and sludge from the bile

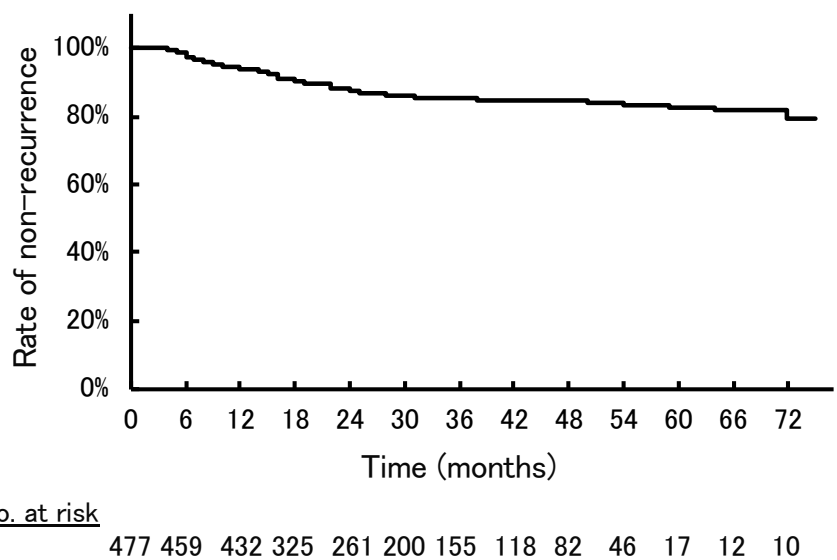

Fig. 3. Kaplan-Meier curves for the cumulative incidence of common bile duct stone recurrence.
During the observation period of 6-75 months, the recurrence of common bile duct (CBD) stones was observed in 99 patients (20.8%). The median time to recurrence of CBD stones was 19.0 months. No.at risk expresses the number of non-recurrence patients whose follow-up extends at least that far into the Kaplan-Meier curves.

Table 2. Patient baseline characteristics.

	Recurrent group (n = 99)	Non-recurrent group (n = 378)	*p* value
Sex (male/female)	55/44	191/187	0.373
Age (years)	81.9 ± 4.9	79.7 ± 10.5	0.099
Prior cholecystectomy: % (n)	14.1 (14)	12.7 (48)	0.693
Maximum CBD diameter (mm)	14.7 ± 5.5	12.5 ± 3.2	< 0.001
CBD angulation (degrees)	142.2 ± 24.0	147.8 ± 11.8	0.013
Periampullary diverticulum: % (n)	62.6 (62)	45.5 (172)	0.004
Need for lithotripsy: % (n)	41.4 (41)	13.5 (51)	< 0.001
Irrigation: % (n)	8.1 (8)	13.8 (52)	0.017

CBD, common bile duct.

Table 3. Univariate analysis for common bile duct stone recurrence.

	Hazard ratio	95% CI	*p* value
Age ≥ 75 (years)	1.207	0.758-1.922	0.427
Gender (male)	1.224	0.784-1.909	0.430
CBD diameter > 15 mm	1.713	1.147-2.559	0.009
CBD angulation < 135º	1.769	1.130-2.769	0.013
Periampullary diverticulum	1.499	0.989-2.270	0.056
Need for lithotripsy	2.313	1.522-3.515	< 0.001
Irrigation	0.475	0.229-0.987	0.046

CBD, common bile duct; 95% CI, 95% confidence interval.

Table 4. Multivariate logistic regression analysis for common bile duct stone recurrence.

	Hazard ratio	95% CI	*p* value
CBD diameter > 15 mm	1.667	0.979-2.841	0.060
CBD angulation < 135º	1.879	1.014-3.482	0.045
Periampullary diverticulum	1.514	0.848-2.703	0.161
Need for lithotripsy	3.500	2.004-6.117	< 0.001
Irrigation	0.207	0.070-0.612	0.004

CBD, common bile duct; 95% CI, 95% confidence interval.

duct (Fig. 2). The clearance rate of stone fragments confirmed by IDUS was 92.4 ± 6.3%.

We retrospectively analyzed 92 patients who required mechanical lithotripsy: 41 patients with recurrent CBD stones and 51 patients without recurrence (Table 2). These patients were divided into two groups: patients treated by subsequent saline solution irrigation (S group, 36 patients) and not treated by irrigation (N group, 56 patients). As shown in Fig. 4, saline solution irrigation after stone removal significantly decreased the recurrence of CBD stones ($p = 0.001$). The recurrence rate of CBD stones at 36 months after the treatment was 13.9% (n = 5) in the S group and 44.6% (n = 25) in the N group.

Discussion

In the present study, we showed that acute angulated CBD and the need for mechanical lithotripsy were significantly related to the recurrence of CBD stones after EST.

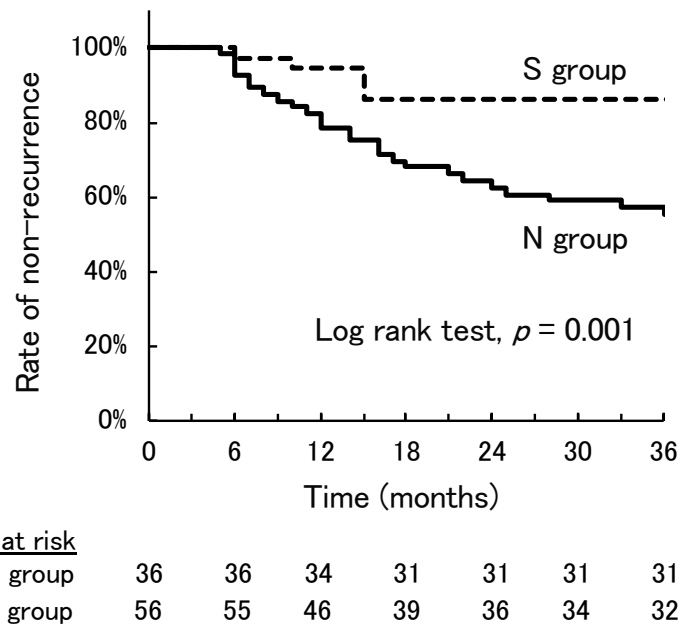

Fig. 4. Kaplan-Meier curves showing the rate of common bile duct stone recurrence in patients requiring lithotripsy. Patients were treated by subsequent saline solution irrigation (S group, 36 patients) and not treated by irrigation (N group, 56 patients). Saline solution irrigation after endoscopic removal of common bile duct (CBD) stones significantly decreased the recurrence of CBD stones (log rank test, $p = 0.001$). The recurrence rate of CBD stones at 36 months after the treatment was 13.9% (n = 5) in the S group and 44.6% (n = 25) in the N group. No. at risk expresses the number of non-recurrence patients whose follow-up extends at least that far into the Kaplan-Meier curves.

The risk factors of recurrent stone were consistent with previous results (Ohashi et al. 1999; Ando et al. 2003; Keizman et al. 2006b). Furthermore, we found that saline solution irrigation with a specially designed biliary catheter reduced the recurrence of CBD stones in the patients who had been treated with lithotripsy. To the best of our knowledge, this is the first study that shows the preventive effect of saline solution irrigation on the recurrence of CBD stones.

Small stone fragments left after lithotripsy may act as a nidus for the stone recurrence (Ando et al. 2003). It had been assumed that even if small stone fragments remained after EST, they would pass spontaneously and not cause any biliary problems. However, studies using IDUS have shown that cholangiography-negative residual small stones may be a cause for stone growth and a complete stone clearance decreases the recurrence rate of CBD stones (Tsuchiya et al. 2008; Jang et al. 2013). The low sensitivity of the cholangiography to detect small stones causes an incomplete clearance of CBD stones (Ohashi et al. 1999; Das et al. 2001; Tseng et al. 2001; Linghu et al. 2004; Moon et al. 2005; Endo et al. 2011; Kim et al. 2014; Ahn et al. 2018). In this study, IDUS detected residual small stones or sludge in all cases who needed mechanical lithotripsy although CBD was considered to be cleared on the cholangiography. It is, therefore, important to flush out tiny fragments from the bile duct even if no stone was seen on the cholangiogram.

We showed that the biliary irrigation was extremely useful in clearing the small residual stones; the clearance rate with 100-ml saline solution irrigation was 92.4%, confirmed by IDUS. There were three clinical trials for irrigation of the CBD using with standard catheters (Ang et al. 2009; Jang et al. 2013; Ahn et al. 2018). Ang et al. (2009) reported that a mean of 48 mL saline and an additional 50 ml irrigation was sufficient to flush out the residual CBD stones. Jang et al. (2013) repeated the injection and aspiration with saline until the retained stones or sludge were cleared on the cholangiography, and the procedure needed approximately 7 min. In our study, the irrigation procedure (20 ml saline solution × five times) with a specially designed irrigation catheter required only 2-3 minutes.

Importantly, the irrigation procedure was safe. Irrigation may increase upstream bile duct pressure and cause cholangitis. Whereas there is no fear with the catheter in which the irrigation streams down out of the papilla and the balloon positioned in the proximal CBD blocks the upstream flow. Practically, there was no increase in adverse events in our series.

There are some limitations in the present study. This was carried out over the introduction of biliary irrigation and so the bias due to the time of entry must be taken into consideration. However, there were no changes before and after the introduction of irrigation in terms of endoscopic procedures for stone removal, patients' risk factors, nor imaging quality. Therefore, we think the time of entry might have little influence on the data analysis. Second, our patients were relatively old and had mostly soft brown stones which were considered to be primary CBD stones. CBD stones in Western countries are typically secondary ones that migrate from the gallbladder (Malet et al. 1988). The difference in the character of stones may affect the effect of biliary irrigation. Third, this was carried out at a single institution, and it was not a randomized controlled trial. Future prospective studies are warranted to apply our findings to practice and confirm the clinical significance of biliary irrigation.

In conclusion, our study demonstrates that the need for mechanical lithotripsy is strongly related to CBD stone recurrence after EST, and a subsequent saline solution irrigation with a specially designed biliary catheter may effectively remove the residua after lithotripsy and decrease the recurrence of biliary stones.

Acknowledgments

The authors wish to acknowledge Dr. Hiroo Naito, Director of South Miyagi Medical Center, for years of encouragement and advice.

Conflicts of Interest

The authors declare no conflict of interest.

References

Ahn, D.W., Lee, S.H., Paik, W.H., Song, B.J., Park, J.M., Kim, J., Jeong, J.B., Hwang, J.H., Ryu, J.K. & Kim, Y.T. (2018) Effects of saline irrigation of the bile duct to reduce the rate of residual common bile duct stones: a multicenter, prospective, randomized study. *Am. J. Gastroenterol.*, **113**, 548-555.

Ando, T., Tsuyuguchi, T., Okugawa, T., Saito, M., Ishihara, T., Yamaguchi, T. & Saisho, H. (2003) Risk factors for recurrent bile duct stones after endoscopic papillotomy. *Gut*, **52**, 116-121.

Ang, T.L., Teo, E.K., Fock, K.M. & Lyn Tan, J.Y. (2009) Are there roles for intraductal US and saline solution irrigation in ensuring complete clearance of common bile duct stones? *Gastrointest. Endosc.*, **69**, 1276-1281.

Das, A., Isenberg, G., Wong, R.C., Sivak, M.V., Jr. & Chak, A. (2001) Wire-guided intraductal US: an adjunct to ERCP in the management of bile duct stones. *Gastrointest. Endosc.*, **54**, 31-36.

Doi, S., Yasuda, I., Mukai, T., Iwashita, T., Uemura, S., Yamauchi, T., Nakashima, M., Adachi, S., Shimizu, M., Tomita, E., Itoi, T. & Moriwaki, H. (2013) Comparison of long-term outcomes after endoscopic sphincterotomy versus endoscopic papillary balloon dilation: a propensity score-based cohort analysis. *J. Gastroenterol.*, **48**, 1090-1096.

Endo, T., Ito, K., Fujita, N., Noda, Y., Kobayashi, G., Obana, T., Horaguchi, J., Koshita, S., Kanno, Y. & Ogawa, T. (2011) Intraductal ultrasonography in the diagnosis of bile duct stones: when and whom? *Dig. Endosc.*, **23**, 173-175.

Jang, S.E., Ahn, D.W., Lee, S.H., Lee, B.S., Jeong, J.B., Hwang, J.H., Ryu, J.K., Kim, Y.T., Lee, K.H. & Kim, Y.H. (2013) Preventive saline irrigation of the bile duct after the endoscopic removal of common bile duct stones. *Dig. Dis. Sci.*, **58**, 2353-2360.

Keizman, D., Ish Shalom, M. & Konikoff, F.M. (2006a) Recurrent symptomatic common bile duct stones after endoscopic stone extraction in elderly patients. *Gastrointest. Endosc.*, **64**, 60-65.

Keizman, D., Shalom, M.I. & Konikoff, F.M. (2006b) An angulated common bile duct predisposes to recurrent symptomatic bile duct stones after endoscopic stone extraction. *Surg. Endosc.*, **20**, 1594-1599.

Kim, D.C., Moon, J.H., Choi, H.J., Chun, A.R., Lee, Y.N., Lee, M.H., Lee, T.H., Cha, S.W., Kim, S.G., Kim, Y.S., Cho, Y.D., Park, S.H. & Lee, H.K. (2014) Usefulness of intraductal ultrasonography in icteric patients with highly suspected choledocholithiasis showing normal endoscopic retrograde cholangiopancreatography. *Dig. Dis. Sci.*, **59**, 1902-1908.

Kim, D.I., Kim, M.H., Lee, S.K., Seo, D.W., Choi, W.B., Lee, S.S., Park, H.J., Joo, Y.H., Yoo, K.S., Kim, H.J. & Min, Y.I. (2001) Risk factors for recurrence of primary bile duct stones after endoscopic biliary sphincterotomy. *Gastrointest. Endosc.*, **54**, 42-48.

Konstantakis, C., Triantos, C., Theopistos, V., Theocharis, G., Maroulis, I., Diamantopoulou, G. & Thomopoulos, K. (2017) Recurrence of choledocholithiasis following endoscopic bile duct clearance: long term results and factors associated with recurrent bile duct stones. *World J. Gastrointest. Endosc.*, **9**, 26-33.

Linghu, E.Q., Cheng, L.F., Wang, X.D., Wang, Z.Q., Yang, Y.S., Li, W., Cai, F.C., Wang, H.Z., Du, H. & Meng, J.Y. (2004) Intraductal ultrasonography and endoscopic retrograde cholangiography in diagnosis of extrahepatic bile duct stones: a comparative study. *Hepatobiliary Pancreat. Dis. Int.*, **3**, 129-132.

Malet, P.F., Dabezies, M.A., Huang, G.H., Long, W.B., Gadacz, T.R. & Soloway, R.D. (1988) Quantitative infrared spectroscopy of common bile duct gallstones. *Gastroenterology*, **94**, 1217-1221.

Moon, J.H., Cho, Y.D., Cha, S.W., Cheon, Y.K., Ahn, H.C., Kim, Y.S., Kim, Y.S., Lee, J.S., Lee, M.S., Lee, H.K., Shim, C.S. & Kim, B.S. (2005) The detection of bile duct stones in suspected biliary pancreatitis: comparison of MRCP, ERCP, and intraductal US. *Am. J. Gastroenterol.*, **100**, 1051-1057.

Ohashi, A., Ueno, N., Tamada, K., Tomiyama, T., Wada, S., Miyata, T., Nishizono, T., Tano, S., Aizawa, T., Ido, K. & Kimura, K. (1999) Assessment of residual bile duct stones with use of intraductal US during endoscopic balloon sphincteroplasty: comparison with balloon cholangiography. *Gastrointest. Endosc.*, **49**, 328-333.

Pereira-Lima, J.C., Jakobs, R., Winter, U.H., Benz, C., Martin, W.R., Adamek, H.E. & Riemann, J.F. (1998) Long-term results (7 to 10 years) of endoscopic papillotomy for choledocholithiasis. Multivariate analysis of prognostic factors for the recurrence of biliary symptoms. *Gastrointest. Endosc.*, **48**, 457-464.

Prat, F., Malak, N.A., Pelletier, G., Buffet, C., Fritsch, J., Choury, A.D., Altman, C., Liguory, C. & Etienne, J.P. (1996) Biliary symptoms and complications more than 8 years after endoscopic sphincterotomy for choledocholithiasis. *Gastroenterology*, **110**, 894-899.

Sugiyama, M. & Atomi, Y. (2002) Risk factors predictive of late complications after endoscopic sphincterotomy for bile duct stones: long-term (more than 10 years) follow-up study. *Am. J. Gastroenterol.*, **97**, 2763-2767.

Tazuma, S., Kanno, K., Kubota, K., Tsuyuguchi, T., Kamisawa, T., Isayama, H., Nakagohri, T. & Inui, K. (2015) Report on the 2013 national cholelithiasis survey in Japan. *J. Hepatobiliary Pancreat. Sci.*, **22**, 392-395.

Tseng, L.J., Jao, Y.T., Mo, L.R. & Lin, R.C. (2001) Over-the-wire US catheter probe as an adjunct to ERCP in the detection of choledocholithiasis. *Gastrointest. Endosc.*, **54**, 720-723.

Tsuchiya, S., Tsuyuguchi, T., Sakai, Y., Sugiyama, H., Miyagawa, K., Fukuda, Y., Ando, T., Saisho, H. & Yokosuka, O. (2008) Clinical utility of intraductal US to decrease early recurrence rate of common bile duct stones after endoscopic papillotomy. *J. Gastroenterol. Hepatol.*, **23**, 1590-1595.

Ueno, N., Ozawa, Y. & Aizawa, T. (2003) Prognostic factors for recurrence of bile duct stones after endoscopic treatment by sphincter dilation. *Gastrointest. Endosc*., **58**, 336-340.