

## Biliary stenting as alternative therapy to stone clearance in elderly patients with bile duct stones

Akira Horiuchi, Masashi Kajiyama, Yasuyuki Ichise, Haruyo Tada, Naoyuki Fujiwara, Naoki Tanaka

Digestive Disease Center, Showa Inan General Hospital, Komagane, Japan.

### Abstract

**Background and study aims :** Endoscopic retrograde cholangiopancreatography with stone retrieval following endoscopic sphincterotomy (ES) is the standard method for the management of choledocholithiasis. However, biliary stenting is used to treat patients with endoscopically irretrievable bile duct stones, especially elderly and high-risk patients. The aim of this study was to evaluate the benefits and risks of biliary stenting versus stone clearance following ES in the management of choledocholithiasis.

**Patients and methods :** Between January 2010 and December 2012, 165 patients with common bile duct stones who underwent biliary stenting or stone clearance following ES were enrolled. One 7 Fr. double-pigtail plastic stent was placed without ES or stone extraction. The procedure time, hospitalization period, adverse events, additional endoscopic interventions required and one-year mortality were evaluated retrospectively.

**Results :** Ninety-nine and 66 patients were included in stenting group and in stone clearance group, respectively. Except for age, number of stones, and use of antithrombotic agents in the stent group, there were no statistically significant difference between groups. The average procedure time and hospitalization period in the stenting group were significantly shorter than those in stone clearance group (mean 21 min vs. 43.9 min,  $P < 0.0001$  ; 3.8 days vs. 6.5 days,  $P < 0.0001$ ). No significant differences were seen in adverse events and additional endoscopic interventions required between both groups for at least a 1.5-year follow-up. No one-year mortality occurred.

**Conclusions :** Biliary stenting using a double-pigtail stent proved to be a useful alternative therapy to stone clearance following ES in the management of choledocholithiasis in elderly patients. (*Acta gastroenterol. belg.*, 2014, 77, 297-301).

**Key words :** biliary stenting, choledocholithiasis, endoscopic sphincterotomy, ERCP.

**Abbreviations :** ERCP, endoscopic retrograde cholangiopancreatography ; ES, endoscopic sphincterotomy ; CBD, common bile duct.

### Introduction

Choledocholithiasis is one of the most common gastrointestinal diseases seen in clinical therapeutic endoscopy practice. Endoscopic retrograde cholangiopancreatography (ERCP) with stone retrieval following endoscopic sphincterotomy (ES) is the standard method for the management of choledocholithiasis. When common bile duct (CBD) stones cannot be completely removed, biliary stenting using is often performed to prevent stones impaction (1). We previously showed that large stones became smaller and/or disappeared following biliary stenting (2) and was consistent with other reports that indwelling endoprosthesis may affect stone size or lead to fragmentation (3,4,5).

Stone extraction following ES is widely performed for patients with CBD stones with an 80-90% success rate and with an adverse event rate of less than 10% (6,7,8). The technical difficulty of stone removal from CBD depends on the size and number of stones ; large stones (i.e., of more than 20 mm) often must be fragmented by mechanical lithotripsy prior to removal (9,10). With large or multiple stone the procedure is often prolonged and may require many sessions to clear difficult stones. It is sometimes difficult to perform complete extraction of CBD stones in elderly patients due to the morphological matters of large bile duct (> 15 mm in diameter) or oblique bile duct (11).

In addition, treatment of elderly patients is often complicated by other medical conditions and the use of anti-coagulants and/or antiplatelet agents for treatment or prevention of cardiovascular or cerebrovascular diseases. The current practice guidelines for ERCP in patients requiring long-term anticoagulation considers ES to be a high-risk procedure and recommends anticoagulation be temporarily discontinued (12). Temporary interruption of anti-coagulants and/or antiplatelet agents for endoscopic procedures is not without its own problems as interruption is a concern for a thromboembolic risk. Our approach has been to perform ERCP without stopping anti-coagulants and/or antiplatelet agents.

The aim of this study was to retrospectively evaluate the benefits and risks of biliary stenting alone versus stone clearance following ES in the management of CBD stones.

### Patients and Methods

#### Patients

This retrospective study was approved by the ethics committee at our hospital. Inclusion criteria were patients underwent ERCP at Showa Inan General Hospital based on the endoscopic filing system between January 2010 and December 2012. Patients with acute suppurative cholangitis were included. The inclusion criteria

Correspondence to : Akira Horiuchi, M.D., Digestive Disease Center, Showa Inan General Hospital, 3230 Akaho, Komagane 399-4117, Japan.  
E-mail : horiuchi.akira@sihp.jp

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were at least 1-year follow-up after the initial endoscopic intervention. Exclusion criteria included an age less than 20 years old, pregnant, and American Society of Anesthesiologists class III or IV. Of 308 patients who underwent ERCP primary stone extraction following ES or biliary stenting was attempted in 194 patients (63%) with CBD stones. 14 patients required at least two sessions of ERCP for stone clearance and 7 patients required biliary stenting following stone retrieval to prevent the impaction of CBD stones. Eight patients had severe comorbidity such as cardiovascular or cerebrovascular diseases. After excluding these 29 patients 165 patients with CBD stones were finally enrolled. In this study period endoscopic nasobiliary drainage tube placement was not performed.

#### *Procedure*

In biliary stenting group, a 7 Fr. double-pigtail side hole plastic stent (Olympus, Tokyo, Japan) was placed without ES or stone extraction. For stone clearance, following ES the stones were fragmented using an endoscopic mechanical lithotripter and basket/balloon catheter. No oral dissolution agents were prescribed in either group. Patients' charts were retrospectively reviewed. In addition to patient demographics, all details regarding clinical presentation, stone characteristics, all interventions and adverse events were recorded. With all enrolled patients the follow-up was performed by means of either direct patients or their family contact by telephone to obtain data on one-year mortality. With regard to the diseases related to the bile duct stone any patients did not admit other hospitals during the follow-up period.

#### *Measurement of number of CBD stones and CBD diameters*

The diameter of CBD stones was measured on the radiographs. For patients with multiple CBD stones, all stones were measured and the number of the stones was counted. The radiograph magnification was corrected by using the endoscope diameter as a reference value and the stone diameter was calculated as : Actual stone diameter = measured stone diameter times actual endoscope diameter/measured endoscope diameter. The radiographs were reviewed independently by two of the authors and the measurements were averaged.

#### *Outcome variables*

The procedure time, hospitalization period, adverse events, additional endoscopic interventions required and one-year mortality were evaluated. In addition, clinical presentation such as abdominal pain and fever and laboratory parameters at 2 days after ERCP were assessed.

#### *Statistics*

Statistical tests to compare the measured results for the two groups were as follows : the Chi-square test, with

Yates' correction for continuity where appropriate, was used for comparison of categorical data. Fisher's exact test was used when the numbers were small. For parametric data, the Student's *t*-test was used when 2 means were compared. Differences were considered significant if the *P* value was less than 0.05. Statistical analysis was performed by using JMP® 9.0.2 version software (SAS Institute Inc.).

## **Results**

Ninety-nine and 66 patients who underwent biliary stenting alone (stenting group) and stone clearance following ES (clearance group) were enrolled, respectively (Table 1). The patients enrolled in stenting group were significantly older than those in stone clearance group (mean age 78.2 (range, 56-92) vs. 67 (range, 44-81),  $P < 0.0001$ ). Twenty patients (20%) in stenting group and 12 (18%) in stone clearance group had previous cholecystectomy. All 54 patients who took anticoagulants and/or antiplatelet agents for the prevention of recurrence of cardiovascular or cerebrovascular diseases were enrolled in stenting group.

On admission, clinical presentation such as right upper quadrant pain, jaundice, and fever was seen similarly in both groups. All laboratory parameters were not significantly different between groups (Table 1). The numbers of patients with acute suppurative cholangitis were similar in both groups. Although the mean size of bile duct stones was almost the same in both groups, the mean number of bile duct stones in stenting group was higher than in the stone clearance group (4.0 vs. 2.1,  $P < 0.0028$ ). Regardless of endoscopic interventions, clinical presentation such as abdominal pain and fever and laboratory parameters promptly improved at 2 days after ERCP. No significant differences were seen in both groups (Table 2).

Both the mean procedure time and hospitalization period in the stenting group were significantly shorter than those in stone clearance following ST group (21 min vs. 43.9 min,  $P < 0.0001$  ; 3.8 days vs. 6.5 days,  $P < 0.0001$ ) (Table 3). Cholangitis (3 patients) occurred following stent placement whereas cholangitis (8 patients) and pancreatitis (3 patients) occurred in the stone clearance group ( $P = 0.079$ ). In addition, there were no significant differences in additional endoscopic interventions required between both groups. Biliary stenting alone enabled 95% of patients not to require any additional interventions for at least 1.5 years. On the other hand, 6 patients (10%) in the stone clearance group required stenting or additional stone retrieval. No one-year mortality occurred in both groups.

## **Discussion**

Biliary stenting alone equaled or surpassed stone clearance following ES in the management of CBD stones in elderly patients, resulting from the data that

Table 1. — Clinical characteristics of patients enrolled

	Stenting group (N = 99)	Clearance group (N = 66)	p value
Mean (SD) age (y)	78.2 (13)	67.0 (16)	< 0.0001
Male gender	74 (74%)	53 (80%)	0.71
Prior cholecystectomy	20 (20%)	12 (18%)	0.16
Anticoagulants/antiplatelet agents use	54 (55%)	0 (0%)	
Presence of gallstone	32 (32%)	20 (30%)	0.80
Clinical presentation			
Right upper quadrant pain	99 (100%)	66 (100%)	
Jaundice	93 (94%)	59 (89%)	0.32
Fever	86 (87%)	56 (85%)	0.74
Acute suppurative cholangitis	14 (14%)	8 (11%)	0.73
Laboratory parameters [mean (SD)]			
Leukocyte count, X10 <sup>3</sup>	9.9 (4)	10.6 (3)	0.69
Total bilirubin, mg/dl	4.2 (2)	4.4 (2)	0.59
Alkaline phosphatase, IU/L	1232 (756)	1203 (882)	0.47
Aspartate aminotransferase, IU/L	371 (210)	330 (123)	0.28
Bile duct stones [mean (SD)]			
Number	4.0 (4.5)	2.1 (2.3)	0.0028
Size (mm)	12.0 (4.4)	11.8 (6.6)	0.42

Values are numbers of patients (percentages) except for mean age, laboratory parameters and bile duct stones.

Table 2. — Clinical findings and laboratory findings at 2 days after ERCP

	Stenting group (N = 99)	Clearance group (N = 66)	p value
Clinical presentation			
Abdominal pain	5 (5%)	8 (12%)	0.18
Fever	0	0	
Laboratory parameters [mean (SD)]			
Leukocyte count, X10 <sup>3</sup>	5.0 (2)	5.4 (2)	0.68
Total bilirubin, mg/dl	1.5 (0.9)	2.5 (2)	0.94
Alkaline phosphatase, IU/L	778 (586)	513 (410)	0.11
Aspartate aminotransferase, IU/L	84 (49)	100 (61)	0.76

Values are numbers of patients (percentages) except for laboratory parameters.

both the average procedure time and hospitalization period in the stenting group were significantly shorter than those in stone clearance group. Importantly, the number of additional endoscopic interventions required over the following year did not differ between groups.

Biliary stenting was first introduced to treat patients with endoscopically irretrievable CBD stones, especially elderly and high-risk patients. Its permanent use has been limited due to many concerns such as recurrent cholangitis, occlusion and stent migration-related gastrointestinal tract perforation (13,14). Its advantages are a success rate of nearly 100% and low early morbidity (15,16). Stent migration remains a potential problem. Most migrated stents pass into the bowel lumen or remain in it for a long period of time and organ perforation resulting from

plastic biliary stents has proven to be very uncommon (17).

Recurrent cholangitis has been regarded the most frequent adverse event in patients with long-term indwelling biliary endoprotheses, being reported in 3.5-40% of patients (13,14,15). In patients followed-up for 3 years, the late adverse event rate was 40% and the mortality rate due to biliary sepsis was 6% (18). Due to the long-term risk of cholangitis, biliary stent insertion alone has often been restricted to treatment of bile duct stones in elderly patients and high-risk patients with short life expectancy (15,18). We used a double pigtail plastic stent as alternative therapy to stone clearance in this study and it is unknown whether a difference of the type of stent (i.e., a straight stent) would have provided similar

Table 3. — Clinical outcomes and adverse events during and after interventions

	Stenting group (N = 99)	Clearance group (N = 66)	p value
Mean observation period (SD) (months)	18 (7)	19 (9)	0.66
Mean procedure time (SD) (min)	21.0 (5.3)	43.9 (15)	< 0.0001
Mean hospitalization period (SD) (day)	3.8 (1.1)	6.5 (1.5)	< 0.0001
Adverse events			
Bleeding	0	0	
Perforation	0	0	
Migration	0	–	
Cholangitis	3 (4%)	8 (12%)	0.079
Pancreatitis	0	3 (5%)	0.080
Additional endoscopic interventions required during the observation period			
None	95 (95%)	60 (90%)	0.89
Stent	3 (3%)	3 (5%)	
Stone clearance	2 (2%)	3 (5%)	
One-year mortality	0	0	

Values are numbers (percentages) of patients except for observation period, procedure time, and hospitalization period.

results. Of interest, we had no occurrence of cholangitis over the more than 1.5 years of observation and no stent migration was observed. Studies are needed to address whether the type of stent is a critical factor in relation to the recurrence of cholangitis or stent migration when used without ES or stone extraction. In addition, it should be addressed whether the outcome would be much better if the stent were changed at some intervals.

Many patients with difficult CBD stones are of older age or have severe associated diseases. For these cases, alternative methods such as EHL or ESWL are often used and it has been reported that peroral endoscopic EHL is effective for managing difficult biliary stone disease with fragmentation rates of 96% and stone clearance rates of 90% (19). These procedures, however, are time-consuming and require delicate instruments, which are often not available in general institutions. The data that the mean procedure time in the stenting group was significantly shorter than that in stone clearance group suggests that this is an excellent approach for elderly and high-risk patients. Then, after the acute episode has resolved considerations can be made for long-term management. However, the most appropriate method for long-term follow-up is unclear when biliary stenting is performed as a stand-alone therapy for choledocholithiasis. We advise that if right upper quadrant pain, jaundice, or fever develops, the patients should visit the clinic as soon as possible.

In our previous study, the short-term use of a 7Fr. double-pigtail stent for 2 months was associated with reduction in stone size and number and even clearance without the addition of oral ursodeoxycholic acid and

terpene (2). The placement of just one stent of the same type was also performed in this study. The shape of double-pigtail may associated with the prevention of recurrent cholangitis, which is based on the speculated mechanism that the shape of double-pigtail may synchronize the bowel movement much better than the straight type of the stent, irrespective of its patency, resulting in the prevention of impaction of CBD stones. This mechanism may explain why biliary stenting alone enabled 95% of patients not to require any additional interventions for at least 1.5 years, although the patency of plastic stent is generally thought to be at least 3 to 4 months.

Our study has some limitations. This study is a retrospective study, with the expected bias this can lead to. The use of one double-pigtail plastic stent without ES or stone extraction was based on the discretion of the endoscopist. It is unclear why the endoscopist chose biliary stenting during the study period and there is a potential for selection bias.

In conclusion, biliary stenting using a double-pigtail stent proved to be a useful alternative therapy to stone clearance following ES in the management of CBD stones in elderly patients. This method appears to be both effective and safe for the management of difficult CBD stones and does not require the use of any special instruments.

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