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## Original

# Safety and Utility of Endoscopic Removal of Common Bile Duct Stones in the Elderly

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**Abstract** : We investigated the safety and utility of endoscopic removal of common bile duct stones (CBDS) in the elderly. In all, 253 patients with CBDS who underwent endoscopic retrograde cholangiopancreatography (ERCP) between January 2007 and December 2011 at Showa University Hospital were evaluated retrospectively. The median age of the patients was 75 years; thus, we divided patients into two groups, those aged  $\geq 75$  years (Group A;  $n = 134$ ) and those aged  $< 75$  years (Group B;  $n = 119$ ). Patients in Group A had significantly higher rates of endoscopic sphincterotomy in palliative ERCP (24.8% vs. 10.7%;  $p = 0.008$ ) and palliative removal of CBDS (34.8% vs. 20.9%;  $p = 0.015$ ) than patients in Group B. However, the median dose of flunitrazepam was significantly lower for patients in Group A than Group B (1 vs. 1.4 mg, respectively;  $p < 0.001$ ). The rate of use of pentazocine (18.5% vs. 54.7%;  $p < 0.001$ ) and scopolamine butylbromide (6.2% vs. 23.9%;  $p < 0.01$ ) was significantly lower in Group A patients, whereas the use of glucagon was significantly higher in this group (43.8 vs. 15.4%;  $p < 0.001$ ). There were no significant differences in the rate of successful endoscopic removal of CBDS, treatment time, complications, and the recurrence of CBDS between the two groups. Endoscopic removal of CBDS in the elderly is a safe procedure with good outcomes if the appropriate treatment is selected.

**Key words** : common bile duct stones (CBDS), elderly, endoscopic removal, endoscopic retrograde cholangiopancreatography, endoscopic sphincterotomy

## Introduction

Advances in medical care, nutrition, and hygiene have resulted in an increased lifespan of the Japanese population. This aging of society will likely increase the incidence of age-related diseases. Thus, the need for endoscopic removal of common bile duct stones (CBDS) in the elderly is likely to increase, because CBDS are more common with aging<sup>1)</sup>. Previous reports suggest that the elderly can safely undergo endoscopic procedures<sup>2-5)</sup>. However, the risk of complications during endoscopic procedures is higher in the elderly than in young patients because of reduced

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cardiopulmonary and immune function.

The aim of the present study was to evaluate the safety and utility of endoscopic removal of CBDS in elderly patients at Showa University Hospital.

## **Methodology**

### *Patients*

Two hundred and fifty-three patients assessed as having CBDS by abdominal ultrasonography, computed tomography, magnetic resonance cholangiopancreatography, or endoscopic ultrasonography were evaluated retrospectively. All patients had a naïve papilla of Vater and had undergone endoscopic retrograde cholangiopancreatography (ERCP) between January 2007 and December 2011 at Showa University Hospital. Information was obtained for all patients regarding their age, gender, diameter of the common bile duct, the number and diameter of CBDS, and the prevalence of gallstones. In addition, we determined, the rate of cholangitis or cholecystitis, the use of oral antithrombotic agents, the rate of endoscopic sphincterotomy (EST) or endoscopic papillary balloon dilation (EPBD), whether the removal of CBDS was successful, the time required for endoscopic removal of CBDS and the endoscopic procedure overall, complications after ERCP, and the rate of recurrence of CBDS.

### *Procedures*

Written informed consent was obtained from all patients for the endoscopic removal of CBDS. This study was approved by the Ethics Review Board of Showa University Hospital.

ERCP was performed with patients in the prone position. Patients were sedated with benzodiazepines; pentazocine was used as an analgesic and scopolamine butylbromide or glucagon were used as antispasmodic agents. If patients were receiving antithrombotic agents, the procedure was performed after discontinuation of the drug.

In most cases, ERCP was performed using a duodenoscope (JF260V; Olympus Medical Systems, Tokyo, Japan), whereas a gastroscope or colonoscope was used in patients with reconstructed gastrointestinal anatomy (Billroth II or Roux-en-Y). The sphincterotomes used for EST were the Autotome RX (Boston Scientific, Natick, MA, USA) and the CleverCut 3V (Olympus Medical Systems); the biliary balloon dilator for EPBD was the Max Force TTS (Boston Scientific); and the guidewire system used was the Jagwire Plus (Boston Scientific) or VisiGlide (Olympus Medical Systems).

In most cases, EST with a small or medium-sized incision of the papilla of Vater was performed for endoscopic removal of CBDS. When EST could not be performed, such as in patients with coagulopathies, those taking antithrombotic medication or those with reconstructed gastrointestinal anatomy (Billroth-II or Roux-en-Y), EPBD was performed. In cases of large stones, EPBD with EST was performed. Balloon and basket catheters or mechanical lithotripsy were used for the endoscopic removal of CBDS.

Patients with acute moderate or severe cholangitis, as determined according to the Flowcharts for the diagnosis and treatment of acute cholangitis and cholecystitis: Tokyo Guidelines<sup>6)</sup>, under-

Table 1. Baseline clinical characteristics and therapeutic results for 253 patients with common bile duct stones who underwent endoscopic retrograde cholangiopancreatography

Age (years)	75 (17–97)
No. men/women	141/112
Diameter of the common bile duct (mm)	11 (4–25)
CBDS diameter	
< 10 mm	65.2% (165/253)
≥ 10 mm	34.8% (88/253)
No. single/multiple CBDS	139/114
Presence of gallstones	67.6% (171/253)
Cholangitis or cholecystitis	56.2% (132/253)
Use of oral antithrombotic agents	8.3% (21/253)
EST	83.8% (212/253)
EPBD	5.1% (13/253)
EPBD with EST	9.9% (25/253)
Successful endoscopic removal of CBDS	97.6% (247/253)
Type of endoscopic removal of CBDS	
Emergency	71.7% (177/247)
Palliative	28.3% (70/247)
Duration of ERCP (min)	30 (7–90)
Post-ERCP complications	
Pancreatitis	2.4% (6/253)
Bleeding	2.8% (7/253)
Perforation	0.8% (2/253)
Recurrence of CBDS	5.6% (14/248)

Unless indicated otherwise, data are given as the median (range) or as a percentage with the number of patients given in parentheses, as appropriate.

CBDS, common bile duct stones; EST, endoscopic sphincterotomy (EST); EPBD, endoscopic papillary balloon dilation; ERCP, endoscopic retrograde cholangiopancreatography.

went emergency ERCP with antibiotic and fluid therapy. Palliative ERCP was performed in all other patients.

### Statistical analysis

Data are given as median values with the range given in parentheses. Statistical analyses were performed using StatMate III version 3.16 (ATMS, Tokyo, Japan). Data were analyzed by the Mann-Whitney *U*-test and Chi-squared test, with two-tailed  $p < 0.05$  considered significant.

### Results

Two hundred and fifty-three patients with choledocholithiasis of a naïve papilla of Vater who underwent ERCP were evaluated retrospectively. As indicated in Table 1, the median age

of patients was 75 years (range 17 ~ 97 years); 141 were male and 112 were female. The median diameter of the common bile duct at the point of cholangiography was 11 mm (range 4 ~ 25 mm). The diameter of common bile duct was < 10 mm in 165 patients (65.2%) and > 10 mm in 88 patients (34.8%). One hundred and thirty-nine patients had a single CBDS, whereas 114 patients had multiple CBDS. Gallstones were present in 171 patients (67.6%), and 132 patients (56.2%) had cholangitis and cholecystitis. Twenty-one patients (8.3%) were taking antithrombotic medication. The rate of EST, EPBD, and EPBD + EST was 83.8% (212/253), 5.1% (13/253), and 9.9% (25/253), respectively. Endoscopic removal of CBDS was successful in 247 patients (97.6%). The rate of emergency endoscopic removal of CBDS was 71.7% (177/247). The median endoscopic treatment time was 30 min (range 7 ~ 90 min). The rate of post-ERCP pancreatitis, bleeding, and perforation was 2.4% (6/253), 2.8% (7/253), and 0.8% (2/253), respectively. The recurrence rate of CBDS was 5.6% (14/248; Table 1).

Because the median age of the patients was 75 years, we divided the patients into two groups, namely those  $\geq 75$  years (Group A;  $n = 134$ ) and those < 75 years (Group B;  $n = 119$ ).

As indicated in Table 2, there were 63 men and 71 women in Group A, compared with 78 men and 41 women in Group B. Thus, there were significantly more women in Group A than in Group B ( $p = 0.003$ ).

Furthermore, the median diameter of the common bile duct was significantly greater in Group A than in Group B patients ( $p < 0.001$ ). Significantly more patients in Group A had CBDS of  $\geq 10$  mm in diameter compared to Group B ( $p < 0.001$ ).

In Group A, 68 and 66 patients had single and multiple CBDS, respectively, compared with 71 and 48 patients, respectively, in Group B. There were no significant differences in the number of CBDS between the two groups.

Gallstones were present in significantly fewer patients in Group A than in Group B ( $p = 0.004$ ). However, there was no significant difference in the rate of cholangitis or cholecystitis between the two groups.

Significantly more patients were on oral antithrombotic agents in Group A than in Group B ( $p = 0.026$ ). There were no significant differences in the rate of EST, EPBD, and EPBD + EST between the two groups. However, the rate of palliative EST was significantly higher in Group A than in Group B ( $p = 0.008$ ).

Endoscopic removal of CBDS was successful in 98.5% (132/134) of patients in Group A and in 96.6% (115/119) of patients in Group B. The rate of palliative endoscopic removal of CBDS was significantly higher in Group A than Group B patients ( $p = 0.015$ ). The median endoscopic procedural time did not differ significantly between the two groups.

The common complications after ERCP were acute pancreatitis, bleeding, and perforation. There were no significant differences in the rate of post-ERCP complications between the two groups, with acute pancreatitis, bleeding, and perforation (Table 2). The rate of recurrence of CBDS in Groups A and B did not differ significantly (Table 2).

As indicated in Table 3, flunitrazepam was used as a sedative during ERCP in 96.9% (126/130) of patients in Group A and in 96.6% (113/117) of patients in Group B. The median

Table 2. Comparison of baseline characteristics and therapeutic results for patients in Group A ( $\geq 75$  years) and Group B ( $< 75$  years)

	Group A (n = 134)	Group B (n = 119)	p-value
Age (years)	82 (75-97)	65 (17-74)	< 0.001
No. men/women	63/71	78/41	0.003
Diameter of the common bile duct (mm)	12 (5-25)	9 (4-20)	< 0.001
CBDS diameter			
< 10 mm	50.7 (68/134)	81.5 (97/119)	< 0.001
$\geq 10$ mm	49.3 (66/134)	18.5 (22/119)	< 0.001
No. single/multiple CBDS	68/66	71/48	NS
Presence of gallstones	59.7% (80/134)	76.5% (91/119)	0.004
Cholangitis or cholecystitis	56.7% (76/134)	47.1% (56/119)	NS
Use of oral antithrombotic agents	11.9% (16/134)	4.2% (5/119)	0.026
EST (%)	81.3% (109/134)	86.6% (103/119)	NS
Emergency EST	75.2% (82/109)	89.3% (92/103)	
Palliative EST	24.8% (27/109)	10.7% (11/103)	0.008
EPBD	6.0% (8/134)	4.2% (5/119)	0.008
EPBD with EST	11.9% (16/134)	7.6% (9/119)	NS
Successful endoscopic removal of CBDS	98.5% (132/134)	96.6% (115/119)	NS
Emergency or palliative endoscopic removal of CBDS			NS
Emergency	65.2% (86/132)	79.1% (91/115)	
Palliative	34.8% (46/132)	20.9% (24/115)	0.015
Duration of ERCP (min)	35 (7-90)	30 (8-85)	0.015
Post-ERCP complications			NS
Pancreatitis	2.2% (3/134)	2.5% (3/119)	
Bleeding	2.2% (3/134)	3.4% (4/119)	NS
Perforation	0.7% (1/134)	0.8% (1/119)	NS
Recurrence of CBDS	6.8% (9/132)	4.3% (5/116)	NS

Unless indicated otherwise, data are given as the median (range) or as a percentage with the number of patients given in parentheses, as appropriate.

CBDS, common bile duct stones; EST, endoscopic sphincterotomy (EST); EPBD, endoscopic papillary balloon dilation; ERCP, endoscopic retrograde cholangiopancreatography.

dose of flunitrazepam used was significantly lower in Group A than in Group B ( $p < 0.001$ ). The rate of use of pentazocine as an analgesic was significantly lower in Group A than in Group B ( $p < 0.001$ ; Table 3). Similarly, the rate of use of scopolamine butylbromide as an antispasmodic agent was significantly lower in Group A than in Group B ( $p < 0.001$ ; Table 3). However, the rate of use of glucagon was significantly higher in Group A than in Group B ( $p < 0.001$ ; Table 3).

## Discussion

Elderly patients are known to have diminished cardiopulmonary and immune function, and a higher incidence of underlying diseases, such as cerebrovascular disease<sup>2)</sup>. In addition, it is thought that the elderly are susceptible to biliary infection because they are prone to cholestasis

Table 3. Comparison of the use of sedative, analgesic, and antispasmodic agents for patients in Group A ( $\geq 75$  years) and Group B ( $< 75$  years).

	Group A (n = 134)	Group B (n = 119)	p-value
Flunitrazepam			
Rate of use	96.9% (126/130)	96.6% (113/117)	NS
Dose (mg)	1 (0.2-2)	1.4 (0.4-2.8)	< 0.001
Pentazocine			
Rate of use	18.5% (24/130)	54.7% (64/117)	< 0.001
Dose (mg)	15 (7.5-22.5)	15 (7.5-22.5)	NS
Scopolamine butylbromide			
Rate of use	6.2% (8/130)	23.9% (28/117)	< 0.001
Dose (mg)	10 (5-20)	20 (5-40)	NS
Glucagon			
Rate of use	43.8% (57/130)	15.4% (18/117)	< 0.001
Dose (mg)	0.5 (0.25-2)	0.5 (0.25-2)	NS

Data are given as the median (range) or as a percentage with the number of patients given in parentheses, as appropriate.

(due to decreased bile secretion and gallbladder contractility) and retrograde infection due to dysfunction of the sphincter of Oddi. Hence, the incidence of CBDS also increases with aging<sup>1)</sup>.

Several studies have reported the usefulness and safety of endoscopic removal of CBDS in elderly patients<sup>2-5)</sup>. In the present study, the time for the endoscopic removal of CBDS, post-ERCP complications (pancreatitis, bleeding and perforation), and the success and recurrence rates for endoscopic removal of CBDS did not differ significantly between patients aged  $\geq 75$  years (Group A) and those  $< 75$  years of age (Group B). These findings may suggest the usefulness and safety of endoscopic removal of CBDS in the elderly. In addition, there are several reports of successful EST and EPBD of the papilla of Vater for endoscopic removal of CBDS in elderly patients<sup>3, 7, 8)</sup>. Because EST is the method of choice for the endoscopic removal of CBDS at Showa University Hospital, the rate of EPBD was less than that of EST in both Groups A and B, with no significant differences between them. Further, the low complication rate following both EST and EPBD in the present study suggests that both procedures can be safely and successfully performed in elderly patients.

Whether endoscopic removal of CBDS should be performed as an emergency or palliative procedure in patients with acute cholangitis is a subject of considerable discussion. The revised Flowcharts for the diagnosis and treatment of acute cholangitis and cholecystitis: Tokyo Guidelines<sup>6)</sup> recommend emergency or early drainage for CBDS with moderate or severe acute cholangitis. In the present study, palliative removal of CBDS was more common in Group A than in Group B.

Furthermore, the number of palliative EST procedures performed in Group A was significantly higher than in Group B. This result could be due to the fact that many of the elderly patients were receiving antithrombotic agents for the treatment of concomitant cardiovascular

or cerebrovascular disease. In the present study, endoscopic removal of CBDS was difficult in some cases. Although patients for whom endoscopic removal of CBDS is likely to be difficult should preferably undergo open surgery; choledochotomy in elderly patients is reportedly associated with significant mortality, a positive rate of blood culture, and a prolonged hospital stay compared with young patients<sup>9</sup>). Hence, long-term biliary stent placement is used to treat some elderly patients in whom endoscopic removal of CBDS is difficult<sup>3</sup>); this procedure is reportedly useful in patients at a later stage and with a short life expectancy<sup>10-11</sup>). However, De Palma *et al.* found that stent placement was not problem free in 40% ~ 41% of patients followed up for a period of 117 days after biliary stenting<sup>12</sup>). Hence, if a biliary stent is placed following difficult endoscopic removal of CBDS, the stent should be replaced regularly.

In the present study, the diameter of the bile duct in Group A was larger than that in Group B. The bile duct is known to expand with age<sup>13</sup>). Furthermore, inflammation of the duodenal papilla and hypofunction of the sphincter of Oddi are more common with aging. The greater incidence of larger CBDS in Group A patients is likely to be secondary to retrograde infection resulting from dysfunction of the sphincter of Oddi and prolonged cholestasis.

There is a tendency for a greater prevalence of gallstones with aging. However, in the present study there were fewer patients with gallstones in Group A than in Group B. This could be due to greater food intake in young people compared with the elderly, resulting in a greater tendency for gallstone formation in young people.

Scopolamine butylbromide was more often used as an antispasmodic agent in Group B, whereas glucagon was more often used in Group A. This could reflect the fact that scopolamine butylbromide is less frequently used in elderly patients with underlying diseases such as hypertension, cardiopathy, glaucoma, and prostatic hypertrophy. The use of flunitrazepam in Group A was less than that in Group B, and this could reflect the fact that the effects of sedatives are exaggerated in the elderly due to impaired hepatic and renal function.

It has been reported that low-dose propofol provides stable sedation for ERCP in patients  $\geq 90$  years of age<sup>14</sup>). A previous study performed in patients aged between 23 and 94 years reported an incidence of cardiopulmonary complications following ERCP of 4.1% in those aged  $< 80$  years, compared with 7.1% in those aged  $\geq 80$  years<sup>15</sup>). Hence, propofol may be a suitable agent for effective sedation in patients aged  $\geq 80$  years. These observations suggest that the use of sedatives in the elderly is safe provided that these agents are used with care.

In conclusion, the time required for the endoscopic removal of CBDS, post-ERCP complications (pancreatitis, bleeding and perforation), the success of the procedure, and the recurrence of CBDS after removal did not differ significantly between the elderly (Group A) and young (Group B) patients in the present study. These findings suggest that, using appropriate sedative, analgesic, and antispasmodic agents, manipulation of the papilla of Vater, and proper timing of endoscopic removal of bile duct stones, ERCP can be performed safely in elderly patients to remove CBDS.

**Conflict of interest**

The authors have declared no conflict of interest.

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