내시경적 큰풍선확장술을 이용한 어려운 담관 결석 추출 시 풍선확장시간에 대한 비교 연구

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A Comparison Study of Ballooning Time between Immediate and Conventional Deflation Method of Endoscopic Papillary Large Balloon Dilation for the Extraction of Difficult Bile Duct Stone

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Background/Aims: The ballooning time in endoscopic papillary large balloon dilation (EPLBD) remains controversial. The aim of this study was to evaluate the significance of the ballooning time comparing an immediate balloon deflation method with a conventional ballooning time of > 45 seconds.

Methods: Between January 2010 and December 2010, 126 patients with bile duct stones treated with EPLBD and endoscopic sphincterotomy were divided according to the ballooning time: the immediate deflation group (n=56) and the conventional inflation group (ballooning time 45s to < 60s) (n=70).

Results: The overall success rate and the success rate of the first attempt of ERCP (endoscopic retrograde cholangio-pancreatography) were 96.4% (54/56) and 80.4% (45/56) in the immediate group and 97.1% (68/70) and 77.1% (54/70) in the conventional inflation group. There were no statistically significant differences in the overall success and the first attempt of ERCP success rate ($p=0.99$, $p=0.66$). The frequency of mechanical lithotripsy was 0% in the immediate deflation group and 7.1% in the conventional inflation group ($p=0.065$). Complications occurred in 3.6% (2/56) patients in the immediate deflation group and 8.6% (4/70) patients in the conventional inflation group ($p=0.298$).

Conclusions: The ballooning time in EPLBD does not affect the outcomes of the treatment for bile duct stones. And the feasibility of the immediate deflation method in EPLBD is acceptable.

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INTRODUCTION

Endoscopic retrograde cholangiopancreatography (ERCP) has been widely accepted as a standard therapy for choledocholithiasis for decades. To facilitate stone removal, destruction or dilation of the bile duct orifice is necessary. Endoscopic sphincterotomy (EST) and endoscopic papillary balloon dilation (EPBD) are well established procedures in the treatment of bile duct stones. However, failure to extract the stones occurs in approximately 10-15% of patients,¹ and these procedures are associated with complications, including bleeding, perforation, and pancreatitis. Large stones, stones that are impacted in the duct, and stones above strictures or in tapered ducts are considered to be difficult to extract.²

In 2003, Ersoz et al.³ first reported using endoscopic papillary large balloon dilation (EPLBD) with a large-diameter (12-20 mm) dilation balloon combined with EST. Since then, this technique has been used to widen the orifice to overcome the challenges associated with the removal of difficult stones using conventional EST or EPBD. According to recent studies,⁴⁻⁹ which include a meta-analysis,⁹ the efficacy and the complications of EPLBD combined with EST for the treatment of bile duct stones have been acceptable. However, the ballooning time in EPLBD remains controversial⁹ and studies on ballooning time during EPLBD are inadequate so far. Although a large size balloon was kept inflated for a time period after the incision of the bile duct orifice in most of the previous studies,^{4-8,10} immediate deflation method is also useful to facilitate stone extraction and may decrease the possibility of complications such as bleeding and perforation. Therefore, we aimed to validate the significance of ballooning time in EPLBD by the analysis of the efficacy and safety of an immediate balloon deflation method compared with a longer ballooning duration method.

MATERIALS and METHODS

1. Patients

Between January 2010 and December 2010, 126 consecutive patients with difficult bile duct stones treated with EPLBD and a limited EST were enrolled in the study. The demographic and clinical data were retrospectively collected by reviewing medical records. In this study, difficult bile duct stone was defined as a stone greater than 12 mm in diameter (if multiple stones were present, the diameter of the largest one was documented) irrespective of the presence of perampullary diverticulum (PAD). All enrolled patients were ≥ 18 years of age and informed consent was obtained prior to ERCP. Exclusion criteria included: concomitant pancreatic or biliary malignant disorders, benign biliary stricture, combined with choledochoduodenal fistula, hepatolithiasis, clinically proven acute pancreatitis, and hemostatic disorders. Bile duct stones that were documented on initial imaging studies (ultrasonography, computed tomography or MRCP) but could not be identified during ERCP were excluded. Incomplete dilation, defined as when the waist of a balloon had not completely disappeared, even when the maximum pressure for the balloon was applied, was also excluded.

2. Methods

ERCP was performed using a side-viewing duodenoscope (TJF-240; Olympus Optical Co, Ltd, Tokyo, Japan). Two experienced endoscopists (Kim YS, Ku YS) who have performed more than 300 ERCP procedures annually for over 10 years performed all the ERCP procedures. Selective bile duct cannulation was achieved using the pull-type papillotome preloaded with a 0.035-inch guidewire or 0.035-inch cannula. Minimal pancreatography was employed only when a guidewire-assisted selective bile duct cannulation could not be obtained. Once the selective bile duct cannulation was achieved, an initial cholangiogram was obtained. Common bile duct (CBD) diameter, stone diameter (the largest one if multiple stones were present) the length of the distal CBD arm and CBD angulations were measured on the

initial cholangiogram. A limited sphincterotomy, defined an incision limited to less than one-third of the length of the papillary roof, was performed and a balloon catheter (CRE Esophageal/Pyloric, maximum diameter 12, 15, 18, or 20 mm; length 5 cm, Boston Scientific, Natick, MA) was introduced and gradually inflated under endoscopic and fluoroscopic guidance; the dilation of the balloon catheter was chosen according to the diameters of the CBD and the stones. The ballooning time was left to endoscopist's discretion. For the conventional inflation group, the balloon remained inflated for longer than 45 seconds but less than 60 seconds after the waist in the balloon had disappeared completely on fluoroscopic guided imaging. Ballooning time was defined as the period between the disappearance of waist of the balloon and deflation of the balloon. In the immediate deflation group, the balloon was deflated immediately after the waist of the balloon had disappeared and was not inflated again.

After balloon deflation, stone extraction was attempted using a retrieval balloon catheter to avoid impaction. If the stone extraction failed after 4 attempts with a retrieval balloon catheter, mechanical lithotripsy was attempted. Complete stone removal was documented using a final cholangiogram. If a residual stone was detected or suspected, a plastic stent (7Fr single- or double-pigtail) was inserted and a second ERCP was attempted within 3 or 4 days. Routine pancreatic stenting was not an intended part of the study protocol. Efficacy was evaluated by assessing the overall success rate for complete stone removal, the stone clearance rate of the first attempt of ERCP session and the frequency of mechanical lithotripsy. Safety was evaluated by assessing the incidence of major post-procedure complications (post-ERCP pancreatitis, bleeding and perforation). Complications were evaluated according to the consensus criteria published by Cotton et al.¹²

3. Statistical analysis

Continuous variables are expressed as the mean $\pm$ standard deviation (SD) or the median with a range when the variable did not show a normal distribution. Student's *t*-test

was used to compare the mean values between the 2 groups. The Mann-Whitney's test was used in the analysis of continuous variables that did not show normal distribution. Chi-square tests were used in the analysis of categorical variables. A *p* value of less than 0.05 was considered statistically significant.

RESULTS

1. Patient characteristics

Of the 126 patients who enrolled in this study, 70 were assigned to the conventional inflation group and 56 were assigned to the immediate deflation group (Table 1). The mean age of the subjects in each group was 70.3 ± 10.2 years in the immediate deflation group and 70.8 ± 12.9 years in the conventional inflation group ($p=0.83$). No significant differences between the groups were noted with regard to the ratio of males to females, the size of the CRE balloon used, bile duct stone size, and CBD diameter. The use of balloons with sizes ≥ 18 mm seemed to be more frequent in the conventional inflation group (31/70 [44.3%]) than in the immediate deflation group (18/56 [32.1%]). However, statistical analysis revealed no significant difference between the groups ($p=0.165$). The presence of PAD and a history of biliary surgery were not significant between the groups. The CBD angles and the lengths of the distal CBD arms, which indicate anatomical variations in the bile duct, were similar in both groups. Initial liver function test were similar in both groups.

2. Efficacy assessment

The overall success rate, the success rate of the first attempt of ERCP session, and the use of mechanical lithotripsy were evaluated to assess the efficacy of the procedures (Table 2). The overall success rate was 96.4% (54/56 patients) and 97.1% (68/70 patients) in the immediate deflation and conventional inflation group. The success rate of the first attempt of ERCP session was 80.4% (45/56 patients) and 77.1% (54/70 patients). There were no statistically sig-

Table 1. Baseline characteristics in both groups

	Immediate Group (n=56)	Conventional Group (n=70)	p-value
Age, yrs	70.3 ± 10.2	70.8 ± 12.9	0.833
Gender			0.748
Male	24 (42.9)	32 (45.7)	
Female	32 (57.1)	38 (54.3)	
Balloon size (mm)			0.42
12	11 (19.6)	11 (15.7)	
15	27 (48.2)	28 (40.0)	
18	14 (25.0)	20 (28.6)	
20	4 (7.1)	11 (15.7)	
CBD stone (mm)	14	14	0.42
Median with range	(12-26)	(12-32)	
CBD diameter (mm)	19.8 ± 6.1	19.1 ± 6.0	0.512
PAD*	26 (46.4)	41 (58.6)	0.589
Length of the distal CBD arm (mm)	35.2 ± 12.2	32.3 ± 9.3	0.151
CBD [†] angle	145.7 ± 17.5	144.7 ± 20.2	0.772
Precut	3 (5.4)	1 (1.4)	0.322
Previous EST [§]	10 (17.9)	18 (25.7)	0.292
Past cholecystectomy	15 (26.8)	27 (38.6)	0.393
Initial lab. Finding			
Total bilirubin (mg/dL)	2.9 ± 2.4	3.4 ± 3.2	0.363
AST (U/L)	194.2 ± 248.7	181.3 ± 247.3	0.773
ALT (U/L)	187.1 ± 193.8	160.1 ± 184.5	0.438
sAPt (U/L)	253.6 ± 218.9	198.6 ± 156.0	0.116

* PAD: periampullary diverticulum.

[†] sAP: serum alkaline phosphatase.[‡] CBD: common bile duct.[§] EST: endoscopic sphincterotomy.^{||} Data are presented as mean±SD or number (%).

nificant differences in the overall success rate and the success rate of the first attempt of ERCP session between two groups ($p=0.99$, $p=0.66$). The use of mechanical lithotripsy tended to be more frequent in the conventional inflation group (5/70 [7.1%]) than in the immediate deflation group (0/56 [0%]), however, the difference was statistically insignificant ($p=0.065$). The number of multiple ERCP sessions (≥ 2) required for complete stone clearance was significantly higher in the conventional inflation group (54.3%) than in the immediate deflation group (21.4%). Failure to extract the stones occurred 4 cases (2 cases in each group) because of tortuous bile duct and all the failed cases underwent surgery.

3. Safety assessment

Major complications occurred in 4 patients (5.7%) in the

conventional inflation group and 2 patients (3.6%) in the immediate deflation group (Table 3). However, there is no statistically significant differences between two groups ($p=0.692$). Post-ERCP pancreatitis occurred in 1 patient (1.8%) in the immediate deflation group and in 3 patients (4.3%) in the conventional inflation group. And severe post-ERCP pancreatitis resulted in one death in the conventional inflation group ($p=0.63$). Bleeding was observed in one patient in the immediate deflation group (1.8%), and no bleeding occurred in the conventional inflation group. No perforations were observed in the immediate deflation group, but one case (1.4%) of EPLBD-related perforation was noted in the conventional inflation group ($p=0.99$). This patient had multiple large CBD stones (maximal diameter of 15mm) and underwent EPLBD with 18mm balloon.

Table 2. Comparison of efficacy between immediate deflation and conventional methods.

	Immediate group (n=56)	Conventional group (n=70)	p-value
Overall success rate	54 (96.4) [†]	68 (97.1)	0.99
Success at first ERCP	45 (80.4)	54 (77.1)	0.662
Number of ERCP sessions			0.001
1	44 (78.6)	32 (45.7)	
2	12 (21.4)	35 (50.0)	
3	0 (0)	3 (4.3)	
Multiple sessions (≥2)	12 (21.4)	38 (54.3)	<0.001
Mechanical lithotripsy	0 (0)	5 (7.1)	0.065

[†]Data are presented as number (%).

Table 3. Comparison of safety between immediate deflation and conventional groups.

	Immediate group (n=56)	Conventional group (n=70)	p-value
EPLBD [†] -related major complications rate [‡]	2 (3.6) [§]	4 (5.7)	0.692
Post-ERCP pancreatitis	1 (1.8)	3 (4.3)	0.628
Mild	0 (0)	2 (2.9)	
Moderate	1 (1.8)	0 (0)	
Severe	0 (0)	1 (1.4) [‡]	
Bleeding	1 (1.8)	0 (0)	0.444
Perforation	0 (0)	1 (1.4)	0.99

[†]EPLBD: endoscopic papillary large balloon dilation.

[‡] Major complications include pancreatitis, bleeding and perforation.

[‡] The patient died from severe pancreatitis.

[§] Data are presented as number (%).

DISCUSSION

Although EST has been widely accepted as the standard therapy for the treatment of bile duct stones for several decades, the treatment of difficult bile duct stones remains challenging. EPLBD creates a large orifice that facilitates the removal of large or multiple stones, and reduces the risk of stone impaction in the distal bile duct.¹¹ Nowadays, EPLBD combined with small EST have been introduced and the reported overall success rate ranges from 80% to almost 100%.^{4-8,10} A recent meta-analysis of patients treated with EPLBD in combination with EST and those treated with EST alone found no statistically differences between the groups in terms of the overall success rates, stone clearance in the first attempt of ERCP session and the use of mechanical lithotripsy.⁹ Overall complications of EPLBD with EST range from 3% to 15%.^{4-8,10,11} They are comparable to those of EST alone. However, a significant reduction in hemorrhage was observed in the EPLBD with EST.⁹ Another study reported that EPLBD decreased procedure times and fluoroscopy times and reduced the need for mechanical litho-

tripsy compared with EST alone.¹³ These results indicate that EPLBD combined with EST is a good alternative to EST alone for the treatment of difficult bile duct stones or in cases with surgically altered anatomy by surgery and PAD.

One area that remains controversial in EPLBD and EPBD is the ballooning time. In one EPBD study longer ballooning durations resulted in better outcomes and fewer complications.¹⁴ In another EPBD study a 20 seconds ballooning time indicated efficacy and safety that were comparable with those obtained using ballooning time of 60 seconds.¹⁵ This concept might be considered to be relevant for either EPBD or EPLBD.¹⁶ In several EPLBD studies, the ballooning time was relatively short (a duration of 10s to < 60s).^{6,8,13,17} On the other hand, a longer time for balloon inflation (≥ 60s) was used in other studies.^{5,6} Although it is generally believed that a longer ballooning duration results in a larger orifice, this study showed that immediate balloon deflation has a similar therapeutic effect with the conventional method.

Although similar results including overall success rates, stone clearance rate of first ERCP and the use of mechanical lithotripsy were noted in the two groups, the number of

ERCP sessions for complete stone clearance was statistically higher in the conventional inflation group. However, it would be premature to conclude that the immediate deflation method is more effective than the conventional inflation method since the sample size in this study was small. Based on the results of this study, the overall efficacy of immediate balloon deflation in EPLBD for bile duct stone clearance was not inferior to the procedure using the conventional ballooning time.

The major complication rates did not differ between two groups (3.6% vs. 5.7%, $p=0.692$). Previous reports demonstrated that although complications appear to be fewer in patients treated with EPLBD in combination with EST than in patients treated with EST alone (5.8 vs. 13.1%, $p=0.0007$),⁹ tearing the ducts while performing EPLBD can cause very serious bleeding¹⁸ and perforation.¹⁹ In this study, there are a few cases of complications. Bleeding occurred in one case of the immediate group, which was easily treated with supportive care. One case of bile duct perforation developed in the conventional inflation group, which was treated with surgical repair, and it is possible that over inflation using inappropriate balloon size (18 mm) against CBD stone (15 mm) might result in common bile duct perforation. In addition, the rate of post-ERCP pancreatitis was similar (0% vs. 4.3%), however, severe post-ERCP pancreatitis leading to mortality occurred in a 76-year-old man in the conventional inflation group. In terms of safety, the results of the immediate deflation group were not inferior to those of the conventional inflation group.

There are several limitations to our study. This study included a small number of cases and is retrospective in design. Also, the enrolled cases were heterogeneous and included those who had undergone a precut procedure for biliary access and patients who had undergone prior EST. Despite the limitations, the efficacy and safety of EPLBD with immediate balloon deflation were very favorable and balloon inflation during EPLBD does not affect the outcomes of the treatment for bile duct stones as suggested in a meta-analysis.⁹ Thus, the findings from this study might be useful in clinical practice.

In conclusion, balloon inflation in EPLBD does not affect the outcomes of the treatment of bile duct stones. Moreover, the efficacy and safety of the immediate balloon deflation method in EPLBD were comparable with the conventional ballooning method. EPLBD with immediate balloon deflation can be considered for routine use. In the near future, a large, prospective study will be required to confirm the present findings.

국문 색인: 큰풍선확장술, 풍선확장시간, 총담관결석증

Conflicts of Interest

The author has no conflicts to disclose.

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