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Impact of Hospital Volume and the Experience of Endoscopist on Adverse Events Related to Endoscopic Retrograde Cholangiopancreatography: A Prospective Observational Study

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Background/Aims: Few studies have addressed the relationship between the occurrence of adverse events (AEs) in endoscopic retrograde cholangiopancreatography (ERCP) and hospital case volume or endoscopist's experience with inconsistent results. The aim of our study was to investigate the impact of hospital case volume and endoscopist's experience on the AEs associated with ERCP and to analyze patient- and procedure-related risk factors for post-ERCP AEs. **Methods:** From January 2015 to December 2015, we prospectively enrolled patients with naïve papilla who underwent ERCP at six centers. Patient- and procedure-related variables were recorded on data collection sheets at the time of and after ERCP. **Results:** A total of 1,191 patients (median age, 71 years) were consecutively enrolled. The overall success rate of biliary cannulation was 96.6%. Overall, 244 patients (20.5%) experienced post-ERCP AEs, including pancreatitis (9.0%), bleeding (11.8%), perforation (0.4%), cholangitis (1.2%), and others (0.9%). While post-ERCP pancreatitis (PEP) was more common when the procedure was performed by less experienced endoscopists, bleeding was more common in high-volume centers and by less experienced endoscopists. Multivariate analysis showed that a less experience in ERCP was significantly associated with PEP (odds ratio [OR], 1.630; 95% confidence interval [CI], 1.050 to 2.531; p=0.030) and post-ERCP bleeding (OR, 1.439; 95% CI, 1.003 to 2.062; p=0.048). **Conclusions:** Our study demonstrated that overall AEs following ERCP were associated with the experience of the endoscopist. To minimize post-ERCP AEs, rigorous training with a sufficient case volume is required, and treatment strategies should be modified according to the endoscopist's expertise. **(Gut Liver 2020;14:257-264)**

Key Words: Cholangiopancreatography, endoscopic retrograde; Adverse events; Hospital volume; Endoscopic experience

INTRODUCTION

Since the introduction of endoscopic sphincterotomy in 1974,[1,2] endoscopic retrograde cholangiopancreatography (ERCP) has evolved from a diagnostic to a therapeutic procedure for the management of various pancreatobiliary disorders.[3] However, ERCP is a relatively invasive procedure associated with potential adverse events (AEs) that range from trivial incidents to major life-threatening crises requiring additional hospital stays or interventional procedures. The major AEs after ERCP are well recognized and the reported incidence varies widely across different studies ranging for 5% to 10% in pancreatitis, 1% to 4% in hemorrhage, 1% to 5% in cholangitis, and 1% to 2% in perforation. The magnitude and independence of the associated risk factors varies widely and are uncertain, but the procedure-related mortality was about 1%.[4-6] Although ERCP procedures are becoming increasingly safer owing to technical advancements and the growing experience of endoscopists, ERCP-related AEs cannot be completely avoided. There may be an association between ERCP case volume and endoscopist's expertise with outcomes and post-ERCP AEs. Several previous univariate and multivariate analyses including large series of patients have identified either patient- or procedure-related risk factors for ERCP-related AEs.[7-12] However, controversy remains

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regarding the impact of the expertise of the endoscopist and the case volume of the center on the outcome of ERCP procedures. This study aimed to investigate whether hospital case volume and endoscopist's experience affect the incidence of ERCP-related AEs and to identify patient- and procedure-related risk factors for ERCP-related AEs using univariate and multivariate analyses.

MATERIALS AND METHODS

1. Patients

This study was conducted as a prospective multicenter observational study in six centers of the Daegu-Gyeongbuk province, South Korea. Among these centers, more than 200 therapeutic ERCP procedures per year were performed in four centers (high-volume centers) and less than 200 procedures per year were performed in two centers (low-volume centers). From January 2015 to December 2015, participating centers enrolled patients with naïve papilla who required diagnostic or therapeutic ERCP procedures. This study was approved by the Medicity Daegu Joint Institutional Review Board (IRB number: DGIRB 2014-07-003-004) and registered in the Clinical Research Information Service (KCT0002993). Informed consent was routinely obtained from all patients prior to performing ERCP.

2. Study protocol and data collection

Patients with any of the following criteria were excluded from the study: aged less than 18 years; pregnancy; previous history of sphincterotomy; underlying chronic pancreatitis; main pancreatic duct dilation of more than 5 mm; medically unstable condition including severe cardiopulmonary disease for conscious sedation; or uncontrolled coagulopathy (i.e., international normalized ratio of >1.5 or platelet count of <50,000/mm^3). Data were recorded on the data collection sheets before ERCP. Details of the ERCP procedures were recorded at the time of the procedure (Supplementary Material 1). Amylase and/or lipase levels were assessed at 6 hours and 24 hours after ERCP. In patients with persistently high 24-hour amylase levels, the enzymatic profile was re-assessed at 48 hours. All patients underwent follow-up until hospital discharge to monitor their clinical conditions and the occurrence of procedure-related AEs. Patients who developed AEs continued to be hospitalized and followed up until their clinical conditions improved.

3. Definitions of observation variables and AEs

Cannulation time was measured from the time when the catheter or papillotome was advanced out of the scope channel in front of the papilla to the time when successful deep biliary cannulation was accomplished under fluoroscopy. Difficult cannulation was defined by the occurrence of any of the following prior to deep biliary cannulation: more than 10 attempts of catheter or guidewire insertion into the pancreatic duct and a cannulation time of more than 5 minutes.[13]

Definitions of individual AEs after ERCP were similar to those reported by Cotton *et al*.,[11] with some modifications made to the severity and classifications. Post-ERCP pancreatitis (PEP) was defined as the occurrence of new-onset or worsened abdominal pain lasting for more than 24 hours that was associated with an increase in serum amylase level of at least 3 times the upper limit of normal at 24 hours after the procedure. We used a modified definition of severity for PEP.[14] Instead of the duration of hospital stay, we evaluated the degree of severity using the number of days before normal feeding resumed. ERCP-related bleeding was defined as intraprocedural when bleeding occurred during the procedure and an additional procedure was required for hemostasis, as immediate when bleeding or a hemoglobin drop of at least 2 g/dL was observed in the first 24 hours, and as delayed when bleeding occurred within 15 days. Perforation was defined when an air or contrast leak into the peritoneal or retroperitoneal cavity was recognized at the time of ERCP or on subsequent chest and/or abdomen plain imaging. Perforation was classified into four types according to the perforation site.[15] As an operator variable, less experience was defined as less than 200 procedures based on the cumulative number of ERCP procedures. The threshold for defining a low-volume center was fewer than 200 annual ERCPs per center.[16,17]

4. Study outcomes

The primary outcome of this study was to investigate overall AEs and to compare the rate of AEs based on hospital case volume and endoscopist's experience. The secondary outcome was to identify patient- and procedure-related risk factors predisposing to the development of AEs.

5. Statistical analysis

Data were described as absolute and relative frequencies for categorical variables and mean with standard deviation or median with range for continuous variables. Differences in the incidence of post-ERCP AEs among groups were compared using the chi-square or Fisher exact test for categorical variables. To identify the independent risk factors for post-ERCP AEs, patient- and procedure-related variables were examined in univariate and multivariate analyses. All variables with a p-value of <0.1 in the univariate analysis were included in a forward stepwise regression multivariate analysis and multiple logistic regression models. The results are shown as odds ratios (ORs) with 95% confidence intervals (CIs). All reported probability values were two-sided, and p-values of less than 0.05 were considered statistically significant. Data were analyzed using SPSS version 22.0 (IBM Corp., Armonk, NY, USA).

RESULTS

1. Baseline characteristics

From January 2015 to December 2015, a total of 1,201 patients with naïve papilla underwent ERCP, and data regarding the patients and procedures were collected from six centers (Table 1). After the exclusion of 10 patients owing to chronic pancreatitis (n=3), previous history of sphincterotomy (n=1), pancreatic duct dilation of >5 mm (n=3), and incomplete protocol completion (n=3), 1,191 patients (median age, 71 years; male:female ratio, 1.38:1) were included in the study; 846 procedures (71%) were performed in the four high-volume centers and 345 (29%) in the two low-volume centers. Among the participating endoscopists, 10 had performed fewer than 200 therapeutic ERCPs and eight had performed more than 200 procedures. Overall, 702 ERCPs (58.9%) were performed by eight expert endoscopists and 489 (41.1%) by 10 less experienced ones. Patient demographics, including comorbidities, previous history of surgery, clinical manifestations at the time of ERCP, indications for ERCP, current history of medication, and prophylactic management, are described in Table 1. Prophylactic medication for the prevention of PEP was administered at the discretion of the attending endoscopist.

2. ERCP-related AEs according to hospital case volume and endoscopist's experience

Overall, ERCP-related AEs developed in 244 patients (20.5%) (Table 2). The occurrence of ERCP-related AEs was statistically higher with less experienced operators than with expert operators (24.7% vs 17.5%, p=0.003), and no difference was observed in the occurrence of these complications between the high-volume and low-volume centers (21.6% vs 17.7%, p=0.133).

After the exclusion of 130 patients with acute pancreatitis at enrollment, PEP occurred in 95 (9.0%). It was classified as mild in 86 cases (8.1%), moderate in seven (0.7%), and severe in two (0.2%). ERCP-related bleeding occurred in 141 cases (11.8%); it was classified as intraprocedural in 134 (11.3%), immediate in five (0.4%), and delayed in two (0.2%). The mean incidence of PEP was 9.4% (69/736 cases) in high-volume centers and 8.0% (26/325 cases) in low-volume centers; the difference was not significant (p=0.560). However, in terms of endoscopist's experience, less experienced operators showed statistically higher rates of PEP compared with experts (12.0% vs 6.8%, p=0.004). This result was attributed to higher rates of difficult cannulation among less experienced operators than among experts (215/433 [49.7%] vs 234/628 [37.3%], p<0.001).

The occurrence of ERCP-related bleeding was more common in high-volume centers (13.8% vs 7.0%, p=0.001) and among less experienced operators (14.5% vs 10.0%, p=0.018). Other AEs included perforation in five patients (0.4%), cholangitis in 11 (1.2%) following the exclusion of 236 patients with acute cholangitis at enrollment, and others in 11 (0.9%).

Table 1. Baseline Characteristics of the Enrolled Patients (n=1,191)

Characteristic	Patients
Age, year	71 (19–101)
Sex, male/female	690/501
Comorbidities	
Cardiovascular disorders	397 (33.3)
Cerebrovascular disorders	112 (9.4)
Pulmonary disorders	51 (4.3)
Diabetes	163 (13.7)
Chronic liver diseases	50 (4.2)
Altered surgical anatomy	54 (4.5)
STG with B-II anastomosis	21 (1.8)
STG with B-I anastomosis	17 (1.4)
Liver transplantation	14 (1.2)
Hepatectomy	2 (0.2)
Clinical presentation at ERCP	
Acute pancreatitis	130 (10.9)
Acute cholangitis	236 (19.8)
Acute cholecystitis	81 (6.8)
Reason for ERCP	
Removal of choledocholithiasis and/or sludges	856 (71.9)
Tissue acquisition for histologic diagnosis	219 (18.4)
Drainage procedure	392 (32.9)
Current history of medication	
None	993 (83.4)
Aspirin	128 (10.7)
Antiplatelet agents	83 (7.0)
Warfarin	16 (1.3)
NSAIDs	8 (0.7)
Prophylactic medication	
None	355 (29.8)
Nafamostate mesilate	342 (28.7)
Ulinastin	243 (20.4)
Gabexate mesilate	223 (18.7)
Indomethacin	28 (2.4)
Presence of diverticulum	359 (30.1)
Type 1/2/3/4	53/164/142/0
Attempts of catheter insertion into main PD	
None / <5 / 5–10 / >10 times	962/189/24/16
Attempts of guidewire insertion into main PD	
None / <5 / 5–10 / >10 times	864/278/35/14
Attempts of contrast injection into main PD	
None / <5 / 5–10 / >10 times	1015/164/12/0
Contact of ampulla before deep biliary cannulation	
None / <5 / 5–10 / >10 times	668/390/89/44
Precut sphincterotomy	94 (7.9)
Infundibulotomy	100 (8.4)

Data are presented as median (range) or number (%).
STG with B-II, subtotal gastrectomy with Billroth-II anastomosis; STG with B-I, subtotal gastrectomy with Billroth-I anastomosis; ERCP, endoscopic retrograde cholangiopancreatography; NSAIDs, nonsteroidal anti-inflammatory drugs; PD, pancreatic duct.

Table 2. Frequencies of ERCP-Related Adverse Events According to Hospital Case Volume and Endoscopist's Experience

	Total	Hospital case volume			Experience of endoscopist		
		High volume	Low volume	p-value	Expert	Less experienced	p-value
	n=1,191	n=846	n=345		n=702	n=489	
Overall	244 (20.5)	183 (21.6)	61 (17.7)	0.133	123 (17.5)	121 (24.7)	0.003
Bleeding	141 (11.8)	117 (13.8)	24 (7.0)	0.001	70 (10.0)	71 (14.5)	0.018
Intraprocedural	134 (11.3)	111 (13.1)	23 (6.7)		68 (9.7)	66 (13.5)	
Immediate	5 (0.4)	5 (0.6)	0		1 (0.1)	4 (0.8)	
Delayed	2 (0.2)	1 (0.1)	1 (0.3)		1 (0.1)	1 (0.2)	
Perforation	5 (0.4)	4 (0.5)	1 (0.3)	1.000	2 (0.3)	3 (0.6)	1.000
Type I/II/III/IV	3/0/0/2	2/0/0/2	1/0/0/0		1/0/0/1	2/0/0/1	
Others*	11 (0.9)	3 (0.4)	8 (2.3)	-	9 (1.3)	2 (0.4)	-
	n=1,061	n=736	n=325		n=628	n=433	
Pancreatitis†	95 (9.0)	69 (9.4)	26 (8.0)	0.560	43 (6.8)	52 (12.0)	0.004
Mild	86 (8.1)	64 (8.7)	22 (6.8)		41 (6.5)	45 (10.4)	
Moderate	7 (0.7)	4 (0.5)	3 (0.9)		1 (0.2)	6 (1.4)	
Severe	2 (0.2)	1 (0.1)	1 (0.3)		1 (0.2)	1 (0.2)	
	n=955	n=650	n=305		n=562	n=393	
Cholangitis‡	11 (1.2)	7 (1.1)	4 (1.3)	0.751	4 (0.7)	7 (1.8)	0.216

Data are presented as number (%).
ERCP, endoscopic retrograde cholangiopancreatography.
*Others included acute cholecystitis (n=4), cerebrovascular accident (n=2), transient fever (n=1), hypoxia (n=1), hypotension (n=1), abnormality of liver battery profiles (n=1), and nausea (n=1). †Data were analyzed after excluding 130 patients with acute pancreatitis at enrollment. ‡Data were analyzed after excluding 236 patients with acute cholangitis at enrollment.

Table 3. Results of Univariate and Multivariate Analyses of Patient-Related Risk Factors for Post-ERCP Pancreatitis (n=1,061)

Variable	Incidence of post-ERCP pancreatitis, %			Multivariate analysis		
	With variable	Without variable	p-value	Exp (B)*	95% CI	p-value
Age (<70 yr)	8.9	9.0	1.000			
Female sex	11.3	7.3	0.029	1.604	1.041–2.470	0.032
Previous history of AP	11.1	8.9	0.572			
Altered surgical anatomy	10.4	8.9	0.611			
Cardiovascular comorbidity	6.6	10.1	0.067	0.588	0.356–0.972	0.038
Cerebrovascular comorbidity	13.5	8.5	0.130			
Pulmonary comorbidity	4.3	9.2	0.428			
Presence of CLD	8.5	9.0	1.000			
Periampullary diverticulum	9.4	8.7	0.726			

ERCP, endoscopic retrograde cholangiopancreatography; CI, confidence interval; AP, acute pancreatitis; CLD, chronic liver disease.
*Exp (B), odds ratios.

The observed overall mortality rates were 0.4% (3/846) and 0.9% (3/345) in the high- and low-volume centers (p=0.364), respectively. However, there was only one case of ERCP-related mortality in a high-volume center. The other causes of mortality were septic shock or hepatic failure; according to endoscopist's experience, there was no significant difference in the mortality rate (0.4% in the less experienced group, 0.6% in the expert group, p=1.000), with one case of ERCP-related mortality in the expert group.

3. Univariate and multivariate analysis for PEP and bleeding

Analysis of risk factors was performed only for PEP and ERCP-related bleeding because the occurrence of the other AEs was too low to be further analyzed in our study. Of the nine patient-related risk factors considered in the study protocol (Table 3), the development of PEP was significantly associated with female sex alone in univariate analysis (p=0.029) and with female sex and cardiovascular comorbidity in multivariate analysis (OR,

1.604; 95% CI, 1.041 to 2.470; p=0.032; OR, 0.588; 95% CI, 0.356 to 0.972; p=0.038, respectively). Among eight procedure-related risk factors, difficult cannulation, acquisition of pancreatogram, pancreatic sphincterotomy, and less experienced operator were significantly associated with PEP in univariate and multivariate analyses (Table 4). Although precut sphincterotomy was identified as a statistically significant risk factor for PEP (p=0.003) in the univariate analysis, the multivariate analysis did not show significance (p=0.082).

The results of the forward stepwise binary logistic regression analysis from the pool of 17 potential risk factors for ERCP-related bleeding identified the following four risk factors by multivariate analysis, one patient- and three procedure-related, all of which were independently associated with ERCP-related bleeding: comorbidity of chronic liver disease, pancreatic sphincterotomy, less experienced operator, and high hospital case volume (Tables 5 and 6).

DISCUSSION

ERCP has been widely practiced as a diagnostic and therapeutic procedure for pancreatobiliary disease. The risk of ERCP-related AEs was recognized early and has been the focus of many studies.[8-12,18-20] Although technical advances and the expanding experience of endoscopists have made the ERCP procedure increasingly safe, it is still associated with a high potential for AEs. Several prospective multicenter studies have described ERCP success rates and related AEs, and these findings have been useful in understanding the patient- and procedure-related risk factors.[6,10,12,21-26] However, most of these studies are not recent and may not reflect the current clinical picture, as ERCP is now routinely performed to treat complex pancreatobiliary diseases and conditions, such as post-liver transplantation complications, and is a technically demanding procedure. These applications increase the risk of ERCP-related AEs. In this study, we aimed to determine whether hospital case volume and endoscopist's experience correlated with ERCP-related AEs.

Table 4. Results of Univariate and Multivariate Analyses of Procedure-Related Risk Factors for Post-ERCP Pancreatitis (n=1,061)

Variable	Incidence of post-ERCP pancreatitis, %			Multivariate analysis		
	With variable	Without variable	p-value	Exp (B)*	95% CI	p-value
Difficult cannulation	14.0	5.2	<0.001	2.341	1.430–3.833	0.001
Pancreatogram	21.3	7.1	<0.001	2.132	1.251–3.633	0.005
Precut incision	19.0	8.1	0.003	1.784	0.928–3.430	0.082
Infundibulotomy	13.2	8.6	0.175			
Biliary balloon dilation	6.8	9.3	0.418			
Pancreatic sphincterotomy	18.9	7.4	<0.001	1.867	1.103–3.160	0.020
Less experienced operator	12.0	6.8	0.004	1.630	1.050–2.531	0.030
Low hospital case volume	8.0	9.4	0.560			

ERCP, endoscopic retrograde cholangiopancreatography; CI, confidence interval.
*Exp (B), odds ratios.

Table 5. Results of Univariate and Multivariate Analyses of Patient-Related Risk Factors for Post-ERCP Bleeding (n=1,191)

Variable	Incidence of post-ERCP bleeding, %			Multivariate analysis		
	With variable	Without variable	p-value	Exp (B)*	95% CI	p-value
Age (<40 yr)	12.7	11.8	0.849			
Female sex	10.6	12.8	0.276			
Previous history of AP	28.6	11.6	0.073	3.331	1.015–10.933	0.047
Altered surgical anatomy	7.4	12.0	0.391			
Cardiovascular comorbidity	12.3	11.6	0.704			
Cerebrovascular comorbidity	12.5	11.8	0.760			
Pulmonary comorbidity	13.7	11.8	0.657			
Presence of CLD	24.0	11.3	0.012	3.074	1.485–6.362	0.002
Medication of anticoagulants	15.2	11.2	0.118			
Periampullary diverticulum	14.5	10.7	0.078	1.447	0.989–2.116	0.057

ERCP, endoscopic retrograde cholangiopancreatography; CI, confidence interval; AP, acute pancreatitis; CLD, chronic liver disease.
*Exp (B), odds ratios.

Table 6. Results of Univariate and Multivariate Analyses of Procedure-Related Risk Factors for Post-ERCP Bleeding (n=1,191)

Variable	Incidence of post-ERCP bleeding, %			Multivariate analysis		
	With variable	Without variable	p-value	Exp (B)*	95% CI	p-value
Difficult cannulation	11.8	11.9	1.000			
Precut incision	6.4	12.3	0.097	0.491	0.208–1.162	0.105
Infundibulotomy	20.0	11.1	0.014	1.685	0.954–2.978	0.072
Biliary balloon dilation	8.7	12.3	0.263			
Pancreatic sphincterotomy	18.8	10.8	0.007	1.766	1.091–2.861	0.021
Less experienced operator	14.5	10.0	0.018	1.439	1.003–2.062	0.048
High hospital case volume	13.8	7.0	0.001	2.016	1.232–3.298	0.005

ERCP, endoscopic retrograde cholangiopancreatography; CI, confidence interval.
*Exp (B), odds ratios.

In addition, we identified a number of patient and procedural correlates with complications in 6 centers in Daegu-Gyeongbuk province, South Korea.

According to previous reports, the incidence of ERCP-related AEs varies from 5% to 12%.[7-10,12,26-29] The discrepancies in the reported rate may be attributed to heterogeneity of the definition and inclusion criteria of ERCP-related AEs, inclusion of diagnostic ERCP, and differences in the experience of the endoscopists. The present study provides up-to-date findings with regard to the differences in post-ERCP AEs according to hospital case volume and endoscopist's experience. The overall success rate for deep bile duct cannulation was 96.6%, with a cannulation success rate of 96.1% (813/846) in patients in high-volume centers compared to 98.0% (338/345) in low-volume centers (p=0.104). The cannulation success rate was higher with expert endoscopists (97.4%) than with less experienced endoscopists (95.5%, p=0.068) and was slightly lower in high-volume centers, but there were no statistically significant differences according to hospital case volume. These results reveal mixed findings between the hospital groups. Similar to the results of a recent systematic review,[20] endoscopist's experience was evaluated in this study and found to be a significant risk factor associated with overall AEs, though there was no significant difference in the overall AEs according to hospital case volume. Owing to sources of bias such as the complexity of case mixes, referral patterns, patient factors, and differences in endoscopist's experience and educational programs for ERCP training, the interpretation of AEs according to hospital volume should be performed with caution.[6,30] In our study, the AEs were generally of minor severity, with additional hospital stay followed by full recovery, and were rarely severe with permanent disability. Low-volume centers were not associated with increased mortality or poor outcomes.

Bleeding is a serious AE of ERCP that is most commonly related to endoscopic sphincterotomy. The exact incidence of clinically significant ERCP-related bleeding is variable and difficult to define in the consensus criteria. The reported occurrence at the time of sphincterotomy of bleeding ranging from oozing to severe bleeding is as high as 10% to 30%, while the rate of post-sphincterotomy bleeding after ERCP is estimated to be 0.1% to 2%.[3,7,10,12,28,31,32]

In the present study, the bleeding rate was 11.8% and most cases of bleeding were intraprocedural or immediate events (95.0% and 3.5%, respectively), which included continuous bleeding for several minutes after the sphincterotomy. These types of bleeding are generally considered mild AEs if significant blood loss, transfusion requirement, or changes in vital signs do not occur. Identified risk factors for post-sphincterotomy bleeding include coagulopathy, thrombocytopenia, anticoagulant treatment, presence of active cholangitis, and low case volume on the part of the endoscopist (performance of not more than 1 sphincterotomy per week).[3,7,31] In the present study, multivariate analysis identified three independent procedure-related risk factors for post-ERCP bleeding: pancreatic sphincterotomy (OR, 1.766; p=0.021), less experienced endoscopist (OR, 1.439; p=0.048), and high hospital volume (OR, 2.016; p=0.005). Presence of chronic liver disease was the only patient-related factor (OR, 3.074; p=0.002). These findings indicate that less experienced endoscopists may control the bleeding less precisely or less effectively and that the volume of hospital cases is not associated with a reduced rate of bleeding. This may reflect the fact that high-volume centers have more patients at clinical high risk of bleeding, with poor general conditions that entail a higher degree of difficulty. These conflicting data regarding the negative impact of high-volume centers on the post-ERCP bleeding rate warrant further well-designed studies.

PEP is one of the most common AEs of ERCP, and it is associated with both patient- and procedure-related factors. Patient-related factors are younger age, female sex, history of previous PEP, non-dilated ducts, normal bilirubin level, and suspected sphincter of Oddi dysfunction. Procedure-related factors are difficult cannulation, multiple pancreatic injections, pancreatic sphincterotomy, precut sphincterotomy, and pancreatic sampling. These factors have been shown to increase the risk of

PEP.[3,8,10,12,18,26-28,31,32] In the present study, the incidence of PEP was similar to that reported in previous studies.[33] In the present study, among the patient-related risk factors, only female sex and cardiovascular comorbidity were significantly associated with PEP in the multivariate analysis. In terms of procedure-related risk factors, difficult cannulation, acquisition of pancreatogram, pancreatic sphincterotomy, and less experienced endoscopist were significantly associated with PEP in univariate and multivariate analyses. These results indicate that endoscopist's experience is a relatively important risk factor for AEs of ERCP (OR, 1.630) from a technical standpoint.

In one large Italian multicenter prospective study, a comparison of high-volume (>200 ERCPs/year) and low-volume centers (<200 ERCPs/year) showed that the risk of PEP was significantly higher in low-volume centers in univariate analysis (relative risk, 2.8).[12] In another recent multicenter study, PEP was not associated with the case volume of either the single endoscopist (3.8% vs 5.5%; expert vs nonexpert, p=0.345) or the center (3.9% vs 3.1%; high-volume centers vs low-volume centers, p=0.379).[25]

The effect of endoscopist's experience is quite difficult to evaluate and interpret. Continuous training and an adequate case volume should be required for the performance of ERCP in practice to reduce AEs. Furthermore, endoscopists must consider if they have an adequate case volume to maintain their ERCP skills and minimize AEs before performing ERCP. The success and outcome of ERCP procedures is critically important, and minimizing AEs has equal significance. Therefore, endoscopist's experience is an essential factor in the success of ERCP, along with a skilled ERCP team consisting of nurses and radiographers. The number of purely diagnostic ERCPs has decreased, and the number of interventional ERCPs, with high risk and complexity, has increased. Endoscopists in high-volume centers are continuously undergoing training and performing ERCP. As a result, endoscopists in low-volume centers or those who are less experienced are performing fewer total procedures annually. Our data showed that endoscopists with less experience have higher rates of AEs. Although increasing endoscopist's experience was associated with low PEP rates, this association was not observed with regard to center volume. Given the greater frequency of more complex and difficult procedures in high-volume centers, these centers are more likely to have a large proportion of patients with a high risk of pancreatitis. Therefore, endoscopist's experience and careful patient selection play an important role in preventing PEP. Rigorous training and a sufficient case volume along with an adequate system of referral to experts for complex cases are required to reduce the incidence of PEP in practice. Appropriate modification of the treatment approach according to the individual endoscopist's experience may be the most important factor.

This prospective multicenter study revealed the incidence of ERCP-related AEs according to different endoscopists' experience and center case volumes. The experience of the endoscopist is associated with the overall incidence rate of AEs. In addition, the current data reveal the patient- and procedure-related risk factors for PEP and bleeding. To minimize the AEs of ERCP, endoscopists should endeavor to ensure an adequate case volume to maintain their technical skills. Before considering performing an ERCP, the endoscopist should be attentive to the selection of patients with appropriate indications, perform individual risk-benefit analyses, and understand how to effectively manage any potential AEs.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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AUTHOR CONTRIBUTIONS

Study concept and design: C.M.C., K.B.C., Y.S.L., H.J.L. Definition of intellectual content: C.M.C. Literature search and clinical studies: C.M.C., K.B.C., Y.S.L., H.J.L. Data and statistical analysis, manuscript preparation: C.M.C., K.B.C., Y.S.L., H.J.L. Data acquisition: C.M.C., M.K.J., J. Heo, T.N.K., K.H.K., H.K., K.B.C., Y.S.L., H.J.L., H.G.K., J. Han, D.W.L. Manuscript editing and review: all authors.

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