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Causes and Management of Endoscopic Retrograde Cholangiopancreatography-Related Perforation: A Retrospective Study

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Background: Endoscopic retrograde cholangiopancreatography (ERCP) is essential for diagnosing and treating biliopancreatic disease. Because ERCP-related perforation can result in death, therapeutic decisions are important. The aim of this study was to determine the cause of ERCP-related perforation and suggest appropriate management.

Methods: Between January 1999 and August 2022, 7,896 ERCPs were performed in our hospital. We experienced 15 cases (0.18%) of ERCP-related perforation and conducted a retrospective review.

Results: Of the 15 patients, 6 were female and 9 were male, and the mean age was 77.1 years. According to Stapfer's classification, the 15 cases of ERCP-related perforation comprised 3 type I (duodenum), 3 type II (periampullary), 9 type III (distal bile duct or pancreatic duct), and no type IV cases. Fourteen of 15 (92.6%) were diagnosed during ERCP. The main cause of perforation was scope-induced damage, endoscopic sphincterotomy, and instrumentation penetration in type I, II, and III cases, respectively. Four patients with severe abdominal pain and extraluminal fluid collection underwent emergency surgery for repair and drainage. One type III patient with distal bile duct cancer underwent pancreaticoduodenectomy on day 6. Three type III patients with only retroperitoneal gas on computed tomography (CT) performed immediately after ERCP had no symptoms and needed no additional treatment. Seven of the 15 patents were treated by endoscopic nasobiliary drainage (n=5) or CT-guided drainage (n=2). There were no deaths, and all patients were discharged after treatment.

Conclusions: Early diagnosis and appropriate treatment are important in managing ERCP-related perforation. (J Nippon Med Sch 2023; 90: 316–325)

Key words: ERCP, perforation, treatment, surgery

Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) is an indispensable technique for diagnosing biliary and pancreatic diseases, and various therapeutic techniques that use ERCP have been developed for clinical settings. However, because ERCP-related procedures generally require advanced technique, the incidence of complications is higher than for upper and lower endoscopy, and complications can be serious, even life-threatening[1–3]. Acute pancreatitis, cholangitis, bleeding, and perforation are the most common complications related to ERCP. Gastrointestinal perforation caused by ERCP is associated with a high mortality rate, and its diagnosis and appropriate treatment is therefore important[4,5].

The aim of this study was to determine the incidence, cause, and outcome of ERCP-related perforation and to identify appropriate management and prevention measures.

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Table 1 Stapfer's classification of iatrogenic perforation during ERCP

Type	Definition
I	Lateral or medial duodenal wall perforations caused by the endoscope
II	Periampullary perforations related to sphincterotomy
III	Distal bile duct or pancreatic duct injuries related to endoscopic instrumentation
IV	Retroperitoneal air alone without periduodenal fluid collection on imaging

Materials and Methods

Between January 1999 and August 2021, 7,896 ERCPs were performed in Nippon Medical School Hospital, of which 15 resulted in ERCP-related perforation (0.18%). Medical records for the 15 patients with documented ERCP-related perforations were identified and reviewed retrospectively. Charts were evaluated for patient age, sex, indications for ERCP, history of abdominal surgery, diagnostic timing, modality, findings at ERCP-related perforation, cause of perforation, radiographic findings, computed tomography (CT) findings after ERCP-related perforation, time to diagnosis, clinical presentation, treatment, and mortality.

ERCP-related injuries were stratified according to the standardized classification system proposed by Stapfer et al.[6], the most common classification system for ERCP-related perforation (**Table 1**). Type I is lateral or medial duodenal wall perforation, Type II is periampullary perforation, and type III perforation is distal bile duct injury. Stapfer et al. did not mention pancreatic duct injury caused by ERCP-related procedures; however, pancreatic duct perforation was classified as type III in this study. Type IV perforation is retroperitoneal air alone, without periduodenal fluid collection on imaging.

This retrospective study was approved by the Ethics Committee of Nippon Medical School Hospital (No. 30-03-1107).

ERCP procedures were performed with an ERCP scope (JF-200, JF-230, TJF-200, JF-260V, TJF-Q260, and TJF-Q290 V; Olympus Corp., Tokyo, Japan) by an special experienced team using standard techniques. However, the ERCP scope used varied during the 20-year study period. Standard cannulation or wire-guided cannulation can be selected by the operator for bile duct access. In case of failure, techniques such as precut sphincterotomy and double-guidewire technique can be used. Ionic contrast medium (diatrizoate meglumine Na, Urografin; Bayer AG, Germany) was used to recognize the bile duct or pancreatic duct.

After the procedure, the ERCP team observed the patient's general condition, including vital signs, for 24 hours to identify any possible ERCP-related complications. Laboratory testing, including a complete blood count, C-reactive protein, and serum amylase, was routinely performed at 3 hours after ERCP and on the morning of the day after the procedure.

In general, patients were managed medically, without a peroral diet, by evaluating abdominal pain, peritoneal irritation sign, elevation of serum amylase, and retroperitoneal or intraperitoneal fluid collection. CT was routinely immediately performed for patients with suspected perforation during ERCP. CT screening was added for patients with severe abdominal pain after ERCP. Patients with ERCP-related perforation were managed surgically when severe abdominal pain or a peritoneal irritation sign accompanied by intraperitoneal or retroperitoneal fluid collection on CT was observed.

Results

Table 2 shows the demographic and clinical features of the 15 patients with ERCP-related perforation. Six were female (40.0%) and 9 were male. Mean age was 77.1 years (range 49-88 years), and 13 of the 15 patients (86.7%), were older than 70 years.

Stapfer's Classification

According to Stapfer's classification, the 15 cases with ERCP-related perforations included type I (n=3, 20.0%), type II (n=3, 20.0%), and type III (n=9, 60.0%) cases but no type IV cases. ERCP indications included choledocholithiasis (n=9), hilar cholangiocarcinoma (n=2), and hepatolithiasis, distal bile duct cancer, distal bile duct stricture, and pancreatic duct stricture (n=1 each). In 4 of the 9 type III cases, choledocholithiasis was included. Five of the 15 patients had a history of abdominal surgery, and 2 of the 3 patients with type I perforation had a history of upper abdominal surgery, including hepatectomy and distal gastrectomy with Billroth I reconstruction. Type III perforation included 2 patients with a history of appendectomy and 1 patient with a history of right hemicolectomy. None of the 15 patients had a history of organ failure or use of anti-inflammatory agents, including corticosteroids and angiogenesis inhibitors. With respect to

Table 2

	Perforation Type (total 15 cases)				
	Type I (n=3)	Type II (n=3)	Type III (n=9)	Type IV (n=0)	Total
Age (years)	70-88 (78.3)	67-87 (77.3)	49-88 (76.7)		49-88 (77.1)
>70 years	3	2	8		13 (86.7%)
Female	1	2	3		6 (40.0%)
ERCP indication					
choledocholithiasis	2	3	4		9 (60.0%)
hilar cholangiocarcinoma	1		1		2
hepatolithiasis			1		1
distal bile duct cancer			1		1
bile duct stricture			1		1
pancreatic duct stricture			1		1
History of abdominal surgery					
	2 (hepatectomy 1) (distal gastrectomy 1)		3 (appendectomy 2) (right hemicolectomy 1)		5 (33.3%)

Stapfer's classification, the sites of ERCP-related type I and II perforation were the duodenum (n=3) and periampullary (n=3), respectively. The sites of type III perforation (n=9) were the distal bile duct (n=7) and pancreatic duct (n=2) (**Table 3**).

Diagnostic Timing, Diagnostic Modality, and Cause of Perforation

Regarding diagnostic timing of ERCP-related perforation, 14 of 15 cases (92.6%) were diagnosed during ERCP. Type I perforation (n=3) was noted by direct endoscopic observation of the abdominal cavity (n=1) and mucosal injury with muscular layer (muscularis propria) exposure (n=2). The former was complete perforation by scope. The latter 2 duodenal injuries were caused by clockwise axial rotation intended to shorten the ERCP fiber, and both patients had a history of upper abdominal surgery. **Figure 1** shows mucosal fissure and red muscular layer exposure caused by clockwise axis rotation to shorten the ERCP scope.

Two of the 3 type II perforations were caused by endoscopic sphincterotomy (EST) and were diagnosed during ERCP by contrast medium extravasation (n=1) and direct endoscopic observation of the retroperitoneal space from the EST cutting area (n=1). A type II case was diagnosed by retroperitoneal gas observed on X-ray on day 1. Type III perforations (n=9) were identified by instrumentation deviation, including the lithotripter (n=3), catheter (n=5) on X-ray, and an endoscopic finding of peroral cholangioscopy (POCS) (n=1). Both cases of 2 pancreatic duct type III perforation were caused by a catheter. In 1 case of type III perforation, POCS showed an unfamiliar extraluminal structure that was not bile duct mucosa; type III perforation was confirmed by extravasation of contrast medium.

Imaging Characteristics and Clinical Presentation

Regarding imaging characteristics on diagnostic CT after ERCP-related perforation (**Table 4**), type I cases (n=3) showed pneumoretroperitoneum with subcutaneous emphysema (n=1), retroperitoneal fluid collection (n=1), and retroperitoneal and peritoneal fluid collection (n=1). The former case of duodenal injury with subcutaneous emphysema only was caused by clockwise axial rotation of the ERCP scope. The area of subcutaneous emphysema was large and extended to the groin. The patient had subcutaneous emphysema only and no abdominal complaints or extraluminal fluid collection. However, 2 type I patients with extraluminal fluid collection reported abdominal pain with a peritoneal irritation sign after ERCP and required surgery. All type II cases (n=3), had pneumoretroperitoneum and retroperitoneal fluid collection. One patient had no symptoms, and 2 patients reported abdominal pain.

Among the type III cases (n=9), 2 patients had pneumoretroperitoneum only, and the other 7 patients exhibited pneumoretroperitoneum and retroperitoneal fluid collection on CT imaging. **Figure 2** shows a case of type III with extravasation of contrast medium on X-ray and CT. Four of the 9 type III patients reported abdominal

Table 3

	Perforation Type (total 15 cases)				
	Type I (n=3)	Type II (n=3)	Type III (n=9)	Type IV (n=0)	Total
Location of perforation					
duodenum	3				3
periampullary		3			3
distal bile duct			7		7
pancreatic duct			2		2
Diagnostic timing					
during ERCP	3	2	9		14
<24 hours after ERCP					0
>24 hours after ERCP		1			1
Diagnostic modality					
Endoscopy	3 (mucosal injury with muscular layer exposure 2) (intraabdominal view 1)	1 (retroperitoneal space exposure 1)	1 (POCS 1)		5
X-ray during ERCP		1 (contrast medium extravasation 1)	8 (instrumentations deviation: lithotripter 3, catheter 5)		9
X-ray after ERCP		1			1
Causes of perforation					
Endoscopy direct perforation	1				1
ERCP shortening procedure (clockwise axis rotation)	2				2
EST		3			3
lithotripter			3		3
catheter			5 (pancreatic duct 2)		5
POCS			1		1

POCS: peroral cholangioscopy
EST: endoscopic sphincterotomy

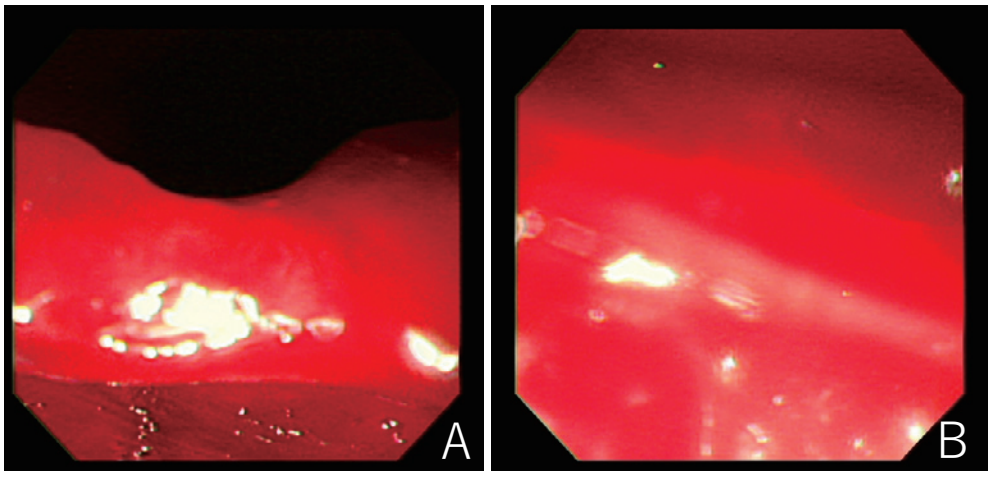


Fig. 1 Stapfer's type I perforation.
A: Mucosal fissure (A) and the muscular layer (B) were observed during a shortening ERCP procedure (clockwise axis rotation). The patient had a history of distal gastrectomy with Billroth I reconstruction.

Table 4

	Perforation Type (total 15 cases)				
	Type I (n=3)	Type II (n=3)	Type III (n=9)	Type IV (n=0)	Total
Imaging characteristics on diagnostic CT after ERCP-related perforation					
only PnRP			2		2
PnRP+SE	1				1
PnRP+ RFC	1	3	7		11
PnRP+PnP+ PFC	1				1
Clinical presentation					
no symptom		1	5		6
AP		2	4		6
AP with PIS	2				2
SE	1				1

POCS: peroral cholangioscopy
PnRP: pneumoretroperitoneum
PnP: pneumoperitoneum
SE: subcutaneous emphysema
RFC: retroperitoneal fluid collection
PFC: peritoneal fluid collection
AP: abdominal pain
PIS: peritoneal irritation sign

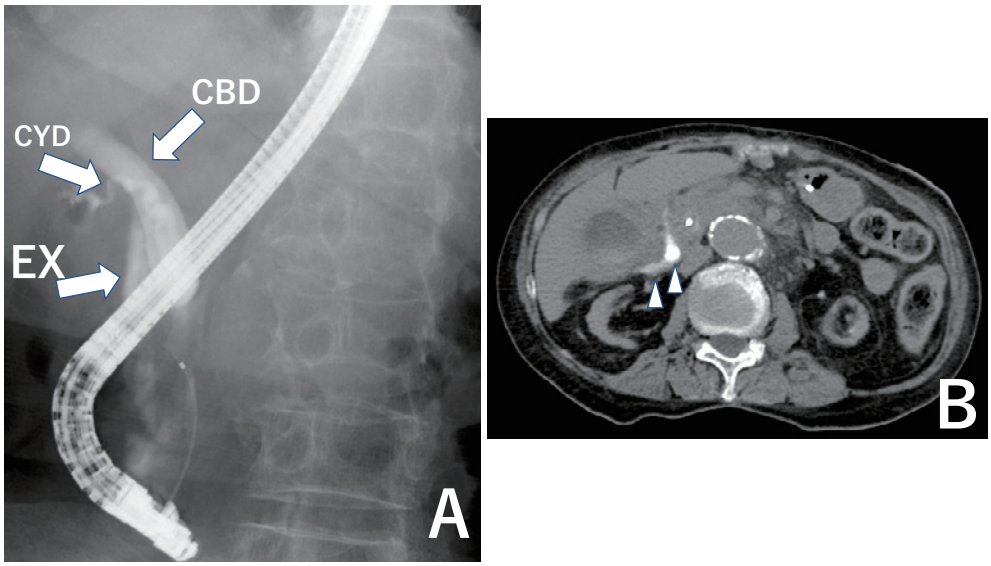


Fig. 2 Stapfer's type III perforation.
A: ERCP demonstrated extravasation of contrast medium near the distal bile duct (EX: extravasation of contrast medium, CBD: common bile duct, CYD: cystic duct)
B: After ERCP, CT showed collection of contrast medium in the retroperitoneal space (arrowheads).

pain; however, 5 patients had no symptoms.

Treatment

In all cases of ERCP-related perforation, pneumoretroperitoneum was observed on CT imaging after ERCP. Both patients with no extraluminal fluid collection in the abdominal and retroperitoneal space reported no abdominal pain. These 2 asymptomatic patients and another patient reporting mild abdominal pain with limited retroperitoneal fluid collection received only conservative medical management without additional treatment. Their courses were uneventful.

As shown in **Table 5**, five (33.3%) of the 15 patients

Table 5

	Perforation Type (total 15 cases)				
	Type I (n=3)	Type II (n=3)	Type III (n=8)	Type IV (n=0)	Total
Treatment					
I. conservative medical treatment			3		3 (20.0%)
II. Endoscopic and radiological treatment	1	2	4		7 (46.7%)
endoscopic nasobiliary drainage	1	1	3		
CT guided retroperitoneal drainage		1 (Day 7)	1		
III. Surgery	2	1	2		5 (33.3%)
PR+RD+BD	1				
PR+CL+ID	1				
PR+CL+RD+BD		1	1		
PD			1 (Day 6)		
Mortality	0	0	0		0 (0.0%)

PR: primary repair
RD: retroperitoneal drainage
CL: choledocholithotomy
ID: intraperitoneal drainage
BD: biliary drainage
PD pancreaticoduodenectomy

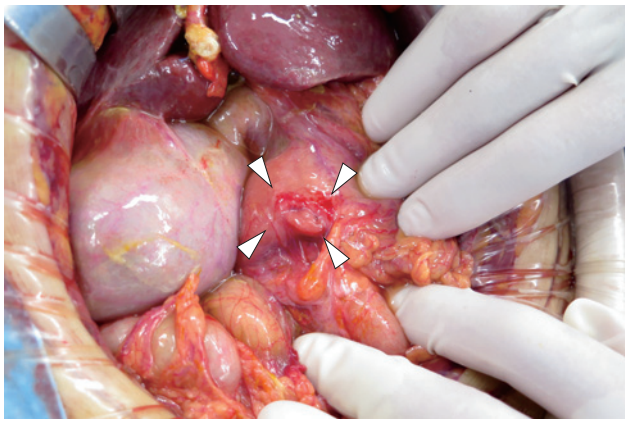


Fig. 3 Stapfer's type I perforation by direct ERCP scope perforation: the arrowheads show a hole approximately 10 mm in diameter.

underwent surgery; 4 of these 5 surgical cases had severe abdominal pain with extraluminal fluid collection and required emergency surgical repair and drainage of the abdominal and retroperitoneal cavity. In 1 case of type I perforation, the duodenal hole was approximately 10 mm in diameter, which was consistent with the size of the ERCP scope, and required primary repair (**Fig. 3**). When necessary, the Kocher maneuver was added to expose structures in the retroperitoneum behind the duodenum and pancreas.

In 1 type II surgical patient with a 3-mm periampullary hole in the retroperitoneal space, the perforated lesion was sutured and closed with the Kocher maneuver. A type III surgical case had a 2-mm perforation of the distal bile duct and required primary repair with the Kocher maneuver. In 4 patients requiring emergent surgery, abdominal or retroperitoneal contamination was not severe because emergent intervention was undertaken without delay. Three of the 4 patients requiring emergent surgery had cholangitis due to choledocholithiasis and choledocholithotomy.

A case of type III perforation was diagnosed pathologically as distal bile duct cancer 3 days after ERCP. The patient had mild abdominal pain with slight retroperitoneal fluid collection on the day of ERCP perforation and was monitored for pain and retroperitoneal fluid accumulation on CT. Abdominal pain and fluid collection gradually resolved. Because diachronic progression of inflammation and infection of the retroperitoneal space was anticipated, the patient underwent pancreatoduodenectomy on day 6 before his planned procedure.

Five (33.3%) of 15 patients underwent endoscopic nasobiliary drainage (ENBD) for decompression of the biliary system. At our center, neither endoscopic clip repair nor metallic stent insertion was used to close a penetrated hole.

In 2 patients, including 1 type II and 1 type III, the retroperitoneal abscess worsened and was treated by CT-guided drainage on day 7, because of worsening inflam-

mation on blood testing and growth of the extraluminal abscess on CT.

All 15 patients with ERCP-related perforation were discharged from the hospital. There were no deaths.

Discussion

ERCP is an indispensable technique, and treatments associated with ERCP are widespread in clinical settings. However, the reported incidence of ERCP-related complications is higher than that of upper and lower gastrointestinal endoscopy, and complications related to ERCP are sometimes fatal[1,2]. We experienced 15 patients with ERCP-related perforation in our hospital and were frustrated by the course of treatment. There is no gold-standard guideline for treatment of ERCP-related perforation, and the characteristics of ERCP-related perforation differ among patients. ERCP is usually performed by gastrointestinal clinicians; however, treatment of complications sometimes requires interventional radiologist or surgeons, which can make decisions regarding treatment more difficult. We believe it is important to determine the incidence, causes, and outcomes of ERCP-related perforation in our institution and to identify appropriate management and prevention.

ERCP complications in Japan were reported in the 6th National Survey Report published by the Japan Gastroenterological Endoscopy Society[1], which classified ERCP as duodenal endoscopy (side-viewing endoscope) or balloon enteroscopy. According to the report, among the 222,365 cases of diagnostic side-viewing endoscopy, including ordinary ERCP, the incidence of accidents was 746 (0.33%) and the number of perforations was 77 (0.035%). Of the 6,710 cases of ERCP treated by balloon enteroscopy, the incidence of accidents was 30 (0.45%), with perforation accounting for 14 accidents (0.21%). Regarding therapeutic ERCP, of 271,531 cases, the incidence of accidents was 2,700 cases (0.99%) and perforation accounted for 293 cases (0.108%). Regarding perforation, EST caused perforation in 0.198% of all ESTs and was highest among ERCP-related perforations. The frequency of perforation in other ERCP procedures was 0.05-0.08% for endoscopic biliary drainage, endoscopic papillary balloon dilatation, and biliary and pancreatic stents.

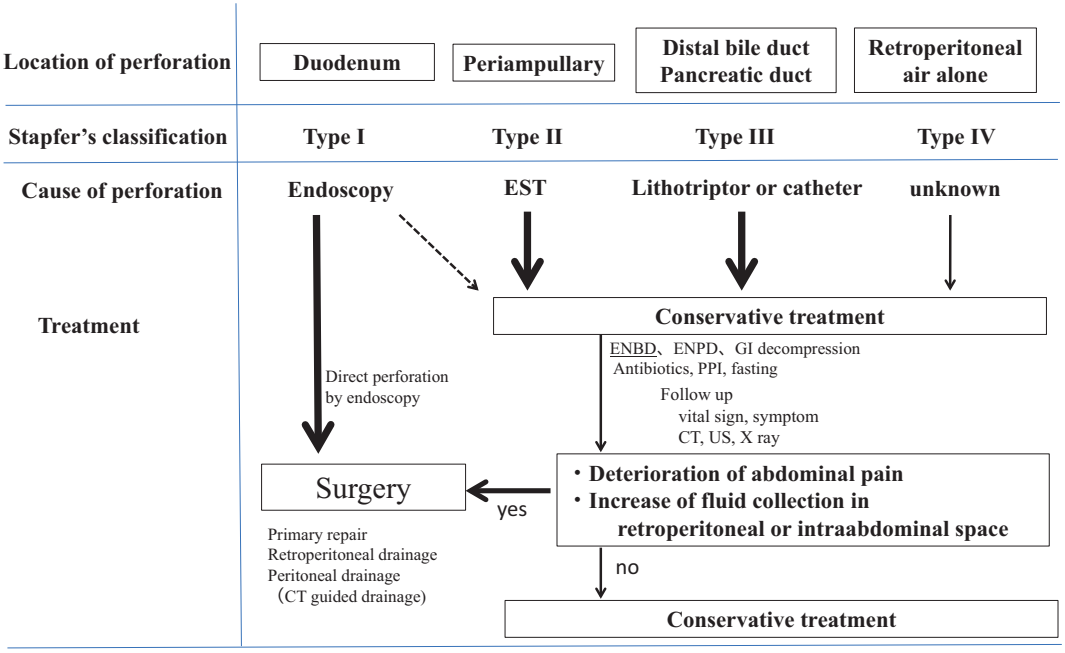
To date, reports of ERCP-related perforation in Japan have largely been retrospective questionnaire surveys; however, prospective studies in Europe and the United States reported a widely differing incidence rate of 0.0-8.3%[4,5,7–11]. The 6th Japanese National Survey Report[1] reported a high mortality rate: 16 (5.5%) of 293 ERCP-related perforations. After ERCP-related perforation, careful treatment decisions must be made, as delayed treatment can be fatal[2,4,12].

According to the classification of ERCP-related perforation reported by Stapfer et al.[6], the site of ERCP-related perforation is roughly classified as the duodenum, periampullary, bile duct, and pancreatic duct. The current report also showed a relationship between perforation site and cause. First, duodenal perforations (type I) were caused by the ERCP scope with direct, complete perforation and a clockwise axial rotation to shorten the ERCP fiber. Clockwise rotation of ERCP in patients with a history of upper abdominal operation may be a risk factor for injury to the duodenal wall by scope-induced twist and should be performed carefully. Type II periampullary perforation was thought to be caused by an overlong incision and an inappropriate EST incision direction. Extreme caution, particularly regarding the incision length and direction when performing EST, reduced the incidence of type II perforation. In type III, damage by the lithotripter and catheter caused distal bile duct perforation, and catheter insertion in pancreatic duct stricture might cause pancreatic duct perforation. It is important to keep in mind that there is a relationship between the site of ERCP-related perforation and the ERCP procedure. To prevent ERCP-related perforation, it is desirable to predict most common complications in each phase, from insertion of the ERCP scope to completion of the therapeutic ERCP treatment.

In almost all cases, it was possible to anticipate and diagnose ERCP-related perforation during ERCP. If perforation is suspected during ERCP, a CT scan should be performed immediately after ERCP to check the severity of perforation, including extraluminal fluid and gas collection. When retroperitoneal perforation is suspected because of the presence of retroperitoneal gas on X-ray during ERCP, it is important not to inflate excessively, so as not to widen the retroperitoneal space. Endoscopists often spend time inserting ENBD or closing the hole by clip after identifying perforation; however, this may cause massive extraluminal emphysema in a wider than expected area. In addition, ERCP under CO_2 insufflation will reduce the volume of extraluminal leakage gas and fluid cavity[13].

In patients with ERCP-related perforation accompanied by post-ERCP pancreatitis, diagnosis and treatment of retroperitoneal perforation is difficult. Multiple simultaneous complications cause complex conditions, make decisions difficult, and affect mortality.

Table 6



EST: endoscopic sphincterotomy, ENBD: endoscopic retrograde biliary drainage,
ENPD: endoscopic retrograde pancreatic drainage, CT: computed tomography, US: ultrasonography
GI: gastrointestinal, PPI: proton pump inhibitor

Table 6 shows the treatment strategy algorithm for ERCP-related perforation in our institution. CT should be performed immediately for cases of suspected perforation during ERCP. CT screening is added for patients with severe abdominal pain after ERCP. Patients with ERCP-related perforation are managed through emergency surgery by closure of the perforated site and abscess drainage when severe abdominal pain is accompanied by intraperitoneal or retroperitoneal fluid collection on CT. Patients without symptoms and extraluminal fluid collection are observed conservatively. Patients with mild abdominal pain and limited extraluminal fluid collection are also monitored. Monitored patients are maintained with fasting under dosing of a proton pump inhibitor and antibiotic agent. Additionally, monitored patients are treated by ENBD, endoscopic nasopancreatic duct drainage (ENPD), and a nasogastric tube, depending on their condition. Indications for ENBD and ENPD should be considered during the concerned ERCP, according to accessibility. Monitored patients are also followed over time for pain and extraluminal fluid accumulation on CT; if symptoms or CT findings worsen, additional treatment, including surgery, may be necessary. In patients with worsening abdominal symptoms and extraluminal fluid collection, emergent intervention including surgical drainage should be considered.

In a previous report[14], pneumoretroperitoneum was observed in 6 of 21 patients (29%) who had no clinical symptoms after EST. These asymptomatic patients with pneumoretroperitoneum alone had an uneventful course and needed no additional treatment. As for the absence of type IV patients in this study, because patients with only retroperitoneal gas had no symptoms and did not undergo CT screening, type IV perforation could not be recognized. Recently, endoscopic ultrasound-fine needle aspiration (EUS-FNA) has been used widely and sometimes causes perforation[15,16]; however, most EUS-FNA procedures are uneventful and require no medical treatment. Clinicians have reached a consensus that asymptomatic endoscopy-related perforation without extraluminal fluid collection does not require emergency intervention[17]. Careful follow-up is sufficient for asymptomatic patients with extraluminal gas collection alone, regardless of Stapfer's classification.

Peripapillary perforation (type II) and perforations of the bile duct and pancreatic duct (type III) are often relatively small and conservative follow-up with biliary drainage may be sufficient[6,18].

Regarding the method of closure or cover of the perforation site, methods for endoscopically closing gastrointestinal perforations that use a clip and an endoloop[18] and the over-the-scope clip method[19] have been reported. A method of temporary covering the perforation with an expandable metal stent has been reported for peripapil-

lary perforation due to excessive EST incision[20]. However, these innovative procedures should be performed at a facility with sufficient knowledge and experience; unnecessarily prolonging ERCP time and aggravating retroperitoneal inflammation should be avoided.

Stapfer et al.[6] reported that duodenal perforation (type I) was expected to cause direct penetrating fiber damage to the intestinal wall and that the perforated area will likely be a large hole with a diameter similar to that of the scope. Therefore, surgical closure of the perforation should be considered as the first choice. However, the area of a duodenal perforation by the ERCP fiber varies, and surgical treatment is considered appropriate for a complete ERCP scope perforation that penetrates the duodenal wall. However, conservative treatment was possible in our case of tearing duodenal injury caused by clockwise axial rotation intended to shorten the ERCP fiber. These perforated cases caused by clockwise axial rotation occurred in patients with a history of upper abdominal surgery and tend to destroy the duodenal wall by twisting force and abdominal adhesion.

In addition to the severity and site of perforation during ERCP, patient symptoms after ERCP, physical findings, and CT images of extraluminal fluid accumulation determine treatment. Extraluminal fluid leakage, including bile and pancreatic juices, exacerbates inflammation and abscess formation. Delayed treatment makes surgery difficult, because of worsened inflammation and abscess formation, it also compromises the patient's general condition and directly affects mortality[2]. Therefore, emergency surgery should be begun immediately in cases requiring surgical intervention.

Careful ERCP-related treatment is important for preventing ERCP-related perforation, but the team should consider possible complications and simulate methods of treatment. In our experience, when suspecting perforation during ERCP, endoscopists become upset and tend not to think clearly. Even in such a tense situation, preliminary simulation and immediate appropriate judgement should avoid the worst outcomes. In addition, after diagnosing ERCP-related perforation, it is important to share the patient's information and communicate closely with interventional radiologists and surgeons, as this will facilitate the best decisions and optimal timing of interventions.

Conflict of Interest: None declared.

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