Gastroenterology Report, 2024, **12**, goae044
https://doi.org/10.1093/gastro/goae044
Original Article

Original Article

Evaluation of ERCP-related perforation: a single-center retrospective study

Feng Zhou[1,†], Xiaoyun Zhan[2,†], Dan Hu[1], Nanzhen Wu[3], Junbo Hong[1], Guohua Li[1], Youxiang Chen[1] and Xiaojiang Zhou[1,*]

[1]Department of Gastroenterology, Digestive Disease Hospital, The First Affiliated Hospital, Jiangxi Medical College, Nanchang University, Nanchang, Jiangxi, P. R. China
[2]Department of Gastroenterology, The Third Hospital of Nanchang, Nanchang, Jiangxi, P. R. China
[3]Department of Gastrointestinal Surgery, Fengcheng People's Hospital, Fengcheng, Jiangxi, P. R. China

*Corresponding author. Department of Gastroenterology, The First Affiliated Hospital of Nanchang University, No.17 Yongwaizheng Street, Nanchang 330000, Jiangxi, P. R. China. Tel: 0791-83969203; Email: yfyzxj1970@ncu.edu.cn

†These authors contributed equally to this work.

Abstract

Background: Endoscopic retrograde cholangiopancreatography (ERCP)-related perforation is a rare and serious adverse event. The aim of our study was to evaluate the risk factors and management of ERCP-related perforation, and to further determine the predictive factors associated with perforation outcome.

Methods: A total of 27,018 ERCP procedures performed at the First Affiliated Hospital of Nanchang University (Nanchang, China) between January 2007 and March 2022 were included in the investigation of ERCP-related perforation. Medical records and endoscopic data were extracted to analyse the risk factors, management, and clinical outcome of ERCP-related perforation.

Results: Seventy-six patients (0.28%) were identified as having experienced perforation following ERCP. Advanced age, Billroth II anatomy, precut sphincterotomy, and papillary balloon dilatation were significantly associated with ERCP-related perforation. Most patients with perforation ($n = 65$) were recognized immediately during ERCP whereas 11 were recognized later on. The delay in recognition primarily resulted from stent migration ($n = 9$). In addition, 12 patients experienced poor clinical outcome including death or hospice discharge ($n = 3$), ICU admission for >3 days ($n = 6$), and prolonged hospital stay for >1 month due to perforation ($n = 3$). Cancer and systemic inflammatory response syndrome (SIRS) are associated with a higher risk of poor outcome.

Conclusions: Advanced age, Billroth II anatomy, precut sphincterotomy, and balloon dilation increase the risk of ERCP-related perforation whereas cancer and SIRS independently predicted poor clinical outcome.

Keywords: endoscopic retrograde cholangiopancreatography; perforation; risk factor; management; clinical outcome

Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) is an invasive endoscopic procedure that is widely employed for the diagnosis and treatment of biliary and pancreatic diseases. Although ERCP has shown a high success rate, it is also associated with various adverse events, including acute pancreatitis, cholangitis, bleeding, and perforation. Among these adverse events, iatrogenic perforation related to ERCP is rare but severe and has been reported in 0.08%–1.5% of patients [1–5], with a mortality rate of ≤20% [4, 6, 7].

Perforation related to ERCP is caused mainly by intestinal luminal injury from endoscopes, sphincterotomy beyond the intramural portion, and bile duct injury from instruments. Different types and degrees of ERCP-related perforation are managed in different ways. Compared with previously emergent surgical repair, the utilization of endoscopic or medical treatment for ERCP-related perforation is considered the priority management approach. The majority of patients can recover from perforation without any serious incidents [3, 8, 9]. Additionally, the importance of immediate recognition in improving patient outcome is gradually being acknowledged, contributing to endoscopic or surgical intervention in the mild stage of the disease [4, 10]. However, some patients still experience a severe clinical course and poor prognosis. Due to the current lack of effective markers, predicting ERCP-related perforation remains challenging.

Therefore, the aim of this study is to evaluate the risk factors and management of ERCP-related perforation and to further determine the predictive factors associated with perforation outcome.

Methods

Study population

ERCP procedures performed at the First Affiliated Hospital of Nanchang University (Nanchang, China) between January 2007 and March 2022 were reviewed. All perforations related to ERCP

Received: 24 July 2023. **Revised:** 5 February 2024. **Accepted:** 14 April 2024

that had supporting evidence with reports from endoscopy, radiology, or surgery were identified in this study. Patients with nonlocal perforation (away from the duodenum and biliopancreatic duct) or incomplete data were excluded. The data, including patient demographics, procedure information, perforation characteristics, laboratory examinations, imaging findings, and management strategies, were extracted from the endoscopy database and medical records. This study was approved by the institutional review board of the First Affiliated Hospital of Nanchang University [(2022)CDYFYYLK(09–030)].

Diagnosis and definition

ERCP-related perforation was diagnosed based on the presence of luminal defects by endoscopic visualization or contrast leakage, extraluminal passage of a guide wire, and free or retroperitoneal gas on fluoroscopy imaging during ERCP. In addition, the detection of gas or luminal contents outside the gastro-intestinal tract through post-procedural plain radiographs or computed tomography (CT) images of the abdomen was also available. Immediate diagnosis of a perforation was defined as recognition of the perforation during ERCP. The delayed diagnosis of perforation was defined as recognition of the perforation through postoperative imaging or the next endoscopic follow-up, such as stent retrieval. Perforation was stratified according to the standardized Stapfer classification system [11]. Perforation caused by migrated stents was described separately, as they pertain to entirely distinct patient groups.

The endoscopic procedures were categorized and divided into four levels by using the American Society for Gastrointestinal Endoscopy (ASGE) difficulty grading system [12]. The peritoneal irritation sign was defined as a combination of abdominal guarding and rigidity, tenderness, and rebound tenderness. Systemic inflammatory response syndrome (SIRS) was defined as the presence of two or more of the following conditions: body temperature of $<36^{\circ}C$ or $>38^{\circ}C$, white blood cell count of $<4\times10^{9}$/L or $>12\times10^{9}$/L, tachycardia with a heart rate of >90 beats per minute, or tachypnea with a respiratory rate of >20 breaths per minute.

Poor outcome was defined as death due to perforation or hospice discharge, ICU admission for >3 days, or prolonged hospital stay for >1 month due to the perforation [13]. A good outcome was defined as recovery from the perforation without any of the poor outcomes stated above.

Perforation treatment

Patients with Stapfer I perforation typically require immediate closure, through either endoscopy or surgical intervention [14]. Conversely, Stapfer II perforation is treated with biliary stenting to divert the bile flow away from the perforation site, with or without clipping of the defect. Stapfer III and IV perforations are initially managed conservatively unless they are identified during endoscopy or they experience clinical deterioration. Conservative medical treatment protocols include fasting, intravenous administration of antibiotics, proton-pump inhibitors, and continuous hemodynamic monitoring.

Statistical analysis

Descriptive statistics were summarized for all clinical variables and are presented as the mean ± standard deviation (SD) for normal data or the median and interquartile range (IQR) for nonnormal data. Categorical variables are presented as counts and percentages (%) and were compared by using the chi-square test or Fisher's exact test. Continuous variables were compared by using the *t*-test or the Mann–Whitney *U* test. Multivariate logistic regression was subsequently used to investigate potential risk factors for perforation. All statistical analyses were performed using SPSS version 24.0 (IBM Corp, Armonk, NY, USA). A two-tailed *P*-value of <0.05 was considered to indicate statistical significance.

Results

A total of 27,018 ERCP procedures were reviewed during the study period from January 2007 to March 2022. There were 78 patients identified as having ERCP-related perforation. Two patients (one with an esophageal perforation and one with a gastric perforation) were excluded due to nonlocal perforation. The remaining 76 patients (0.28%) with perforation were included in our study (Figure 1).

Overall characteristics of patients with ERCP-related perforation

The mean age of the patients with ERCP-related perforation was 64.5 ± 14.4 years and 41 patients (53.9%) were female (Table 1). Eight patients (10.5%) had previously undergone Billroth II gastrectomy and 25 patients (32.9%) had a periampullary diverticulum. The most common indication for perforation in patients was a common bile duct stone (75.0%), followed by biliary stricture (15.8%). The procedural difficulty was focused mainly on grade 2 and grade 3 (35.5% and 48.7%, respectively). Endoscopic sphincterotomy (57.9%) and papillary balloon dilatation (36.8%) were widely used in the perforation group.

According to the multivariate logistic regression analysis, advanced age, Billroth II anatomy, precut sphincterotomy, endoscopic papillary balloon dilatation, and mechanical lithotripsy were associated with a higher risk of ERCP-related perforation. However, mechanical lithotripsy was no longer significantly associated with a higher risk after adjustment for confounding factors.

Classification of ERCP-related perforation

Stapfer I perforation was found in 22 patients, while Stapfer II perforation occurred in 37 patients (Table 2). Additionally, four patients with Stapfer III perforation and four patients with Stapfer IV perforation were detected. Among the seven patients with Billroth II anatomy, three patients with perforation were located within the afferent loop. There were no significant differences in the number of patients with altered anatomy or the number of emergent admissions between the Stapfer I and Stapfer II perforation groups.

Most patients with perforation ($n=65$) were recognized immediately during ERCP and delayed recognition was observed for only two patients with Stapfer II perforation. Although the patients with Stapfer I perforation exhibited a slightly longer hospital stay than those with Stapfer II perforation (15.5 ± 15.1 vs 11.3 ± 4.1 days), the difference did not reach statistical significance. Stapfer III perforation showed a long duration due to severe bleeding.

Endoscopic closures were performed in 17 patients who underwent Stapfer I perforation without secondary interventions. Surgical duodenal repairs were promptly performed in another four patients with duodenal perforation, one of whom experienced a failed intraoperative attempt at complete endoscopic closure. The remaining patient, who had a suspected small perforation in the duodenal diverticulum, was treated conservatively and eventually recovered. In contrast, all Stapfer II perforation patients underwent endoscopic treatment without

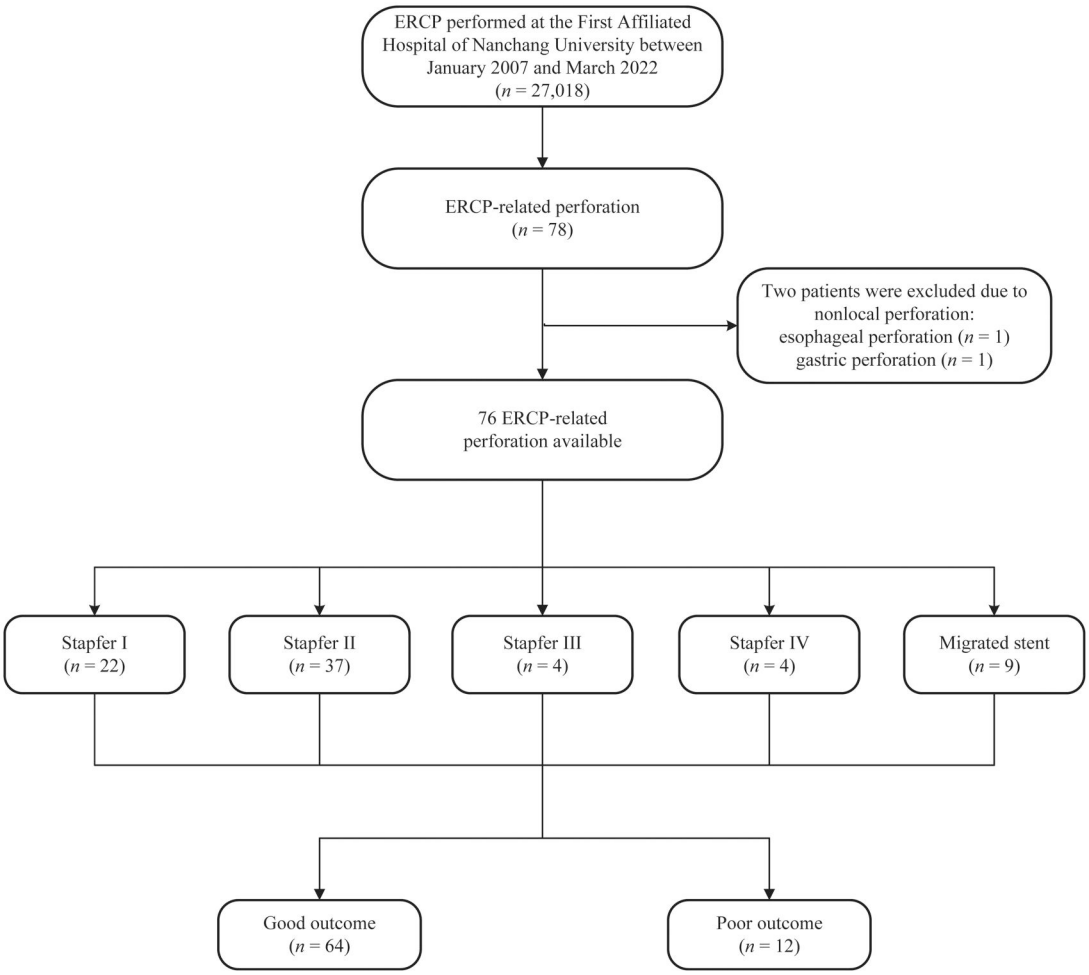

Figure 1. Flowchart of the patient selection.

reintervention, except for one patient who was managed conservatively due to failed biliary cannulation.

Clinical outcome of ERCP-related perforation

To clarify the factors associated with outcome, we divided the patients into two groups (Table 3). After excluding one patient who had perforation caused by migrated stents, 11 patients experienced poor clinical outcome, including death or hospice discharge ($n = 2$), ICU admission for >3 days ($n = 6$), and prolonged hospital stay for >1 month due to perforation ($n = 3$). Poor outcome was observed in six patients with Stapfer I perforation and five patients with Stapfer II perforation.

Our results showed that cancer significantly increased the risk of a poor outcome ($P < 0.05$). However, there was no difference in the indications or type of perforation between the groups. Delayed recognition was not significantly associated with poor outcome. Compared with post-ERCP pancreatitis and abdominal pain, the peritoneal irritation sign and SIRS were significantly more common in the poor outcome group ($P < 0.05$). When the factors were investigated by using multivariate analysis, only cancer and SIRS were found to be significant risk factors for poor outcome.

Similarly, clinical outcome was not associated with any of the different treatment measures. Among the six patients with Stapfer I perforation with poor outcome, two underwent surgical repair and four underwent endoscopic clipping. Five patients of Stapfer II perforation underwent routine placement of nasobiliary tubes or stents, with delayed recognition in two patients.

Stent migration-related perforation

There were nine patients identified with perforation (seven duodenums and two bile ducts) associated with migrated stents (Table 4). Based on the stent types, straight stents were found in seven patients, whereas Tannenbaum and fully covered metal stents were each found in one patient. The stents were positioned intrahepatically left in four patients (44.4%), intrahepatically right in two patients (22.2%), and extrahepatically within the duct in three patients (33.3%). Most of the stents had a length of >10 cm (55.6%) and a diameter of 8.5 French (55.6%). Although all patients received endoscopic treatment, one patient experienced a severe infection after endoscopic closure and was discharged to hospice care.

Discussion

Iatrogenic perforation is the most serious adverse event after ERCP and is associated with a high risk of mortality. Due to the rarity of perforation, only a few studies have focused on this specific adverse event with limited cohort sizes [4, 15, 16]. Additionally, as the application of ERCP continues to expand, the

Table 1. Overall characteristics of patients with ERCP-related perforation.

Characteristic	Perforation ($n = 76$)	Non-perforation ($n = 26,942$)	Univariable analysis		Multivariable analysis	
			OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Age, years, mean ± SD	64.5 ± 14.4	59.0 ± 15.4	5.46 (1.99–8.94)	0.002	1.02 (1.00–1.04)	0.030
Sex, female, *n* (%)	41 (53.9)	13,534 (50.2)	1.16 (0.74–1.82)	0.518		
Billroth II anatomy, *n* (%)	8 (10.5)	434 (1.6)	7.19 (3.43–15.04)	<0.001	5.41 (2.53–11.56)	<0.001
Periampullary diverticulum, *n* (%)	25 (32.9)	8,249 (30.6)	1.11 (0.69–1.79)	0.667		
Admission type, *n* (%)						
Scheduled	18 (23.7)	4,632 (17.2)	Reference			
Urgent	58 (76.3)	22,310 (82.8)	0.67 (0.39–1.14)	0.134		
Indication, *n* (%)						
Common bile duct stone	57 (75.0)	17,995 (66.8)	Reference			
Biliary stricture	12 (15.8)	5,141 (19.1)	0.74 (0.40–1.37)	0.335		
Acute pancreatitis	7 (9.2)	2,834 (10.5)	0.78 (0.36–1.71)	0.534		
Others	0 (0.0)	972 (3.6)	1.05 (1.05–1.06)	0.120		
Procedural difficulty, *n* (%)						
Grade 1	5 (6.6)	2,362 (8.8)	Reference			
Grade 2	27 (35.5)	13,585 (50.4)	0.94 (0.36–2.44)	0.805		
Grade 3	37 (48.7)	9,996 (37.1)	1.75 (0.69–4.45)	0.235		
Grade 4	7 (9.2)	999 (3.7)	0.31 (1.05–10.45)	0.051		
Endoscopic procedure, *n* (%)						
Sphincterotomy	44 (57.9)	15,175 (56.3)	1.07 (0.68–1.68)	0.783		
Precut	10 (13.2)	1,417 (5.3)	2.73 (1.40–5.32)	0.007	2.68 (1.37–5.26)	0.004
Papillary balloon dilatation	28 (36.8)	4,905 (18.2)	2.62 (1.04–4.80)	<0.001	2.02 (1.22–3.36)	0.007
Biliary stricture dilatation	7 (9.2)	1,197 (4.4)	1.26 (0.46–3.45)	0.084		
Mechanical lithotripsy	11 (14.5)	1,554 (5.8)	2.48 (1.27–4.82)	0.012	1.85 (0.91–3.80)	0.091

OR = odds ratio, CI := confidence interval.

Table 2. Classification of ERCP-related perforation.

Characteristic	Stapfer I ($n = 22$)	Stapfer II ($n = 37$)	Stapfer III ($n = 4$)	Stapfer IV ($n = 4$)	*P*-value[a]
Age, years, mean ± SD	69.5 ± 12.9	63.5 ± 14.0	59.3 ± 17.3	64.0 ± 13.2	0.110
Sex, female, *n* (%)	14 (63.6)	21 (56.8)	1 (25.0)	3 (75.0)	0.603
Billroth II anatomy, *n* (%)	3 (13.6)	3 (8.1)	1 (25.0)	0 (0.0)	0.501
Periampullary diverticulum, *n* (%)	9 (4.1)	12 (32.4)	0 (0.0)	2 (50.0)	0.512
Admission type, *n* (%)					
Urgent	3 (13.6)	8 (21.6)	2 (50.0)	3 (75.0)	Reference
Scheduled	19 (86.4)	29 (78.4)	2 (50.0)	1 (25.0)	0.450
Indication, *n* (%)					
Common bile duct stone	17 (77.3)	29 (78.4)	3 (75.0)	4 (100.0)	Reference
Biliary stricture	0 (0.0)	6 (16.2)	1 (25.0)	0 (0.0)	>0.99
Acute pancreatitis	5 (22.7)	2 (5.4)	0 (0.0)	0 (0.0)	0.741
Recognition, *n* (%)					
Early	22 (100.0)	35 (94.6)	4 (100.0)	4 (100.0)	Reference
Delayed	0 (0.0)	2 (5.4)	0 (0.0)	0 (0.0)	>0.99
Hospital stay, days, mean ± SD	15.5 ± 15.1	11.3 ± 4.1	13.5 ± 8.1	9.8 ± 2.5	0.271
Treatment, *n* (%)					
Endoscopic	17 (77.3)	36 (97.3)	4 (100.0)	4 (100.0)	Reference
Surgical	4 (18.2)	0 (0.0)	0 (0.0)	0 (0.0)	>0.99
Conservative	1 (4.5)	1 (2.7)	0 (0.0)	0 (0.0)	>0.99
Outcome, *n* (%)					
Good	16 (72.7)	32 (86.5)	4 (100.0)	4 (100.0)	Reference
Poor	6 (27.3)	5 (13.5)	0 (0.0)	0 (0.0)	0.3197

[a] Stapfer I vs Stapfer II.

absolute number of ERCP-related perforations is likely to increase [5, 17]. Therefore, further evaluation of the ERCP-related perforation is warranted.

In this study, we examined 76 patients with ERCP-related perforation during a 15-year study period. The incidence of perforation following ERCP was 0.28%, which is consistent with the literature [15, 18, 19]. Advanced age, Billroth II anatomy, precut sphincterotomy, and papillary balloon dilatation were identified as major risk factors for perforation. The elevated rate of perforation in elderly patients may be attributed to the reduced mechanical strength of their intestinal wall [20, 21]. Surgical alterations in anatomy also make ERCP challenging and further increase the risk of perforation. Precut sphincterotomy is mainly performed to enlarge the papillary orifice when standard methods of cannulation fail [22]. In addition to direct injury by the precut sphincterotomy itself, extensive edema and injury following multiple prior cannulation attempts leave the papilla more vulnerable to secondary perforation. Our results also showed that balloon dilatation significantly increased the risk of perforation. In fact, compared with the median diameter of the distal common bile duct, which was 13.0 mm (range: 7–23 mm), the median diameter of the balloon dilation was 14.0 mm (range: 8–15 mm) in the Stapfer

Table 3. Factors associated with clinical outcome for ERCP-related perforation.

Characteristic	Poor outcome ($n = 11$)	Good outcome ($n = 56$)	Univariable analysis		Multivariable analysis	
			OR (95% CI)	P-value	OR (95% CI)	P-value
Age, years, mean ± SD	70.9 ± 14.5	64.2 ± 13.5	1.04 (0.99–1.10)	0.143		
Sex, female, *n* (%)	6 (54.5)	33 (58.9)	1.20 (0.33–4.39)	0.79		
Cancer, *n* (%)	4 (36.4)	5 (8.9)	5.83 (1.26–27.02)	0.024	17.27 (1.57–189.87)	0.038
Admission type, *n* (%)						
Urgent	2 (18.2)	14 (25.0)	Reference			
Scheduled	9 (81.8)	42 (75.0)	0.67 (0.13–3.46)	>0.99		
Indication, *n* (%)						
Common bile duct stone	9 (81.8)	44 (78.6)	Reference			
Biliary stricture	1 (9.1)	6 (10.7)	0.82 (0.09–7.62)	>0.99		
Acute pancreatitis	1 (9.1)	6 (10.7)	0.82 (0.09–7.62)	>0.99		
Perforation type, *n* (%)						
Stapfer I	6 (50.0)	16 (28.6)	Reference			
Stapfer II	5 (41.7)	32 (57.1)	0.42 (0.11–1.58)	0.197		
Stapfer III	0 (0.0)	4 (7.1)	–	>0.99		
Stapfer IV	0 (0.0)	4 (7.1)	–	>0.99		
Recognition, *n* (%)						
Early	9 (81.8)	56 (100.0)	Reference			
Delayed	2 (18.2)	0 (0.0)	–	>0.99	–	
Post-ERCP pancreatitis[a], *n* (%)	1 (9.1)	7 (12.5)	1.43 (0.16–12.93)	0.751		
Peritoneal irritation sign, *n* (%)	8 (72.7)	16 (28.6)	6.67 (1.57–28.34)	0.010	2.66 (0.29–24.35)	0.388
SIRS, *n* (%)	9 (81.8)	16 (28.6)	11.25 (2.19–57.89)	0.004	17.27 (1.58–189.87)	0.020
Treatment, *n* (%)						
Endoscopic	8 (72.7)	54 (96.4)	Reference			
Surgical	2 (18.2)	2 (3.6)	6.75 (0.83–54.90)	0.074		
Conservative	1 (9.1)	0 (0.0)	–	>0.99		

[a] 1 and 6 patients, respectively, with preoperative acute pancreatitis were excluded.
OR = odds ratio, CI = confidence interval, SIRS = systemic inflammatory response syndrome.

Table 4. Distal and proximal perforation caused by migrated stents.

Characteristic	Distal migration ($n = 7$)	Proximal migration ($n = 2$)
Age, years, mean ± SD	61.9 ± 18.4	64.5 ± 16.3
Sex, female, *n* (%)	2 (22.2)	0 (0.0)
Indication, *n* (%)		
Benign disease	6 (77.8)	1 (50.0)
Malignant disease	1 (22.2)	1 (50.0)
Stent shape, *n* (%)		
Straight	6 (77.8)	1 (50.0)
Tannenbaum[a]	1 (11.1)	0 (0.0)
Fully covered metal	0 (11.1)	1 (50.0)
Stent location, *n* (%)		
Intrahepatic left	3 (44.4)	1 (50.0)
Intrahepatic right	2 (22.2)	0 (0.0)
Extrahepatic	2 (33.3)	1 (50.0)
Stent length[b], *n* (%)		
≤10 cm	2 (33.3)	1 (100.0)
>10 cm	5 (55.6)	0 (0.0)
Stent diameter[b], *n* (%)		
7 French	3 (33.3)	0 (0.0)
8.5 French	4 (55.6)	1 (100.0)
Treatment, *n* (%)		
Endoscopic	7 (100.0)	2 (100.0)
Surgical	0 (0.0)	0 (0.0)
Conservative	0 (0.0)	0 (0.0)
Outcome, *n* (%)		
Good	6 (88.9)	2 (100.0)
Poor	1 (11.1)	0 (0.0)

[a] Consisting of multiple anchoring flaps without any side holes.
[b] Excluding a 60 mm × 10 mm fully covered metal stent.

II perforation group. The expected maximum target diameter of the balloon should be determined based on the maximum stone diameter but it should not exceed the diameter of the distal bile duct, to mitigate the risk of perforation [23, 24].

Duodenal perforations are typically characterized by larger wounds and continuous leakage of digestive fluid into the retroperitoneal or intraperitoneal space. In our study, when compared with Stapfer II perforation, Stapfer I perforation clearly exhibited a longer hospital stay and a greater percentage of poor outcome. However, hospital stay was connected to the impact of other concomitant adverse events to some extent, preventing the establishment of a significant difference related to the type of perforation.

Except for nine patients with stent migrations, almost all patients with perforation (65/67, 97.0%) were recognized immediately through endoscopic visualization or fluoroscopy imaging. Immediate recognition provides a great opportunity for prompt endoscopic or surgical intervention and improves the clinical course in patients with perforation [4, 25]. The remaining two patients who had delayed recognition induced by sphincterotomy both achieved poor outcome. Wound closure helps to limit the leakage of luminal contents and prevent severe complications, such as sepsis and multiple organ failure [26]. The high detection rate confirmed the feasibility of immediate recognition during ERCP. This benefit was mainly from routine abdominal radiography at the end of the procedures. The evidence for extravasation agent of contrast and the presence of retroperitoneal or intraperitoneal air under fluoroscopy can suggest the occurrence of perforation. Relatively small perforations may exhibit less distinct radiographic changes, making them more prone to being overlooked. Endoscopists, meanwhile, tend to concentrate their attention on the narrowed regions of endoscopic views and/or biliary/pancreatic imaging in the monitor. Moreover, less experienced endoscopists are more unfamiliar with imaging changes associated with perforation due to the low incidence of perforation. Regardless, after completing all endoscopic procedures, careful examination and fluoroscopy are crucial for identifying perforation. Suspected perforation may be further determined by using post-procedural CT scans, especially for retroperitoneal perforation.

Delayed detection primarily arises from perforation caused by migrated stents. Stent migration itself was considered a late adverse event of ERCP and relevant perforation was reported in <1% of patients with stent placement [27, 28]. Perforation caused by migrated stents occurred more frequently within the intrahepatic left biliary system and among longer stents. Previous studies have indicated that the sharper anatomical features and more curved positioning of left intrahepatic stents encourage straight stents to migrate outward [28, 29]. Pig-tail or Tannenbaum stents with side flaps or barbs impose limitations on the mobility of the stent and may serve as alternative methods to mitigate the risk of stent migration [27].

The clinical outcome of perforation is strongly correlated with the patient's underlying conditions. Of those, cancer was significantly associated with an increased incidence of poor outcome. Although advanced age was found to be a risk factor for perforation in our study, the difference in age between the two outcome groups was not significant. Some studies have also indicated that ERCP is safe for elderly patients [30–32]. While the presence of peritoneal irritation symptoms is considered a strong indicator of perforation, the abdominal presentation of perforation patients is usually not entirely typical initially. Obesity, a decreased level of consciousness, and injuries in the retroperitoneal region can influence peritoneal irritation symptoms, leading to the disregard of their prognostic significance according to multifactorial analyses. Relying solely on peritoneal irritation signs to guide decisions also results in delayed clinical intervention due to their late-stage nature. In contrast, tracking changes in the extent and intensity of these signs may be capable of providing a more accurate reflection of the severity of the perforation.

SIRS was identified as another reliable predictor of poor outcome. Despite timely recognition and interventions to prevent continuous leakage in nine patients, the extravasation of digestive fluids or contrast agents can induce a local inflammatory response. When this inflammation is not effectively cleared by the body and gradually progresses systemically, it leads to the development of SIRS, especially in elderly or immunocompromised patients [33, 34]. As a consequence of an overactive response, SIRS can compromise the function of distinct organ systems, leading to multiple organ dysfunction syndrome, which has a mortality of 4.3%–10% [35–37].

Compared with other studies that are focused on the management of perforation [4, 15, 16], our study found no significant advantage for any treatment. Regardless of whether employing internal medicine or surgical interventions are used, immediate recognition and defect closure are essential for limiting the leakage of luminal contents and preventing severe complications, such as sepsis and multiple organ failure. It is advisable to conduct an abdominal CT scan and biochemical tests within 24 hours after closure to promptly detect any treatment failure for secondary interventions [8, 38]. Intervention at the earliest opportunity is considered helpful in reducing the systemic inflammatory reaction caused by persistent leakage to some extent. Overall, the most important effort should be directed toward the prevention of perforation.

There were several limitations in our study. The retrospective design limited by the low incidence of perforation may have introduced inherent selection bias. Asymptomatic or mild patients with delayed perforation could have been missed before discharge. The limited cohort size resulted in certain perforation sets being somewhat statistically underpowered. Moreover, the rarity of perforation forced us to extend the study period and prevented us from determining the influence of the experience of the endoscopists on perforation with increasing procedural volume.

In conclusion, advanced age, Billroth II anatomy, precut sphincterotomy, and papillary balloon dilatation were risk factors for ERCP-related perforation. In addition to perforation caused by migrated stents, routine postoperative abdominal fluoroscopy helps to achieve immediate recognition of most perforations. Cancer and SIRS were associated with poor outcome. Early monitoring and intervention may be required to optimize clinical outcomes in patients who are at risk of poor prognosis.

Data availability

All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

Authors' Contributions

F.Z.: study design, acquisition of data, drafting of the manuscript. X.Z., D.H., and N.W.: acquisition of data. J.H., G.L., Y.C., and X.Z.: endoscopic procedures. X.Z.: study design, interpretation of data, critical revision of the manuscript. All authors have approved the publication of this article.

Funding

This research was supported by the National Natural Science Foundation of China [no. 81860099] and the Natural Science Foundation of Jiangxi Province, China [no. 20202ACBL206009].

Conflicts of Interest

All authors have no conflicts of interest or financial ties to disclose.

References

1. Kodali S, MöNKEMüLLER K, Kim H *et al.* ERCP-related perforations in the new millennium: a large tertiary referral center 10-year experience. *United European Gastroenterol J* 2015;**3**:25–30.
2. Cotton PB, Garrow DA, Gallagher J *et al.* Risk factors for complications after ERCP: a multivariate analysis of 11,497 procedures over 12 years. *Gastrointest Endosc* 2009;**70**:80–8.
3. Patil NS, Solanki N, Mishra PK *et al.* ERCP-related perforation: an analysis of operative outcomes in a large series over 12 years. *Surg Endosc* 2020;**34**:77–87.
4. Weiser R, Pencovich N, Mlynarsky L *et al.* Management of endoscopic retrograde cholangiopancreatography-related perforations: Experience of a tertiary center. *Surgery* 2017;**161**:920–9.
5. Radlinski MJ, Strand DS, Shami VM. Evolution of interventional endoscopic ultrasound. *Gastroenterol Rep (Oxf)* 2023;**11**:goad038.
6. Langerth A, Isaksson B, Karlson BM *et al.* ERCP-related perforations: a population-based study of incidence, mortality, and risk factors. *Surg Endosc* 2020;**34**:1939–47.
7. Jin YJ, Jeong S, Kim JH *et al.* Clinical course and proposed treatment strategy for ERCP-related duodenal perforation: a multicenter analysis. *Endoscopy* 2013;**45**:806–12.
8. Ansari D, TORéN W, Lindberg S *et al.* Diagnosis and management of duodenal perforations: a narrative review. *Scand J Gastroenterol* 2019;**54**:939–44. 44.

9. Avgerinos DV, Llaguna OH, LO AY *et al.* Management of endoscopic retrograde cholangiopancreatography: related duodenal perforations. *Surg Endosc* 2009;**23**:833–8.
10. Enns R, Eloubeidi MA, Mergener K *et al.* ERCP-related perforations: risk factors and management. *Endoscopy* 2002;**34**:293–8.
11. Stapfer M, Selby RR, Stain SC *et al.* Management of duodenal perforation after endoscopic retrograde cholangiopancreatography and sphincterotomy. *Ann Surg* 2000;**232**:191–8.
12. Cotton PB, Eisen G, Romagnuolo J *et al.* Grading the complexity of endoscopic procedures: results of an ASGE working party. *Gastrointest Endosc* 2011;**73**:868–74.
13. Kim J, Lee SH, Paik WH *et al.* Clinical outcomes of patients who experienced perforation associated with endoscopic retrograde cholangiopancreatography. *Surg Endosc* 2012;**26**:3293–300.
14. Paspatis GA, Arvanitakis M, Dumonceau JM *et al.* Diagnosis and management of iatrogenic endoscopic perforations: European Society of Gastrointestinal Endoscopy (ESGE) Position Statement—Update 2020. *Endoscopy* 2020;**52**:792–810.
15. Cirocchi R, Kelly MD, Griffiths EA *et al.* A systematic review of the management and outcome of ERCP related duodenal perforations using a standardized classification system. *Surgeon* 2017;**15**:379–87.
16. Kumbhari V, Sinha A, Reddy A *et al.* Algorithm for the management of ERCP-related perforations. *Gastrointest Endosc* 2016;**83**:934–43.
17. Bazerbachi F, White RM, Forbes N *et al.* Endo-anesthesia: a primer. *Gastroenterol Rep (Oxf)* 2022;**10**:goac069.
18. Andriulli A, Loperfido S, Napolitano G *et al.* Incidence rates of post-ERCP complications: a systematic survey of prospective studies. *Am J Gastroenterol* 2007;**102**:1781–8.
19. Mariani A, Segato S, Anderloni A *et al.* Prospective evaluation of ERCP performance in an Italian regional database study. *Dig Liver Dis* 2019;**51**:978–84.
20. Watters DA, Smith AN. Strength of the colon wall in diverticular disease. *Br J Surg* 1990;**77**:257–9.
21. Wess L, Eastwood MA, Wess TJ *et al.* Cross linking of collagen is increased in colonic diverticulosis. *Gut* 1995;**37**:91–4.
22. Navaneethan U, Konjeti R, Lourdusamy V *et al.* Precut sphincterotomy: efficacy for ductal access and the risk of adverse events. *Gastrointest Endosc* 2015;**81**:924–31.
23. Kim JH, Yang MJ, Hwang JC *et al.* Endoscopic papillary large balloon dilation for the removal of bile duct stones. *World J Gastroenterol* 2013;**19**:8580–94.
24. Yamauchi H, Iwai T, Okuwaki K *et al.* Risk Factors for Perforation During Endoscopic Papillary Large Balloon Dilation and Bile Duct Stone Removal. *Dig Dis Sci* 2022;**67**:1890–900.
25. Bill JG, Smith Z, Brancheck J *et al.* The importance of early recognition in management of ERCP-related perforations. *Surg Endosc* 2018;**32**:4841–9.
26. Schmidt A, Fuchs KH, Caca K *et al.* The endoscopic treatment of iatrogenic gastrointestinal perforation. *Deutsches Arzteblatt Int* 2016;**113**:121–8.
27. Kawaguchi Y, Ogawa M, Kawashima Y *et al.* Risk factors for proximal migration of biliary tube stents. *World J Gastroenterol* 2014;**20**:1318–24.
28. Yuan XL, Ye LS, Liu Q *et al.* Risk factors for distal migration of biliary plastic stents and related duodenal injury. *Surg Endosc* 2020;**34**:1722–8.
29. Stassen PMC, DE Jong DM, Poley JW *et al.* Prevalence of and risk factors for stent migration-induced duodenal perforation. *Endosc Int Open* 2021;**9**:E461–e9.
30. Fritz E, Kirchgatterer A, Hubner D *et al.* ERCP is safe and effective in patients 80 years of age and older compared with younger patients. *Gastrointest Endosc* 2006;**64**:899–905.
31. Hu KC, Chang WH, Chu CH *et al.* Findings and risk factors of early mortality of endoscopic retrograde cholangiopancreatography in different cohorts of elderly patients. *J Am Geriatr Soc* 2009;**57**:1839–43.
32. Nassar Y, Richter S. Management of complicated gallstones in the elderly: comparing surgical and non-surgical treatment options. *Gastroenterol Rep (Oxf)* 2019;**7**:205–11.
33. Balk RA. Systemic inflammatory response syndrome (SIRS): where did it come from and is it still relevant today? *Virulence* 2014;**5**:20–6.
34. Barichello T, Generoso JS, Singer M *et al.* Biomarkers for sepsis: more than just fever and leukocytosis-a narrative review. *Crit Care* 2022;**26**:14.
35. Brun-Buisson C. The epidemiology of the systemic inflammatory response. *Intensive Care Med* 2000;**26 Suppl 1**:S64–74.
36. Churpek MM, Zadravecz FJ, Winslow C *et al.* Incidence and Prognostic Value of the Systemic Inflammatory Response Syndrome and Organ Dysfunctions in Ward Patients. *Am J Respir Crit Care Med* 2015;**192**:958–64.
37. Prasad PA, Fang MC, Abe-Jones Y *et al.* Time to recognition of sepsis in the emergency department using electronic health record data: a comparative analysis of systemic inflammatory response syndrome, sequential organ failure assessment, and quick sequential organ failure assessment. *Crit Care Med* 2020;**48**:200–9.
38. Al Ghossaini N, Lucidarme D, Bulois P. Endoscopic treatment of iatrogenic gastrointestinal perforations: an overview. *Dig Liver Dis* 2014;**46**:195–203.

Gastroenterology Report, 2024, 12, 1–7
https://doi.org/10.1093/gastro/goae044
Original Article