ERCP Induced Perforation; A Revisit After Half a Century

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Research Article

Keywords: ERCP, duodenal perforation, Stapfer classification, Obstructive jaundice, Choledocholithiasis

Posted Date: January 12th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1196966/v1

Abstract

Background

One of the most feared complications of endoscopic retrograde cholangiopancreatography (ERCP) is duodenal perforation. We aim to discuss the incidence and risk factors of ERCP induced perforation in light of pertinent literature and review therapeutic options of different perforation types.

Methods

In this case-control study, we reviewed the charts of all patients with ERCP-induced duodenal perforation between January 2016 and June 2020 and compared them to a control group without perforation. Data regarding patients' demographics, comorbidities, indication for endoscopy, ERCP findings, presumed risk factors for complicated procedures, clinical presentation of perforation, radiologic findings, time to diagnosis and perforation type according to the Stapfer classification were collected. Treatment approach, additional interventions, length of hospital stay (LOS), morbidity and mortality were also documented.

Results

A total of 996 ERCP procedures were performed, 13 patients were diagnosed with ERCP-induced perforation (EIP). The most common indication for ERCP was obstructive jaundice. The most significant risk factor of duodenal perforation was failure or difficult cannulation (P = .003). 5 patients were treated surgically, the majority of them had type I perforation, whereas type IV was the most common in those treated conservatively. ICU admission rates and LOS in the ICU were higher among the surgical patients. The overall mortality rate was 15% with a slightly higher rate in the surgical group.

Conclusion

ERCP-induced duodenal perforation carries significant morbidity and mortality. Conservative management yields favorable outcomes in selected patients compared to the surgical approach.

Introduction:

Endoscopic retrograde cholangiopancreatography (ERCP) is one of the most commonly utilized procedures for both diagnostic and therapeutic indications. It was first developed in clinical practice in 1968 as a diagnostic tool [1]. Cannulation of the ampulla and sphincterotomy were introduced in the early 1970s with consequent evolution of ERCP into a therapeutic procedure [1, 2]. Nowadays ERCP is almost exclusively indicated for the therapy of hepatobiliary disorders since other less invasive diagnostic modalities (for example: MRCP) which possesses similar sensitivity, are widely available.

In spite of the valuable contribution of ERCP in patients' management, it is not a complication-free intervention. The ERCP-related morbidity was estimated to be 6.9%; it also carries a mortality rate of 0.33% [3]. The spectrum of complications includes pancreatitis being the most common, followed by cholangitis, bleeding and perforation. The incidence of severe complications is approximately four times higher in ERCP than in other endoscopic procedures [4].

One of the most feared complications is ERCP-induced perforation (EIP). Although EIP is uncommon, it is potentially fatal. Moreover, the treatment of such complication is still controversial.

In this paper, we aim to report the incidence rate, risk factors and outcomes of EIP at our institution. We also aim to discuss the management approach from a surgical perspective. To our knowledge, this is the first analysis of EIP from Jordan.

Materials And Methods:

Study design

This is a retrospective study in which gastroenterology, surgery, anesthesiology, and intensive care data were collected from the electronic medical charts of patients who underwent ERCP during the period of January 2016 to June 2020.

The following information was extracted: patient demographics, comorbidities, indication for endoscopy, ERCP findings, presumed risk factors for difficult procedure (sphincterotomy vs. precut, dilatation procedures, failed cannulation and relevant past anatomy-altering operation). In addition, clinical presentation of perforation, radiologic findings, time to diagnosis, as well as perforation type according to the Stapfer classification [5] (Type I: lateral –free wall- or medial duodenal wall perforation, type II: peri-Vaterian injuries, type III: distal bile duct or pancreatic duct perforation, type IV: retroperitoneal air alone) were all documented. The treatment approach (conservative or operative), need for additional interventions (e.g. percutaneous drainage), length of hospital stay (LOS), morbidity, and mortality are also reported.

Inclusion criteria

Patients who were diagnosed to have endoscopic perforation (EP) either during ERCP or by imaging studies such as computed tomography [CT] were included. As a control group, 43 patients without ERCP-related complications were randomly selected as a control group from the same time period. The randomization process was done by selecting a control patient from every 23 patients after arranging the 966 patients chronologically by ERCP date.

Ethics

The study protocol was reviewed and approved by the Institutional Review Board at King Abdullah University Hospital and by the Committee of Research on Human Subjects at the Jordan University of

Science and Technology. (Non-funded research No: 20200428). Patients' data were kept anonymous and confidential. All study procedures were conducted according to the World Medical Association Declaration of Helsinki.

Procedures

The management plan was dictated by the attending surgeon on call. Patients who were treated conservatively were kept nil per OS and received intravenous fluids, broad spectrum antibiotics and placement of a nasogastric tube. Failure to improve with conservative management, alarming CT findings and the presence of diffuse peritonitis were considered indications for operative treatment. Patients received percutaneous drainage for intra-abdominal collections and enteral or parenteral feeding as appropriate.

Statistical analysis

Data were managed and analyzed using JMP (version 15). Statistical summaries were presented. Q-Q plots were used to examine normality assumption for continuous variables. Afterward, significant differences in participants' characteristics were analyzed using a t-test, Fisher exact test or logistic regression. Additionally, odds ratios were used for significant results. Alpha was set at 0.05.

Results:

A total of 996 ERCP procedures were performed by three endoscopists. Thirteen patients (1.34%) were diagnosed with EIP. 43 other patients who also underwent ERCP, but with no endoscopic induced perforation were randomly selected as a control group (Table 1).

EIP group: There were 9 women (69%) and 4 men (31%) with a mean age of 52.6 years. Approximately two-thirds (69%) of patients had hypertension, 18.9% had diabetes mellitus while none were diagnosed to have ischemic heart disease. Only two patients (15%) had a history of abdominal surgery both of which were laparoscopic cholecystectomy. One patient had pancreatic adenocarcinoma and another patient was known to have cholangiocarcinoma.

ERCP indications: By far, the most common indication for ERCP was obstructive jaundice (61%), followed by Choledocholithiasis (23%).Other indications included gallstone pancreatitis and bile leak after cholecystectomy (Table 2).

ERCP characteristics: Dilated common bile duct (CBD) was observed in 31% of cases and 15% had a filling defect. Precut papillotomy was performed for 85% of the EIP group, 23% had a stone extracted during ERCP. Failure of cannulation was experienced in half of patients (6 patients, 46%).

Risk factors for perforation:

Patient's characteristics: Notably, a higher number of patients had hypertension in the EIP group compared to the Non-EIP group (69% vs 47%) but fewer had diabetes mellitus (18.9% vs 22.5%) with no

statistical significance (Table 1).

Indications for ERCP: The presence of obstructive jaundice and post-cholecystectomy bile leak were more common indications in the EIP compared to the Non-EIP group (61% vs. 53% and 7% vs. 2% respectively). Choledocholithiasis (23% vs. 28%), cholangitis (4% vs. 0%) and gallstone pancreatitis (7% vs 11%) were more common indications in the Non-EIP group. However, the observed differences in the ERCP indications did not reach statistical significance (Table 2).

ERCP characteristics: Failure to cannulate the common bile duct showed significant association with EIP in contrast to the Non-EIP (46% vs 6%; P = .003). Interestingly, patients who underwent CBD dilatation experienced substantially lower rates of EIP (31% vs 67%: P= .0214). The presence of CBD dilatation and filling defects was less common among the EIP group (31% vs 46% and 15% vs 26% respectively) but with no statistical significance. We found that the most significant risk factor and predictor of duodenal perforation during ERCP was failure of cannulation with an odds ratio of 11.4 (P = .003).

Diagnosis and management: The majority of patients (11 patients, 84%) were diagnosed with EIP using computerized tomography scan (CT scan) while the remaining two patients (16%) were diagnosed during ERCP. One of the two patients developed extensive surgical emphysema during the operation while the other was diagnosed by directly visualizing the contrast extravasation through the duodenum. Of the patients diagnosed after the procedure, the most common symptom was abdominal pain (11 patients, 84%) with the remaining two patients (14%) presenting in the form of peritonitis.

Conservative treatment was preferred for 8 patients (61%), while 5 patients (39%) were treated operatively; (Table III). Operatively treated patients were younger in age and had less comorbidities such as hypertension and diabetes which might have influenced the choice of management. Moreover, half of the conservatively-treated group had a history of abdominal surgery, namely laparoscopic cholecystectomy, compared to only one patient (20%) in the surgical group, which could also have affected the surgeon's choice of treatment. Conservatively managed patients had more dilated CBD as opposed to the surgically treated (37% vs. 20%). Papillotomy, dilatation of CBD and stone extraction were much more commonly performed in the conservatively-treated group (100% vs. 60%, 50% vs. 0% and 37.5% vs. 0%, respectively). Otherwise, there was no significant differences in ERCP characteristics between the surgical and the conservatively treated groups (Tables 3).

Treatment according to perforation type: Seventy-five percent of patients who had Type I perforation were treated surgically whereas none of patients with type III or type IV perforation were operated. Type II perforation was divided between conservative treatment (2 patients) and surgical management (1 patient).

Perforation type by treatment: The majority (80%) of the surgically treated patients had type I perforation. Of those treated conservatively, 3 had type IV perforation, 2 had type II perforation, 2 had type I perforation and 1 had type III perforation (Table 4).

LOS, morbidity and mortality: surgically treated patients stayed longer in the hospital with an average of 24 days compared to 17.25 days for the conservatively-treated group; (Table 4). Additionally, ICU admission rates and the average LOS in the ICU were both higher among the surgically treated patients (60% vs. 25% and 7.94 vs. 3 days). Major complications were noted in slightly higher rates among the surgical group. Of those treated surgically, one patient (20%) suffered from an intra-abdominal abscess requiring drainage and another patient (20%) developed pneumonia. On the other hand, one patient (12.5%) of the conservatively treated patients had an intra-abdominal abscess requiring drainage and another patient (12.5%) sustained acute kidney injury. About half of the patients in both groups received enteral or parenteral feeding at some point of their hospital stay. The overall mortality rate was 15% with a slightly higher rate in the surgical group (20% vs. 12.5%).

Discussion:

In this study, we investigated the incidence rate of duodenal perforation among patients undergoing ERCP and compared patients' and procedure's characteristics to a control group. Our results revealed that perforations occurred in a comparable rate (1.34%) to published series. Our study also disclosed that failure to cannulate the CBD was the main predictor of perforation during ERCP.

The reported incidence of ERCP related perforations varied between 0.11% and 2.4%[6] [7]. In one large analysis of 21 prospective surveys of post-ERCP complications in adults (16,855 patients) between 1977-2006, 101 patients experienced perforation (0.60%). The mortality rate in that study was 9.9% [3]. In another review of 18 (mainly retrospective) studies conducted between 2000-2014, the incidence rate of EIP was 0.39%, with an overall mortality of 7.8% [8]. Surprisingly, published numbers did not seem to decline significantly over the last 20 years as ERCP became more popular and widely available.

Published data revealed that the incidence rate of ERCP perforations corresponds with volume of cases at each institution, as highest volume centers (which perform more than 1000 ERCPs per year) reported lower incidence rates (Bill et al. 0.44%, Jin et al. 0.27%, Kim J et al. 0.61%, Howard et al. 0.6%, Dubecz et al. 0.09%) [9–13], compared to the lower volume ones (less than 500 ERCPs per year) (Turner et al. 2.4%, Stapler et al. 1%, Miller et al. 1.65%, Rabie et al. 1.67%, Koc et al. 0.94%) [5, 6, 14–16]. The correlation between incidence of perforation and volume of ERCP cases needs further analysis to elaborate statistical significance. These observations, however, indicate that ERCP remains an invasive procedure which may carry significant morbidity and mortality, even in skilled hands or at high volume units.

"Difficult cannulation" is a term employed to describe failure to gain access into bile duct by the conventional cannulation technique. Factors that may contribute to this difficulty include presence of periampullary diverticula, altered anatomy and bulky papilla. In many studies, this situation has been defined as a leading cause of perforation [17]. The risk is highest as precut papillotomy (or sphincterotomy) is attempted by the endoscopist to overcome this challenge. In Vezakis et al. review, endoscopic sphincterotomy was responsible for 41% of perforations [8]. Another study by Stapfer and colleagues found that cannulation of the ampulla was considered difficult by the endoscopist in 10 of 14

patients who had perforations (out of 1413 ERCPs) [5]. In their review of 21 prospective reports of ERCP complications, Andriulli et al. found that the overall complication rate was significantly higher whenever therapeutic interventions were utilized during ERCP [3]. Complications were also significantly higher in studies with a precut sphincterotomy rate of over 10%. Fifty years after the advent of therapeutic ERCP, difficult cannulation is still a condition that is frequently encountered, which may –although rarely- predispose to perforation and subsequent morbidity and death.

There appears to be a consensus on electing surgery for the treatment of free duodenal wall perforations (type I), which commonly present with signs of peritonitis [12, 18–20]. In our group of patients with perforation, surgery was required in 5/13(38%), 4/5 of the operated patients had type I (free wall) perforation. Surgical intervention is conducted in higher risk injuries that are more likely to progress into sepsis, which explains –in part- the higher morbidity observed in this subgroup. Because duodenal or duct wall defect identification during surgery might be very challenging, especially if diagnosis is delayed (>6 hours post ERCP) [21, 22], surgery can be limited to perform proper drainage and debridement of unhealthy tissue, which can reduce the risk of systemic manifestations and sepsis. Diversion surgeries (Roux-en-Y bypass) have been reported in management of large duodenal perforations [5]. However, in ERCP most perforations are small, unless caused by the scope itself.

Endoscopic repair of duodenal perforations, particularly small defects(<10mm) that are recognized during ERCP has been reported [23, 24]. The latter development of endoscopic clipping (through-the-scope clips), suturing and closure devices (ligation band, fibrin glue, and endo-loops) as well as covering luminal stents has made endoscopy more efficient in treating injuries similar to perforations and bleeding [25–31]. With the growing body of evidence supporting the use of these techniques for the management of ERCP complications, endoscopist expertise, perforation type and diameter remain important predictors of the outcomes.

In other types of perforation, i.e. types I, II and IV, the injury is less likely to manifest as peritonitis, but rather as retroperitoneal (and to a less extent intraperitoneal) fluid or air accumulation. Conservative measures in such circumstances vary from simply restricting oral intake with parenteral nutrition, hydration and coverage with broad spectrum antibiotics to percutaneous drainage of collections under ultrasound or CT guidance.

It is critical to recognize if leakage has stopped after the endoscopy or still ongoing, as the patient may have experienced transient fluid extravasation during the procedure due to duct or duodenal wall puncture. The presence of enlarging pockets of pus or fluid collections, especially in the retroperitoneal space, does not necessarily indicate an active leakage, which can usually be excluded utilizing CT scan with water soluble contrast (Gastrografin), or fluoroscopic imaging (meal). This may instead indicate inadequate drainage or persistent infection that mandates repositioning of the drain, upgrading the size of the drain or placing another drain. It may also be helpful to consider adding antifungals after submitting samples for cultures.

The following are literature-based guidelines which can be driven to conclude when and how to intervene in patient with suspected or proved ERCP-induced perforation;

- Suspicion is raised whenever cannulation is difficult, the threshold for obtaining a post ERCP CT scan to exclude perforation has to be lowered, since early detection may improve outcomes.
- Active intraperitoneal contrast extravasation from duodenal wall on CT scan is considered a reasonable indication for prompt operative exploration.
- The main target of surgical exploration is to control sepsis by drainage of accumulated fluids. Repair of the defect, if identified, is another target with special attention to prevent occlusion of the ducts.
- The presence of free fluids inside the peritoneum or in the retroperitoneal space is an indication for drainage, this can be achieved by interventional radiology (IR) under CT scan or ultrasound guidance, or by surgery if IR service is not available or the collection is not accessible.
- Most of bile duct perforations can be managed by internal biliary stents, along with drainage of any collection. External nasobiliary drainage is considered a valid alternative for internal stenting.
- Failure of non-operative measures, which can be defined as the persistence of abdominal sepsis (significant pain, tenderness and ileus), as well as fever and continuous elevation of inflammatory markers (leukocytes, CRP, ESR, etc.), indicates prompt conversion into surgical approach.
- Prolonged restriction of oral intake may not be of any help if there is no evidence of an ongoing leakage.
- ERCP perforation remains an event that has to be approached by both surgeons and endoscopists.

This study has some limitations. Firstly, it is a retrospective study. Secondly, the sample size of patients with EIP was relatively small to evaluate risk factors with statistical significance. Thirdly, we assume that a small group of patients with type IV perforation may have not been detected, due to lack of abdominal or systemic manifestations.

In conclusion, fifty years after introduction of ERCP for therapy, it remains an invasive procedure which may carry significant morbidity and mortality, even in skilled hands or at high volume units. Selection of patients for ERCP must be strict, it has to be done for therapeutic indications. Difficult cannulation is still a condition that is frequently encountered, and considered the main risk factor for perforation. Early diagnosis and appropriate surgical or percutaneous drainage yield favorable outcomes.

Declarations

The study protocol was reviewed and approved by the Institutional Review Board at King Abdullah University Hospital and by the Committee of Research on Human Subjects at the Jordan University of Science and Technology. (Non-funded research No: 20200428). Patients' data were kept anonymous and confidential. The need for consent was waived by the Research committee and deemed unnecessary according to national regulation.

***Consent for publication*:**

Not Applicable

Competing interests:

I declare that the authors have no competing interests as defined by BMC, or other interests that might be perceived to influence the results and/or discussion reported in this paper.

***Funding*:**

No funding was obtained for this study.

Authors' contributions:

A. R. A. A. M: Idea, Design, Interpretation of the data, drafting of work. H. M. H: Analysis, Interpretation of the data, drafting of work. T. M: Design, Interpretation of the data, drafting of work. Z. M: Design, Interpretation of the data, drafting of work. A. H: Design, Interpretation of the data, drafting of work. K. J: Interpretation of the data, drafting of work. M. b. h: Interpretation of the data, drafting of work. N. A. F: Interpretation of the data, drafting of work. S. K. S: Data collection, drafting of work. J. F: Interpretation of the data, drafting of work.

All authors have read and approved the manuscript.

All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. all authors have read and approved the manuscript

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Tables

Table 1. Patients characteristics

Characteristics	*Non -EIP(n=43)*		*EIP* (n = *13)*		P value
Sex - female (%)	20	(47%)	9	(69%)	[d] NS
Age (mean ± [e] SD)	52.60± 20.48		48.77±15.27		NS
Comorbidities					
[a] HTN - n (%)	17	(47%)	9	(69%)	NS
[b] DM - n (%)	15	(22.5%)	7	(18.9%)	NS
[c] IHD - n (%)	2	(2%)		0 (0%)	NS
Past relevant surgery - n (%)	9	(21%)	2	(15%)	NS
Laparoscopic cholecystectomy - n (%)	7	(16%)	2	(15%)	NS
Hydatid cyst resection - n (%)	1	(2%)	0	(0%)	NS
Whipple procedure - n (%)	1	(2%)	0	(0%)	NS
Relevant Neoplasm	8	(19%)		2 (15%)	NS
Pancreatic carcinoma - n (%)	3	(7%)		1 (8%)	NS
Cholangiocarcinoma- n (%)	4	(9%)	1	(8%)	NS
Gastric carcinoma - n (%)	1	(2%)		0(0%)	NS

[a] HTN, hypertension; [b] DM, diabetes mellitus; [c] IHD, ischemic heart disease; [d] NS, not Significant; [e] SD, standard deviation.

Table 2. ERCP indications and characteristics

	Non- EIP (n = 43)		*[d] EIP (n = 13)*		*P value*
Indications					
Choledocholithiasis - n (%)	12	(28%)	3	(23%)	NS
Cholangitis - n (%)	2	(4%)	0	(0%)	NS
Obstructive jaundice - n (%)	23	(53%)	8	(61%)	NS
Gallstone pancreatitis - n (%)	5	(11%)	1	(7%)	NS
Leak after cholecystectomy - n (%)	1	(2%)		1(7%)	[c] NA
Characteristics					
Dilated CBD - n (%)	20	(46%)	4	(31%)	NS
Filling defect - n (%)	11	(26%)	2	(15%)	NS
Papillotomy - n (%)	3	4 (79%)	11	(85%)	NS
CBD balloon dilatation - n (%)	29	(67%)	4	(31%)	.0214
Stone extraction - n (%)	15	(19%)	3	(23%)	NS
Sludge extraction - n (%)	13	(30%)	4	(31%)	NS
Stent placement- n (%)	14	(33%)	2	(15%)	NS
Pus - n (%)	1	(2%)	0	(0%)	NS
Failure of cannulation - n (%)	3	(6%)	6	(46%)	.003
Premature termination of procedure - n (%)	3	(6%)	6	(46%)	.003

[a] CBD, Common bile duct; [b] NS, not significant, [c] not applicable, [d] EIP, Endoscopic Induced Perforation.

Table 3. Conservative vs. operative treatment: Patient and ERCP characteristics

	Surgical group		Conservative group		
	(n = 5)		(n = 8)		P- value
Sex - female (%)	3	(60%)	6	(75%)	[e] NS
Age (mean ± [g] SD)	42.00±14.24		53.00±15.19		NS
Comorbidities					
[a]HTN - n (%)	2	(40%)	6	(75%)	NS
[b]IHD - n (%)		0(0%)	0	(0%)	[f] NA
[c]DM - n (%)	0	(0%)	2	(25%)	NS
Previous abdominal surgery - n (%)	1	(20%)	4	(50%)	NS
Cholecystectomy - n (%)	1	(20%)	4	(50%)	NS
Relevant neoplasm - n (%)					NS
Pancreatic cancer - n (%)	0	(0%)	1	(12.5%)	NS
Cholangiocarcinoma - n (%)	1	(20%)	0	(0%)	NS
ERCP characteristics					
Dilated [d] CBD - n (%)	1	(20%)	3	(37.5%)	NS
Filling defect - n (%)	1	(20%)	1	(12.5%)	NS
Papillotomy - n (%)	3	(60%)	8	(100%)	NS
CBD balloon dilatation - n (%)	0	(0%)	4	(50%)	NS
Stone extraction - n (%)	0	(0%)	3	(37.5%)	NS
Sludge extraction - n (%)	1	(20%)	3	(37.5%)	NS
Stent placement- n (%)	2	(40%)	0	(0%)	NS
Pus - n (%)	0	(0%)	0	(0%)	NA
Failure of cannulation - n (%)	2	(40%)	4	(50%)	NS
Premature termination of procedure - n (%)	2	(40%)	4	(50%)	NS

[a] HTN, hypertension; [b] IHD, ischemic heart disease; [c] DM, diabetes mellitus; [d] CBD, Common bile duct; [e] NS: not significant; NA, [f] not applicable; [g] SD, standard deviation.

Table 4. Conservative versus operative treatment: Perforation type, morbidity and mortality.

	Surgical group		Conservative group		
	(n = 5)		(n = 8)		P value
Perforation type					
Type I (free wall) - n (%)		4 (80%)	2	(25%)	NS
Type II (peri-vaterian) - n (%)	1	(20%)	2	(25%)	NS
Type III (distal [a] CBD) - n (%)		0(0%)	1	(12.5%)	NS
Type IV (RP free air) - n (%)		0(0%)	3	(37.5%)	NS
[c] LOS (days, mean ± SD)	24±17.71		17.25±11.69		NS
Morbidity					
[f] ICU admission- n (%)	3	(60%)	2	(25%)	NS
Duration of ICU admission (days, mean ± [d] SD)		7.94 ±4.58		3.00 ±0.00	NS
Intra-abdominal abscess requiring drainage - n (%)	1	(20%)	1	(12.5%)	NS
[e] TPN/enteral feeding - n (%)	3	(60%)		4 (50%)	
Acute kidney injury - n (%)	0	(0%)	1	(12.5%)	NS
Pneumonia - n (%)	1	(20%)	0	(0%)	NS
Mortality - n (%)	1	(20%)	1	(12.5%)	NS

[a] CBD, Common bile duct; [b] RP, retroperitoneal; [c] LOS, length of hospital stay; [d] SD, Standard deviation.; [e] TPN: Total parenteral nutrition; [f] ICU, Intensive Care Unit.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- RawData.xlsx