ERCP RELATED PERFORATIONS; INCIDENCE, RISK FACTORS AND OUTCOMES OF MANAGEMENT, A RETROSPECTIVE COHORT STUDY

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Abstract:

Significance: ERCP is an important therapeutic modality for pancreatico-biliary disorders. Perforation is the most dreaded complication with reported incidence of 0.14- 2.36%. Since it is uncommon, there are few studies on incidence, risk factors, and outcomes of management. We aimed to determine the incidence, risk factors and outcomes of management of ERCP related perforations.

Methodology: This retrospective cohort study reviewed ERCP database of all patients who underwent ERCP at UERM Hospital from June 2015 to November 2016. The charts of patients with perforation were reviewed for data on management and outcome. The data was analyzed in Microsoft Excel for means and IBM SPSS Statistics software for Odds Ratio, CI and Pearson chi square tests.

Results: 306 ERCPs were done during the study period and 4 had perforation with incidence of 1.3%. The analysis showed higher risk for perforation in presence of a duodenal mass (OR 14.04; CI: 1.295 - 152.4), precut sphincterotomy (OR 17.87; CI: 2.36- 135.23), sphincterotomy extension (OR 53.6; CI: 5.278-544.85) and failed cannulation (OR 57.4; CI: 5.63-585.22). 2 patients with Type II perforation were surgically managed with no perforation identified intraoperatively, 1 Type III perforation was managed conservatively without any complication. The mean hospital stay was 13.25 days with no mortality.

Conclusions: The limitation of this study was small sample size as perforation is a rare adverse event. We recommend 2 measures to decrease the risk of perforation and 6 measures for management of ERCP related perforation. A prospective study with larger sample size is recommended.

Keywords: Retrospective Cohort, ERCP, ERCP Complications, ERCP Perforation, ERCP Perforation Management, ERCP Perforation Outcome

Introduction:

Endoscopic retrograde cholangio-pancreatography (ERCP) is now an essential part of the therapeutic armamentarium in managing pancreatic and biliary disorders. With the availability of non-invasive imaging techniques such as magnetic resonance cholangiopancreatography (MRCP) and endoscopic ultrasonography (EUS), ERCP has become primarily a therapeutic procedure.[1] ERCP is associated even though rarely, with complications, most commonly pancreatitis, infection, post-sphincterotomy bleeding and perforation.[3,5] Perforation is one of the most dreaded complications of ERCP, with a reported incidence of 0.14- 2.36%.[2,3,4,5,6] The Studies from prospective databases in the current era of therapeutic ERCP are few.[5] Thus there is no strong concensus or guidelines for management of ERCP related perforations.

Stapfer et al proposed a classification for ERCP related perforations based on a retrospective study of 14 ERCP related perforations with incidence of 1%. Type I was classified for lateral duodenal wall injury, Type II for injury at the sphincter of oddi, Type III for ductal injuries, and Type IV for retroperitoneal air. *(See Table 2)* They recommended that all type I injuries undergo surgery immediately and nonsurgical management for type II and III injuries was acceptable if an early contrast study demonstrated minimal extravasation or a sealed perforation without associated fluid collection. Patients with retroperitoneal air alone (type IV) probably do not need additional treatment or workup if the findings of the abdominal examination are normal. [4]

Objective: We aimed to determine the incidence, risk factors, the outcomes of management in ERCP related perforations, among patients who underwent ERCP at the UERM Memorial Hospital and compared them with the management of perforations as recommended by *Stapfer et al.*[4]

Patient and Methods:

This is a retrospective cohort study where records of patients who underwent ERCP from June 2015 to November 2016 at the UERM Memorial Hospital were reviewed. We identified the patients' demographic data, and possible risk factors for perforation such as duration of the procedure, presence of a duodenal mass, a normal looking papilla, the presence of paravaterian diverticle, the use of catheter only or sphincterotome for cannulation, use of needle knife for precut sphincterotomy, extension of previous sphincterotomy and pancreatic sphincterotomy from review of ERCP database.

In the patients with perforation, chart review was done to review the indications for the procedures, the endoscopic and cholangiopancreatogram findings, the time of diagnosis of the perforation, other further imaging tests done, intraoperative findings in patients who underwent surgical management, the outcome of management and duration of hospital stay.

We defined perforation as the presence of air or contrast material in the intraperitoneal or retroperitoneal space with or without frank endoscopic visualization of the peritoneum during the procedure.

Statistics:

The data was encoded, analyzed in Microsoft Excel 2015 Version 15.13.3 for means, standard deviation and subsequent data analysis was done with IBM SPSS Statistics Version 23.0.0.0 for Odds ratio, 95% Confidence Intervals and Pearson chi square tests.

Results:

During the study period, a total of 306 ERCPs were performed due to various indications. Out of these procedures, there were four perforations with an incidence of 1.3%, which was comparable to those reported in the literature (0.14- 2.36%).[2,3,4,5,6] The mean age was 53.1 $\pm$17.16 years (range 12-91 years), 128 (41.83%) were male and 178 (58.16%) were female. 8 (2.6%) patients had a duodenal mass, 49 (16%) patients had a paravaterian diverticle. 18 cases had failed cannulation (5.88%) in this study.

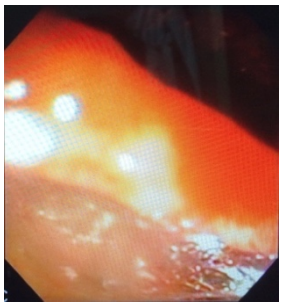
There was a higher risk for perforation in the presence of a duodenal mass (OR 14.04; 95% CI: 1.295 - 152.4), a paravaterian diverticle (OR 1.76; 95% CI: .180- 17.31), sphincterotome use for cannulation (OR 4.119; 95% CI: .568- 29.84), precut sphincterotomy (OR 17.87; 95% CI: 2.36- 135.23), extension of sphincterotomy (OR 53.6; 95% CI: 5.27- 544.85) and failed cannulation (OR 57.4; 95% CI: 5.63-585.22).

Normal looking papilla (OR .88; 95% CI: .123- 6.383) and use of ERCP catheters for cannulation (OR .112; 95% CI: .011- 1.094) showed tendency for lower risk of perforation. Among the studied risk factors, Pearson chi square test confirmed the presence of duodenal mass, precut sphincterotomy, sphincterotomy extension and failed cannulation were not independent variable from perforation, hence there is increased the risk of perforation (Chi^2 >7.8, df=1; p=.000). *(See Table 1)*

Among the 4 patients who had a perforation, 3 were female and 1 was male. The indication for ERCP were obstructive jaundice secondary to pancreatic head mass/malignancy for one patient who had Type I perforation, suspicion of bile duct stones in two patients who had Type II perforation, and choledocholithiasis on CT Scan in one patient who had type II I perforation. *(See Table 3)*

Table 1: Demographic data and risk factors assessment

Variables	No Perforation (n=302) (Mean± SD/ Frequency)	Perforation (n=4) (Mean/ Frequency)	Odds Ratio/ 95% CI for Perforation	Pearson Chi-Square
Age	52.85 ± 17.12	61 ± 21.08		
Sex	M (127)/ F (175)	M (1)/ F(3)		
Duration of Procedure	35.49 ± 25.77	56.5 ± 44.65		
Duodenal Mass	7	1	**14.048** (1.295 - 152.4)	7.977 (p= .005)
Normal looking Papilla	160	2	**.888** (.123- 6.383)	.014 (p= .906)
Paravaterian Diverticle	48	1	**1.764** (.180- 17.31)	.243 (p= .622)
Catheter only used for Cannulation	226	1	**.112** (.011- 1.094)	5.119 (p= .024)
Sphincterotome for Cannulation	59	2	**4.119** (.568- 29.84)	2.295 (p=.13)
Pre-Cut Sphincterotomy	16	2	**17.875** (2.36- 135.23)	14.249 (p=.000)
Sphincterotomy Extension	16	3	**53.625** (5.27-544.85)	32.934 (p=.000)
Failed Cannulation	15	3	**57.40** (5.63-585.22)	34.973 (p=.000)
Pancreatic Sphincterotomy	1	0	**N/A**	



Patient 1, endoscopic view of perforation

Patient 1, Pneumoperitoneum

Patient 3, Endoscopic view after pre-cut

Patient 3: Extravasation of contrast

Patient 2: Pneumoperitoneum

Patient 4, Opening in bile duct

Patient 4, Pneumoperitoneum

Diagnosis of Perforation:

All the perforations were diagnosed during the procedure. The Type I (n=1, 25%) perforation was instrument related and occurred during positioning of the duodenoscope at the lateral duodenal wall. Direct visualization of the peritoneum or omental fat associated with finding of pneumoperitoneum in fluoroscopy were seen. The Type II (n=2, 50%) perforations were sphicterotomy related and needle knife was used for bile duct access in both cases. These were diagnosed with extravasation of the contrast material while attempting cannulation after pre cut papillotomy and extension of sphincterotomy without deep cannulation. On fluoroscopy, both patients had pneumoperitoneum. In the Type III perforation (n=1, 25%) an extension of previous sphincterotomy was done. After balloon stone extraction, an opening was noted in the bile duct and pneumoperitoneum was seen on fluoroscopy.

Management and outcome:

Three patients with Type I and II perforations (75%) underwent surgical exploration. None of the patients had endoscopic closure of perforation. One Type I perforation (Patient 1) was managed with primary repair of the duodenal perforation, peritoneal lavage and drainage. Choledochojejunostomy was also done for biliary diversion as patient had ampullary mass.

In the two patients with Type II perforations, the intraoperative findings in the first patient (patient 2) were a dilated common bile duct on intraoperative cholangiogram with suspicious filling defect. CBD exploration was done with no stone identified. So, T-tube was placed in the bile duct. The site of perforation could not be identified. The papilla could not be localized even after duodenostomy. In the second patient (Patient 3), no bile leak was found, the bile duct was non dilated with no palpable stones. Empiric omental patching was done on the anterior and posterior duodenal wall. In both cases, perforation could not be identified intraoperatively.

One type III perforation (patient 4) was successfully managed conservatively by putting the patient on NPO, IV fluids, antibiotics, analgesics, and radiological monitoring with follow up X-ray and CT scan with IV and water soluble oral contrast. The mean duration of hospital stay was 13.25 days (range 5- 22 days) without any complications or mortality. *(See table 3)*

Discussion:

ERCP related perforation is one of the dreaded complication for therapeutic endoscopists and has traditionally been managed surgically. The limitation in our study was the relatively small sample size and low event rate. The risk factors that we identified which could possibly increase the risk of perforation during perforation were (1) doing pre-cut sphincterotomy, (2) extension of precut sphincterotomy without deep cannulation, (3) prolonged procedures with failed cannulations and (4) presence of a duodenal mass which will limit the endoscopic movements, make identification of the ampulla difficult or make

Table 2: Stapfer Classification of Perforation, correlation of Outcome

Perforation Type	Location	Mechanism	Recommended Treatment	No. of Patients	Treatment Done
I	Lateral wall	injury remote to ampulla due to endoscope	Surgical Repair	1	Surgical Repair
II	Peri-ampullary	Sphincterotomy Related	Conservative; Surgery in case of large fluid collections only	2	Surgical
III	Ductal	Related to wire or basket instrumentation	Conservative	1	Conservative
IV	Retroperitoneal air alone	Minor injuries	Conservative		

Table 3: Details of Patients with perforation and their Outcome

No	Age	Sex	Indication	Diagnosis of perforation	Type	Mechanism	Management	Hospital Stay
1	70	F	Jaundice with abdominal pain. Ultrasound finding of dilated biliary tree	Endoscopic Visualization of perforation/ Pneumoperitoneum on fluoroscopy	Type I	Duodenoscope related (While positioning)	Surgical: repair of anterolateral duodenal wall perforation, lavage	22 days
2	30	F	Jaundice with abdominal pain; S/P Open Cholecystectomy 3 weeks back	Precut papillotomy done; Extravasation of contrast on fluoroscopy	Type II	Precut/ Sphincterotomy related	Surgical; Dilated CBD, note of bile leak, no perforation identified; Duodenostomy and closure	8 days
3	77	M	Recurrent epigastric pain with jaundice; Refused MRCP	Precut papillotomy done; Extravasation of contrast on fluoroscopy	Type II	Precut/ Sphincterotomy related	Surgical; No bile leak, non dilated CBD, no perforation identified; Omental patching done on anterior and posterior duodenal wall	18 days
4	67	F	CT Scan: Dilated CBD with bile duct stone S/P ERCP	Sphincterotomy extension; Gaping noted in opening of bile duct after balloon stone extraction, Pneumoperitoneum on fluoroscopy	Type III	Injury to bile duct during stone extraction	Medical; NPO, IV fluids and antibiotics, No NGT/NBT placed	5 days

CBD: Common bile duct; NGT: Nasogastric tube; NBT: Nasobiliary tube, S/P: status Post, NPO: Nil per orem, IV: Intravenous

duodenal wall friable due to tumor infiltration. In our study normal looking papilla was not significantly associated with duodenal perforation. The use of standard biliary catheter for cannulation showed tendency for lower risk of perforation whereas use of sphincterotome for cannulation showed tendency for higher risk of perforation. These maneuvers however are operator dependent and might be useful tools for experienced endoscopists.

The management of ERCP related perforations has traditionally been surgical. A study published by *Kodali et al* reviewed 12 perforations out of a total of 8264 ERCPs with a perforation rate of 0.14%, had 5 surgical and 7 conservative treatments with no mortality and thus had similar conclusions.[5] A study published in the Canadian Journal of Surgery had 11 perforations out of 12,232 ERCPs (0.08%), 7 were managed conservatively (3 Type II, 3 Type IV and 1 Type 1) with mortality in 2 patients who refused surgical therapy. They suggested in contrary to the suggestions by Stapfer et al,[4] large abdominal fluid collections are not obligatory indications for surgery, as these are almost always well managed by CT-guided drainage, avoiding unnecessary surgery.[6] Another study done in China had 16 perforations out of 8504 ERCPs (0.18%). They closed 3 Type I perforations using hemoclips, 1 lateral duodenal wall and 3 afferent limb perforations were managed surgically and remaining perforations were managed conservatively with no mortality.[7] A study from Australia reported 5 perforations in 211 (2.36%) ERCPs with 1 mortality in the surgical group and 1 successful conservative management in Type II perforation.[8] H.M. Wu et al reported 30 perforations in 6620 ERCPs (0.45%) and recommended that peri-ampullary perforations were associated with high morbidity and mortality, and therefore should have aggressive endoscopic bile diversion from the site of perforation. Delay in diagnosis and surgery resulted in a worse outcome.[9]

Type I perforations should be managed surgically unless endoscopic closure can be done using hemo-clips if the expertise is available. Type II perforations in our study were managed surgically but the perforation

site could not be identified in both cases. There were no complications and both patients recovered and were discharged from the hospital. In retrospect and upon reviewing the published literature, they could have been assessed with MRCP before procedure and possibly managed conservatively. For Type III perforation, patients can be more confidently managed conservatively. The type IV perforations are not considered as true perforation as they can be incidental finding of free air during or after the procedure and can be just monitored and followed up closely.

Recommendation:

Based upon our experience reported here and the literature, we propose the following recommendations:

1. ERCP should not be use for diagnostic purpose alone , rather it should be considered as a therapeutic intervention as it carries significant associated risks. MRCP may be used for diagnostic purposes.
2. The use of high risk maneuvers such as the use of pre-cut sphincterotomy, extension of sphincterotomy without deep cannulation, extension of previous sphincterotomy, persistently attempting cannulation despite prolonged procedure should be avoided if possible.
3. In case of endoscopically identified perforation, it should be well documented and for Stapfer type I perforation, endoscopic closure with clipping may be attempted depending on the availability of the expertise. In case of unsuccessful endoscopic closure, surgical management is strongly recommended with primary oversew closure of the duodenal wall defect if surgery is done within <12 hours. If the duration to surgery is >12 hrs, we recommend oversew closure with duodenal diversion.
4. For Type II perforations, initial conservative management by placing the patient on NPO, administering intravenous fluids and antibiotics, total parenteral nutrition for undernourished patients and patients who are not expected to be enterally fed within 7 days. Placement of a nasogastric tube or nasobiliary tube can be done if there is suspicion of fluid extravasation due to a large defect. A biliary stent can be placed if there is a quick access to the biliary tree. We recommend CO_2 Insufflation to be preferred over air insufflation for any endoscopic intervention after suspicion of perforation.
5. Patients with type III and IV can be managed conservatively as recommended for Type II perforations with close monitoring and frequent assessment along with serial abdominal X-rays.
6. Patients on conservative management should be evaluated for abdominal pain, tenderness, presence of leukocytosis, and sepsis. Serial abdominal X-Rays can be done to monitor cases with pneumoperitoneum. If there is suspicion of infection, a CT scan with IV and water soluble oral contrast should be done. In case of large amount of fluid collection or abscess, a CT Guided drainage catheter can be placed. If with no improvement is observed despite these measures, surgical management should be considered.
7. Surgical intervention is also needed in patients having Type II, III or IV perforation who have biliary obstruction due to choledocholithiasis or impacted instruments.
8. In patients without identified perforation during ERCP, but in whom one is suspected should be closely monitored and investigated with water soluble contrast upper GI series or abdominal CT scan with IV and water soluble oral contrast.

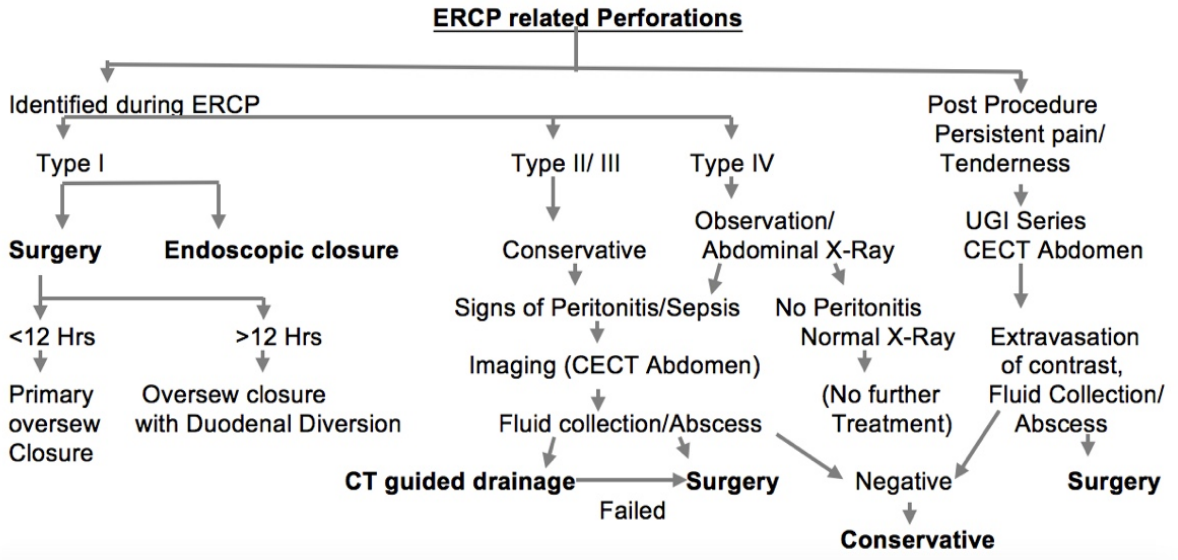


Figure 1: Algorithm for management for ERCP related perforations

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