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Endoscopic Retrograde Cholangiopancreatography (ERCP) perforations, management and outcome

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Abstract

Introduction: ERCP (endoscopic retrograde cholangiopancreatography) with and without endoscopic sphincterotomy has become a worldwide common procedure in the era of interventional management of biliopancreatic disorders. Although considered as a safe procedure, it carries fatal complications, associated with significant mortality. Common complications are pancreatitis, cholangitis, bleeding, and perforation.

Patients and Methods: Patients who performed ERCP and complicated with perforation were included in the study. Study variables included indication for ERCP, presentation at the time of surgical admission, diagnostic procedures, time to diagnose, site of injury, management, duration of hospital stay, postoperative morbidity and its management and survival.

Results: Between January 2012 and December 2015, a total of 612 ERCPs were performed at the gastrointestinal endoscopy center. Nine iatrogenic duodenal perforations (1.47%) were identified (3 male, 6 female). The mean patient age was 47 years. Injury was suspected during the procedure in three patients; it passed unnoticed in six patients. The decision to conserve or operate was based on clinical and radiological backgrounds. Conservative management preferred in two patients and operative intervention was indicated in seven patients. The two patients treated conservatively were recovered. One of the seven patients underwent surgery died after exploratory laparotomy. The other survived six, underwent multiple procedures and had long inpatient stays. The mortality rate in patients treated surgically was 14.3% (1 of 7 patients). The overall mortality rate was 11.1% (1 of 9 patients).

Conclusion: Iatrogenic duodenal perforations are associated with significant complications and mortality. Diagnosis may be easy, but attention must be paid to it. Immediate surgical evaluation and close monitoring is needed. Early perforations may be recovered with conservative management. Most intraperitoneal perforations need surgery. The time between the onset of perforation and the surgical interference is of great importance. Mortality increased dramatically with delayed surgical management.

Keywords: Endoscopic retrograde cholangiopancreatography (ERCP), Duodenum, Perforation, Peritonitis

1. Introduction

Complications are not uncommon in the performance of endoscopic procedures and more so for ERCP. Knowledge of expected ERCP complications, their frequency, and the risk factors associated with their occurrence may help to recognize and to decrease the incidence and severity of these complications. Endoscopists are expected to carefully select their patients for the appropriate intervention, be familiar with the specified procedure and available technology, and be ready to manage any adverse events that may complicate the procedure. Once a complication discovered, early recognition and proper intervention may minimize the morbidity and mortality associated with this complication. Review of complications and their management as part of a continuing quality improvement process may serve to educate endoscopists, help to decrease the risk of future complications, and improve the overall quality of ERCP [1].

Endoscopic retrograde cholangiopancreatography (ERCP) is fundamental in everyday surgical practice. Despite this, as an invasive procedure, it has its own morbidity and mortality, the most scarring of which is periduodenal perforations. Perforation related to ERCP occurs in 0.3% to 1% of patients, and this carries a mortality rate of 16% to 18%. ERCP is widely accepted as a safe procedure, but the associated rate of major complications approaches 6-7%. Although the incidence of duodenal perforations associated with ERCP has decreased since its introduction in 1968 from more than 2% to less than 0.5% [2], most likely because of improved experience and skill of the endoscopists, severe and fatal cases continue to occur [3].

Three distinguished types of perforation have been described: guidewire-induced perforation, periampullary perforation during sphincterotomy, and luminal perforation at a site away from the papilla. Risk factors for perforation specified in a large retrospective study included: performance of a sphincterotomy, previous Billroth II operation, intramural injection of contrast, prolonged duration of the procedure, biliary stricture over-dilation, and sphincter of Oddi dysfunction [4]. However, in a more recent multicenter prospective study, mostly malignancy and precut access were associated with an increased risk of perforation [5]. Prompt and early recognition of periampullary perforation and treatment with aggressive biliary and duodenal drainage (by means of nasogastric and nasobiliary tubes) coupled with broad-spectrum antibiotics can result in clinical resolution without the need for operative intervention in as many as 86% of patients [6].

The proper management of perforation will depend on many factors, such as the site and location, clinical status of the patient, and radiographic imaging. Early identification and rapid management of a perforation have been shown to decrease associated morbidity and mortality. Perforations related to endoscopy are best approached and managed in collaboration with surgical colleagues [7].

Several studies have suggested conservative, radiologic,

endoscopic, or surgical management. However it is not well-known which patients require surgery, and when these patients should receive surgery. Consensus is lacking since these injuries are uncommon and reported patient populations are not comparable [8].

In the present study, a prospective analysis of a series from a single center will be reported and a management algorithm for ERCP-related duodenal perforations based on clinical and radiographic findings at presentation will be defined.

2. Patients and Methods

A total of 612 ERCPs were performed at the department of gastrointestinal endoscopy center (The Digestive Endoscopy Centre of Al-Azhar faculty of medicine, Assiut) from January 2012 to December 2015. Al-Azhar University Hospital in Assiut is a secondary referral hospital in Upper Egypt. It serves population of Upper Egypt especially Assiut. All the cases were looked after prospectively in this period. A total of 9 perforations (1.47%) were identified. Patient demographics including sex, age, and comorbidities such as coronary heart disease (CHD), chronic obstructive pulmonary disease (COPD), chronic renal failure, and malignancy were identified. The indication for ERCP, ERCP findings, clinical and radiological presentation of the perforation, injury related data, diagnostic methods, time to diagnosis and surgery, location of the duodenal injury, methods of treatment, surgical procedures, complications, length of stay in hospital, and the final outcome including late morbidity were also recorded and analyzed.

All patients consenting to eventual surgical treatment were transferred to the department of general surgery. Generally, patients managed conservatively if diffuse peritoneal signs were not present.

Abdominal computed tomography (CT) were performed in patients with elevated inflammatory parameters or fever. Enteral nutrition was resumed at normalization of laboratory parameters and bowel movements. Patients were discharged when completely asymptomatic at oral food intake. Surgery was performed in patients with diffuse abdominal rebound tenderness and guarding regardless of mechanism and site of injury.

2.1 Classification

There are two important classifications of ERCP-related perforations. Howard *et al.,* [9] classified perforations into three distinctive types: type I, guide-wire perforation; type II, periampullary perforation; type III, duodenal perforation away from the papilla. Stapfer *et al.,* [10] classified ERCP-related perforations into four types, based on the mechanism of injury, anatomical location and severity, which may predict the need for surgery. Type I, medial or lateral wall duodenal perforation; type II, perivaterian injuries; type III, distal bile duct injuries related to guide-wire-basket instrumentation and type IV, retroperitoneal air alone. Type IV is questionable and it is not a true perforation. Stapfer classification was selected to be used in the present study.

At the end of every ERCP procedure, thorough control for any possible perforation was performed. The endoscopist will inspect the entire circumference of the duodenum carefully and meticulously check the X-ray for the presence of retroperitoneal air. This concern is valuable when the procedure is technically difficult; needle-knife precut has been performed; and in the presence of variations in the usual anatomy due to previous surgical interventions and stricture dilatation. If there is high suspicion, contrast was infused through the endoscope to facilitate identification of the injury site.

Patients with undetected leaks presented hours after the ERCP with pain, fever and leukocytosis. In cases of type I perforations (intraperitoneal), the diagnosis is usually clear with severe pain and signs of peritonitis. When a patient experiences severe pain after ERCP, differentiation between acute pancreatitis and perforation should be made. In cases of retroperitoneal perforations the diagnosis may be not so obvious. The patient may complain of mild epigastric pain but signs of peritonitis may develop several hours after ERCP or may not develop at all, depending on the size and rate of the leak. The presence of subcutaneous emphysema may be evident very early, especially at right abdominal wall, back or even cervix uteri. Tachycardia is a constant finding, but it may be caused by other factors including pain. Leukocytosis and fever are often seen 12 hours or more after the procedure. Serum amylase may be mildly elevated from the absorption of pancreatic juice from the retroperitoneal space.

In cases with suspicion of perforation, a CT scan with oral contrast was done. The presence of retroperitoneal air can also be detected by plain x-ray films, but CT scan is more sensitive [11], it usually delineate the leak and the presence of fluid collections.

2.2 Treatment

After the recognition of ERCP-related perforation, the first dilemma is to choose conservative treatment or surgery. That depends on the mechanism of injury, degree and site of the leak and patient condition [12, 13]. Endoscope related perforations (type I) will be referred for immediate surgery without hesitation. In cases of endoscopic sphincterotomy perforations (type II) detected during the procedure, biliary drainage will be mandatory in order to prevent leakage of bile from the injury site.

When a sphincterotomy related perforation was suspected after the procedure it will be assessed by a CT scan with oral contrast to demonstrate the degree of leak. Major contrast leak will be an indication for immediate surgery, whilst minimal or no leak will be treated conservatively. Non-operative treatment included nil by mouth, nasogastric tube, intravenous fluids, broad spectrum antibiotics, and radiologic interventions for percutaneous drainage of collections. Total parenteral nutrition may be recommended in undernourished patients or when adequate enteral feeding will be impeded for more than seven days. Generally, indications for surgery will be: major contrast leak; sepsis despite conservative measures; presence of retroperitoneal fluid collections not amenable to percutaneous drainage; and unsolved problems like stones or retained hardware (baskets). The clinical condition of the patient will be always the key factor determining the mode of treatment.

A clinical index score to predict the opportunity for operative intervention devised by Knudson *et al.,* [14] was used. This 4-point scoring system assigned 1 point for each of the following parameter: fever, tachycardia, guarding on examination and leukocytosis. Score equal to or greater than 3 indicate operative management.

In the literature there were no prospective comparative studies between different surgical techniques for ERCP-related perforations. Thus surgical technique depended on site and size

of the defect, timing of surgery, and clinical parameters of the patient. The main aim of immediate surgery was repair of the perforation with diversion of bile and gastric juice, if indicated. Duodenal perforations (type I) will be closed primarily in one or two layers, following debridement of necrotic tissue. The closure will be oriented transversely to avoid compromising the duodenal diameter. In patients with large defects the options will be jejunal serosal patch closure or tube duodenostomy. Leak from the duodenal closure line was a major concern and duodenal diversion will be advisable in delayed diagnosis or large defects. The reasonable choice is to divert the gastrointestinal fluids and proteolytic enzymes from the duodenal repair site. In type II sphincterotomy related perforations, a non-operative approach was followed. When the clinical condition of the patient or the diameter of the leak requires immediate surgery, a transduodenal approach and repair, by performing sphincteroplasty, will be indicated.

The main goals of delayed surgery were control of sepsis, repair of the perforation if possible, and diversion, if required. Delayed surgery was performed in patients who remain septic despite non-surgical treatment, and debridement and drainage of the retroperitoneal space was required. That should be done through extraperitoneal approach (right posterior laparostomy) or transperitoneal approach when cholecystectomy, common bile duct exploration with T-tube drainage or diversion techniques are required. The perforation may not be found in delayed surgery or the tissues are too edematous and fragile for primary repair. The transduodenal approach is not advisable for delayed surgery.

Diversion of gastric and duodenal secretions is mandatory and will be achieved by: insertion of nasogastric or nasoduodenal tube; tube duodenostomy; pyloric exclusion and gastrojejunostomy; gastrojejunostomy alone; T-tube placement for bile diversion; and duodenal diverticulization. Duodenal diverticulization include Billroth II gastrectomy, placement of a draining catheter into the duodenum, closure of duodenal wound and drainage. The main disadvantage of duodenal diverticulization is that it is an extensive procedure which may be inappropriate in septic, fragile patients. Pyloric exclusion is a less invasive alternative. This procedure consists of duodenal perforation repair, closure of the pylorus with a running suture or by stapler and gastrojejunostomy. Pyloric exclusion is not an extensive procedure, less time consuming, results in less physiological disturbances and it is advocated by most clinicians, when duodenal diversion is required.

In the present study, conservative management preferred in two patients and operative intervention was indicated in seven patients. One patient of the conservative management group underwent computed tomography guided drainage of a retroperitoneal abscess.

3. Results

Nine perforations were identified among 612 patients underwent ERCP from January 2012 to December 2015. The mean age of the study population was 47 (36-62) years. Patients with perforations were 3 men and 6 women. ERCP indications were CBD stones in 382 patients (62.42%), cholangitis in 39 patients (6.37%), malignant jaundice in 87 patients (14.21%), chronic pancreatitis in 54 patients (8.82%), dilated CBD in 6 patients (0.98%), and post cholecystectomy in 44 patients (7.19%) (Table 1).

Table 1: Indications of ERCP.

Indication	No (%)
CBD stone	382 (62.42%)
Solitary	102 (16.67%)
Multiple	280 (45.75%)
Cholangitis	39 (6.37%)
Malignant jaundice	87 (14.21%)
Pancreatic tumor	21 (3.43%)
Periampullary	48 (7.84%)
Cholangiocarcinoma	6 (0.98%)
Porta hepatis tumor	12 (1.96%)
Chronic pancreatitis	54 (8.82%)
Dilated CBD	6 (0.98%)
Post cholecystectomy	44 (7.19)
Leak	18 (2.94%)
Obstruction	12 (1.96%)
Leak with obstruction	14 (2.29%)

Morbidity and mortality of all patients underwent ERCP were 87 patients (14.22%) and 8 patients (1.31%) respectively. Perforation occurred in 9 patients (1.47%), bleeding in 12 patients (1.96%), cholangitis in 23 patients (3.76%), pancreatitis in 26 patients (4.25%), and death in 8 patients (1.31%) (Table 2).

Table 2: Morbidity and mortality of ERCP procedures.

Complication	No (%)
Perforation	9 (1.47%)
Bleeding	12 (1.96%)
Cholangitis	23 (3.76%)
Pancreatitis	26 (4.25%)
Death	8 (1.31%)
Total complications	87 (14.22%)

ERCP indications of the 9 patients developed perforation, their clinical presentation, and site of perforation are presented in table 3. Seven patients had CBD stones, one patient had cholangiocarcinoma, and one patient had post laparoscopic cholecystectomy leak. One patient presented with abdominal pain, four patients presented with peritonitis, and four patients with surgical emphysema. Lateral duodenal perforation occurred in five patients, and retroperitoneal perforation occurred in four patients.

Table 3: ERCP indications, clinical presentation, and site of perforation.

ERCP indication	Clinical presentation	Site of perforation
CBD stone	Abdominal pain	Lateral duodenal perforation
CBD stone	Emphysema	Retroperitoneal perforation
CBD stone	Emphysema	Retroperitoneal perforation
CBD stone	Peritonitis	Lateral duodenal perforation
CBD stone	Emphysema	Retroperitoneal perforation
CBD stone	Emphysema	Retroperitoneal perforation
CBD stone	Peritonitis	Lateral duodenal perforation
Cholangiocarcinoma	Peritonitis	Lateral duodenal perforation
Post cholecystectomy leak	Peritonitis	Lateral duodenal perforation

Knudson score of each perforated patient is presented in table 4. Four patients had score of 4, three patients had 3, and two patients had 2.

Table 4: ERCP indications, site of perforation, and Knudson score.

ERCP indication	Site of perforation	Knudson score
CBD stone	Lateral duodenal perforation	3
CBD stone	Retroperitoneal perforation	2
CBD stone	Retroperitoneal perforation	4
CBD stone	Lateral duodenal perforation	4
CBD stone	Retroperitoneal perforation	2
CBD stone	Retroperitoneal perforation	3
CBD stone	Lateral duodenal perforation	3
Cholangiocarcinoma	Lateral duodenal perforation	4
Post cholecystectomy leak	Lateral duodenal perforation	4

Conservative management applied to 2 patients one of them needed CT guided aspiration of pus, primary closure performed as a sole maneuver in 2 patients, primary closure with T-tube drainage of CBD performed in 2 patients, tube duodenostomy and pyloric exclusion with gastrojejunostomy in 3 patients. Management of each patient is summarized in table 5.

Table 5: ERCP indications, site of perforation, and management.

ERCP indication	Site of perforation	Management
CBD stone	Lateral duodenal perforation	Primary closure.
CBD stone	Retroperitoneal perforation	Conservative.
CBD stone	Retroperitoneal perforation	Tube duodenostomy and pyloric exclusion.
CBD stone	Lateral duodenal perforation	Primary closure with T-tube drainage of CBD.
CBD stone	Retroperitoneal perforation	Conservative with CT guided aspiration.
CBD stone	Retroperitoneal perforation	Primary closure with T-tube drainage of CBD.
CBD stone	Lateral duodenal perforation	Primary closure.
Cholangiocarcinoma	Lateral duodenal perforation	Tube duodenostomy and pyloric exclusion.
Post cholecystectomy leak	Lateral duodenal perforation	Tube duodenostomy and pyloric exclusion.

Eight patients were recovered and survived and one patient died. The 2 conservatively managed patients had 7 and 8 days of hospital stay, the 2 primarily closed patients had 9 and 12 days of hospital stay, the 2 primarily closed patients with T-tube drainage of CBD had 16 and 18 days of hospital stay, and the 3 patients underwent tube duodenostomy and pyloric exclusion had 22, 27 (died) and 32 days of hospital stay. Outcome and hospital stay of each patient are collected in table 6.

Table 6: ERCP indications, site of perforation, outcome, and hospital stay.

ERCP indication	Site of perforation	Outcome	Hospital stay
CBD stone	Lateral duodenal perforation	Recovered	9 days
CBD stone	Retroperitoneal perforation	Recovered	7 days
CBD stone	Retroperitoneal perforation	Recovered	32 days
CBD stone	Lateral duodenal perforation	Recovered	18 days
CBD stone	Retroperitoneal perforation	Recovered	8 days
CBD stone	Retroperitoneal perforation	Recovered	16 days
CBD stone	Lateral duodenal perforation	Recovered	12 days
Cholangiocarcinoma	Lateral duodenal perforation	Died	27 days
Post cholecystectomy leak	Lateral duodenal perforation	Recovered	22 days

All perforations were confirmed in the procedure of ERCP by X-ray fluoroscopy and/or endoscopy and followed up with ultrasound and CT. Of the four patients with retroperitoneal perforations, 2 resulted from papillotomy, and 2 resulted from inserting balloon or basket into CBD after papillotomy during stone removal. These patients suffered from CBD stones, and the stones were removed in the first ERCP attempt. After the initial ERCP, they immediately treated with conservative management. They all received nasogastric suction, intravenous nutrition, somatostatin and broad-spectrum antibiotics. Two of them recovered successfully by conservative management and two needed surgical intervention.

4. Discussion

ERCP is an important therapeutic modality for biliary and pancreatic diseases. Perforation is one of the most dreadful complications of ERCP and endoscopic sphincterotomy. A meticulous MEDLINE search was performed by Vezakis and his colleagues [6] from 2000-2014 using the keywords “perforation”, “ERCP” and “ERCP sphincterotomy”. Articles included nine cases or more were reviewed.

They reviewed 18 studies (including 142847 patients), the incidence was 0.39% with an associated mortality of 7.8%. According to Stapfer classification, 25% were type I, 46% were type II and 22% were type III. Overall mortality was 7.8% [6].

The diagnosis of perforation was made during ERCP in 73% of cases. The pathogenesis, site and extension of injury, suggested by clinical data and radiography, should point to operative or non-operative management. Type I perforations indicate early surgical repair, unless endoscopic closure can be achieved. Type II perforations treated initially non-operatively. Conservative treatment included biliary stenting, fasting, intravenous fluid resuscitation, broad spectrum antibiotics, nasogastric drainage, and drainage of fluid collections (percutaneous). Non-operative treatment was successful in 79% of patients belonging to type II injuries, with mortality of 9.4%. Non-operative treatment was sufficient in all patients with injuries of the type III. Nature of surgical technique depends on time of interference, site and size of defect and clinical status of the patient [6].

Due to excessive compression of air in the duodenum, air bubbles can leak through the sphincterotomy area outside the duodenal wall, into the retroperitoneal space. The presence of air in the retroperitoneal plane is a common finding after ERCP sphincterotomy. Computed tomography scan, when used routinely following ERCP and sphincterotomy, retroperitoneal air may be detected in 13% to 29% of patients [15, 16]. In the absence of clinical abnormalities, it has no significance and these patients do not need any further intervention.

In the present study morbidity and mortality of 612 patients underwent ERCP were 87 patients (14.22%) and 8 patients (1.31%) respectively. Perforation occurred in 9 patients (1.47%), bleeding in 12 patients (1.96%), cholangitis in 23 patients (3.76%), pancreatitis in 26 patients (4.25%), and death in 8 patients (1.31%).

4.1 Incidence and Risk Factors

Duodenal perforations are difficult to diagnose during ERCP because they usually occur in the lateral duodenal wall by side view endoscope [17]. Sedation use during the procedure makes the diagnosis more difficult because it masks the symptoms [17, 18]. However, recent several reports identified perforation by meticulous direct vision when carefully looked for or documented by contrast extravasation [14, 18]. Careful identification of this complication during ERCP is warranted should the procedure be therapeutic or technically difficult due to various factors. These include when dilatation is carried out or in patients with local anatomical variations [14, 18, 19]. Specific symptoms and signs suspicious of perforation are upper abdominal and back pain (more intense than usual), tenderness with or without peritoneal signs (generally rebound tenderness), tachycardia, fever, and surgical emphysema, although the last three findings tend to be late [14, 18, 19]. Tachycardia is a constant physical finding but because it can be caused by other factors including pain, it may not be a reliable indicator. Leukocytosis and fever are often seen 12 hours or more after completion of ERCP. Manifestations of peritonitis usually appears after several hours when sufficient duodenal contents extravasate into the peritoneal cavity [20, 22].

A multivariate analysis was performed to reveal risk factors in two studies [23, 24]. Precut, intramural injection of contrast, and Billroth II gastrectomy were significant risk factors for retroperitoneal duodenal perforation by Loperfido *et al.* [23] Enns *et al.,* [24] study suggested that factors existing prior to ERCP which predicted perforation included dysfunction of sphincter of Oddi and a dilated common bile duct. Duration of procedure, biliary stricture dilation and performance of a sphincterotomy were predictive factors related to ERCP itself.

In the present study ERCP indications were CBD stones in 382 patients (62.42%), cholangitis in 39 patients (6.37%), malignant jaundice in 87 patients (14.21%), chronic pancreatitis in 54 patients (8.82%), dilated CBD in 6 patients (0.98%), and post cholecystectomy in 44 patients (7.19%).

In the present study perforation occurred during stone CBD extraction in 7 cases, stent insertion in one case of cholangiocarcinoma, and in one case of post-cholecystectomy leak. All these cases were difficult and consumed long duration.

4.2 Etiology

Vezakis *et al.,* [6] found the mechanism of injury in 573 patients from 18 studies. Endoscopic sphincterotomy was responsible for the majority (41% of perforations), insertion and manipulations of the endoscope for 26%, guide-wire for 15%, strictures dilation for 3%, other instruments for 4%, stent insertion or migration for 2% and the etiology was unknown in 7% of cases.

In the present study endoscopic sphincterotomy was responsible for 4 cases of perforation (44.4%), guide-wire injury in 2 cases (22.2%), dilation of strictures in one case (11.1%), stent insertion in one case (11.1%), and the etiology was unknown in one case (11.1%).

4.3 Diagnosis

Early detection and prompt treatment of post ERCP duodenal perforation, is the essence for better outcome. The signs of suspicion should be high, in those patients with post procedure undue pain and fever. In these patients prompt diagnosis and institution of systemic antibiotics and intravenous fluid resuscitation is more than mandatory [21, 25]. The best diagnostic measure is radiographic. Urgent plain X-ray of the abdomen would detect free intraperitoneal air, extraluminal

retroperitoneal air and/or contrast [16, 26]. CT scan of the abdomen and pelvis with oral contrast is the most sensitive and specific diagnostic modality to evaluate for the presence of perforation [16, 26]. It can effectively demonstrate retroperitoneal or intraperitoneal air and fluid or extravasation of oral contrast [17, 26]. Free intraperitoneal air implies an uncontained leak that is likely to require surgical interference. Isolated retroperitoneal air is suggestive of a sphincterotomy site perforation [19, 26]. The amount of air may not correlate well with the size of perforation but rather with the degree of insufflation of air during the endoscopic procedure. Intraperitoneal or retroperitoneal fluid without air is more suggestive of acute pancreatitis than perforation which always results in extraluminal gas attributable to insufflations [10, 11]. Patients with significant retroperitoneal air and fluid managed non-operatively should be monitored by repeated imaging as persistent infected fluid collection can result in non-healing of the perforation site. Large fluid collection may require CT guided or surgical drainage [8, 10, 13].

Delayed diagnosis as a definition was inconsistent between studies, but it was considered to be associated with gloomy prognosis [27]. Type 1 perforations can be diagnosed from direct visualization of the retroperitoneal space or the abdominal cavity. In cases with bleeding and unclear endoscopic view, the use of fluoroscopy with or without contrast injection confirm the diagnosis. Perforations of type II suspected after a large or wrong direction sphincterotomy and confirmed by fluoroscopy. It will reveal the presence of retroperitoneal air, especially around the right kidney with marking of kidney margin and occasionally the outlining of psoas muscle. Contrast injection can also show leaking from the sphincterotomy site. Perforations of type III can be diagnosed by the unusual passage of the guide wire or by contrast injection.

In the present study 3 cases of perforation were recognized and diagnosed immediately during ERCP, and 6 cases recognized later on after the procedure. One patient presented with abdominal pain, four patients presented with peritonitis, and four patients with surgical emphysema. Four patients had Knudson score of 4, three patients had 3, and two patients had 2. Lateral duodenal perforation occurred in five patients, and retroperitoneal perforation occurred in four patients.

All perforations were confirmed by X-ray fluoroscopy and/or endoscopy and followed up with ultrasound and CT. Of the four patients with retroperitoneal perforations, 2 resulted from papillotomy, and 2 resulted from inserting balloon or basket into CBD after papillotomy during stone removal. These patients suffered from CBD stones, and the stones were removed in the first ERCP attempt. After the initial ERCP, they immediately treated with conservative management. They all received nasogastric suction, intravenous nutrition, somatostatin and broad-spectrum antibiotics. Two of them recovered successfully by conservative management and two needed surgical intervention. The five patients with intraperitoneal perforation underwent surgery.

4.4 Treatment

The first objective in the management would be to determine whether the patient could be managed conservatively or need surgical interference according to patient’s condition, mechanism of injury, site and degree of leak [28-32, 37]. It may not always be possible to determine the site and mechanism of perforation despite several investigations [30, 37]. However, these patients irrespective of method of treatment would need an effective nasobiliary and gastrointestinal drainage to decrease the leak of digestive fluid that would otherwise gradually accumulate in the intraperitoneal and retroperitoneal spaces. Indication of surgery include type I injury, generalized peritonitis not amenable to percutaneous drainage, major contrast leakage, documentation of ERCP perforation with choledocholithiasis or retained hardware (e.g., Dormia basket), extensive subcutaneous emphysema and failure of non-surgical treatment [11, 13]. Aims of the surgical treatment of ERCP induced perforation include: sepsis control (drainage of the retroperitoneal, intra-abdomen collection and drainage of the biliary tree, removal of stones of the bile ducts or retained basket; and to repair the perforation with or without diversion. Recently management has shifted towards selective approach [28, 37].

Management approach depends on the site and mechanism of injury [30, 32]. Type I injury (duodenal perforation) will require surgical intervention [31, 32]. Perforations are closed primarily (one or two layers) following debridement of necrotic tissues. Perforations less than 1 cm which present early are treated with primary repair [28, 30]. Closure is performed transversely to ensure a patent duodenal lumen. For larger duodenal perforation, jejunal serosal patch is an option. However, repair of perforation when large or when delayed is fraught with danger. Nearly 6 liters of fluid including saliva, gastric and pancreaticobiliary juice traverse the duodenum daily will lead to high output fistula in the event of dehiscence of duodenal repair, a possibility when the wall is friable and edematous [28, 29]. Thus, duodenal diversion is reserved for high risk patients with delayed diagnosis or larger defects in duodenal wall. This divert the gastrointestinal contents and enzymes rich secretions from the duodenal repair site and in case of duodenal fistula facilitates management by having a controlled fistula.

Duodenal diversion techniques includes tube decompression, duodenal diverticulation and pyloric exclusion [28-30, 37]. The use of tube decompression is controversial. Its disadvantages include new perforation being made in the intestinal tract and inefficiency of the duodenostomy/jejunostomy tube in decompressing the duodenum properly. Duodenal diverticulation is another method of complete diversion, it includes a distal Billroth II gastrectomy, closure of duodenal injury, insertion of a decompressive catheter into the duodenum and generous drainage of the duodenal repair. Biliary drainage and truncal vagotomy may also be added [28-30]. Duodenal diverticulosis is an extensive procedure which is not suitable for hemodynamically unstable patients. Pyloric exclusion is an alternative to the above extensive procedure. It consists of duodenal wound repair, closure of the pylorus through a gastrostomy with suture or by stapling and side to side gastrojejunostomy at the site of gastrostomy [28-30]. Sutures closing the pylorus breaks down after several weeks and gastrointestinal continuity re-establishes. The procedure is less extensive, less time consuming and causes less physiological disturbances. Most surgeons advocate pyloric exclusion procedure if duodenal diversion is needed [28-30].

Perforation of type II and III caused by guide-wire or basket instrumentation tend to be small and well contained and usually heal spontaneously and hence are usually managed by non-operatively [30, 37]. Identification of the perforation site during exploration is noted in only 7.9% of the patients in the literature review [30, 37]. Management of periampullary

perforation in general remains controversial [37-43]. Some surgeons prefer immediate endoscopic management once the retroperitoneal perforation is identified [28, 30]. Internal biliary stent or nasobiliary stent divert bile and pancreatic secretion away from the site of perforation [28-30]. Biliary decompression with percutaneous transhepatic biliary drainage is an alternative. Regular contrast scan helps to detect retroperitoneal abdominal collection which may require percutaneous or surgical drainage.
In the present study conservative management applied to 2 patients one of them needed CT guided aspiration of pus, primary closure performed as a single maneuver in 2 patients, primary closure with T-tube drainage of CBD performed in 2 patients, tube duodenostomy and pyloric exclusion with gastrojejunostomy in 3 patients. Eight patients were recovered and survived (8/9, 88.9%) and one patient died (1/9, 11.1%). The 2 conservatively managed patients had 7 and 8 days of hospital stay, the 2 primarily closed patients had 9 and 12 days of hospital stay, the 2 primarily closed patients with T-tube drainage of CBD had 16 and 18 days of hospital stay, and the 3 patients underwent tube duodenostomy and pyloric exclusion had 22, 27 (died) and 32 days of hospital stay.
Novel management of ERCP induced perforation have been reported [44-46]. an endoclipping device have been used successfully in some patients [46]. these patients need to be carefully selected and the method is applicable in small well defined injuries, detected early and having m*et al*l the criteria for conservative management such as the absence of abdominal manifestations and collections. Another recent report also presents the successful endoscopic sealing of small lateral duodenal perforations using fibrin glue [45].
In Enns *et al* study [24]. 5/13 patients with type II injuries were managed either with plastic biliary stents or percutaneous transhepatic biliary drainage. In Alfieri *et al* study [47]. 12/30 patients with early diagnosis were successfully treated conservatively with nasobiliary drainage.
Fully covered self-expandable metallic stents (SEMS) in sphincterotomy related perforations. SEMS have the advantage of covering the perforation and permit free flow of bile into the duodenum instead of into the retroperitoneal space. It is better to use a covered SEMS because plastic stents or nasobiliary drains may not completely prevent bile flow into the perforation site. SEMS can also be used later with a repeat ERCP when the leak persists [48-51].
Vezakis *et al.,* [6] reviewed 11 studies, after initial non-surgical treatment, surgery was required in 29/137 (21%) of patients with type II perforations, with an overall mortality of 9.4%. The mortality of patients who required surgery was high (38%). Conservative management was successful in all patients with type III perforations. In Machado review [46] conservative management was successful in 92.9% of patients with both types of injuries, treated initially non-operatively, with a final mortality of 0.6%.
Comparing the present series of retroperitoneal perforations to that reported by others [53, 54], a surprisingly low mortality was demonstrated. Mortality rate was 0% versus 5%–37.5% in other's series [53, 54]. The superior results in the present study may be due to three factors: the small number of cases, early diagnosis, and effective management which reduced stimulation and exudation of gastric acid, bile, and pancreatic liquid in perforation site. Recent literature from the year 1999 onwards, which had more than 20 cases with ERCP-related perforation was reviewed [55]. It was found that 87.9% of retroperitoneal perforations could recover by conservative treatment (total mortality was 2.9%), and 80.8% of peritoneal perforations received surgery (total mortality was 24.7%). This supports opinion of the present study that most retroperitoneal perforations can recover by conservative treatment, and most peritoneal perforations need surgical interference unless the perforation can be sutured under endoscope which was not available in the present study.
Sepsis was the leading cause of death in 85.7% of patients with ERCP-related perforation, and 81.8% of patients who died had peritoneal perforation [55]. It may be an important method to reduce mortality by adequate drainage of exudation, and decreasing the exudation by reducing the secretion of gastric acid, bile, and pancreatic liquid. From the data of the present study and literature analysis, a protocol (Figure 1) is suggested as early perforations management schedule. In the present series, all patients with perforations were diagnosed early (3 cases during ERCP procedure and 6 cases within 12 hours after the procedure). The patients' peritoneal cavity and retroperitoneal space had little exudate accumulation. If retroperitoneal space had large fluid exudation, the effective drainage is required by surgery or percutaneous drainage. Patient with perforation should shift to surgery if he was worsening within 48 h by conservative measures. Delayed surgical operation more than 48 h after perforation have high mortality [56]. Although the present study had little experience for late perforations, the effective treatment should not only include the above management, but also include draining the fluid exudation by surgery or percutaneous drainage, preventing or treating infections by using broad-spectrum antibiotics, and early enteral nutrition (EEN) by placing nasojejunal catheter.

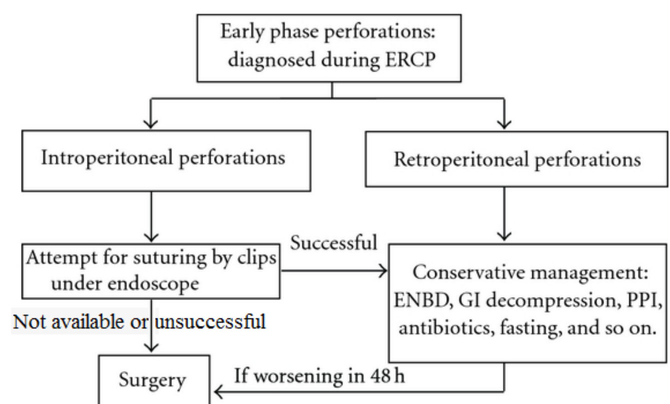

Fig 1: Early management algorithm of ERCP-related perforation.

5. Conclusion

Duodenal perforation complicating ERCP is uncommon but has severe consequences if not adequately and properly managed. The clinical syndrome of abdominal pain, fever and leukocytosis after ERCP especially after difficult and prolonged procedure and the fluoroscopic features of retroduodenal air with fluid would suggest the diagnosis. The pathogenesis and extension of injury proved by clinical and radiographic progressive features would guide towards a more selective approach of conservative or surgical treatment. The interval between the perforation and operation in patients who require surgical interference, is of utmost significance as mortality increases dramatically if there is any delay in

intervention. The best operation for duodenal perforation following ERCP appears to be primary repair and duodenal diversion with pyloric exclusion and gastrojejunostomy. If the perforation is diagnosed and managed early, primary repair of the injury without diversion has similar results, provided there is minimal peritoneal contamination. Type I perforations may require immediate surgical interference. Type II or III perforations may often be managed conservatively. However, they require meticulous observation supported by flouroscopic investigation to differentiate between satisfactory progressed patients from those require surgical intervention. Delayed diagnosis and interference, salvage surgery after failure of conservative management, repeated operations and older age patients contributed significantly to the poor prognosis. However, the outcome in recent years has significantly improved due to early detection, appropriate management strategies, and novel methods of managing ERCP induced perforation as endoclipping devices, fibrin glue, plastic biliary stents, and fully covered self-expandable metallic stents.

6. References

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