Impact of completion of primary biliary procedure on outcome of endoscopic retrograde cholangiopancreatographic related perforation

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ABSTRACT

Background and aims Perforation is one of the worst complications of therapeutic endoscopic retrograde cholangiopancreatography (ERCP). We aimed to study the epidemiology of ERCP related perforation and the impact of completion of intended procedure on the outcome of this complication.

Methods ERCP records from January 2007 to April 2012 were independently evaluated by two investigators for the occurrence of procedure related perforations. A total of 11 500 patients underwent therapeutic ERCP during the study period. The case records of 171 (1.5 %) patients with ERCP related perforations were reviewed to analyze the epidemiology and risk factors associated with poor outcome.

Results Of the 171 patients included in this study, the majority of perforations (n = 129, 75.4 %) were related to use of the needle-knife precut technique. Female gender (1.9 % vs 0.7 %, $P < 0.001$), age >40 years (1.7 % vs 1.1 %, $P < 0.01$), and benign disease (1.7 % vs. 1.1 %, $P < 0.01$) were risk factors for ERCP related perforation. Most of the perforations (n = 135, 79 %) were detected during the procedure. The majority of patients were managed conservatively (n = 164, 96 %). Although 159 patients recovered, 12 patients (7 %) did not survive. Completion of intended biliary procedure for primary disease was associated with low risk of mortality (2 % vs 15.4 %, $P < 0.001$).

Conclusions ERCP related perforation is uncommon. The majority of patients can be managed conservatively. The risk of mortality is low and completion of the intended biliary procedure decreases the risk of mortality.

Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) enables the diagnosis and treatment of various biliopancreatic disorders but is associated with a small risk of ERCP related complications. The risk of major complications ranges from 5.4 % to 23.0 % and the overall mortality ranges from 0.1 % to 1 % [1 – 8]. ERCP related perforations occur in less than 1 % of patients, but are associated with a mortality rate of 16 – 18 % [1 – 8]. Delay in the diagnosis and intervention following duodenal perforation may lead to significant mortality (8 – 23 %) as a consequence of sepsis and multiorgan failure [9]. Howard et al. [9] classified ERCP related perforation into three distinct groups: group I, guidewire related perforation; group II, periampullary perforation; and group III, duodenal perforation remote from the papilla. A recent classification proposed by Stapfer et al. [10] is based on the mechanism, anatomical location, and severity of injury which may predict the need for surgery. Sphincterotome induced and/or guidewire related perforation constitute the majority (up to 80 %) and rarely need intervention [10]. Guidewire or stent-related perforations can usually be treated endoscopically by providing adequate ductal drainage beyond the leak site [1, 9]. Endoscopic sphincterotomy (ES) related perforation remains the most challenging complication to avoid and treat.

Risk factors for ES related perforation have been difficult to quantify due to a lack of well designed studies. Bowel perfora-

tion is more common in patients with Billroth II or Roux-en-Y anatomy, whereas ES related perforation is more common after needle-knife precut (NKP) techniques, and in patients with suspected sphincter of Oddi dysfunction [1]. Literature is sparse with regard to management of patients with ERCP related perforation. Several studies advocate surgical management as the primary approach for this complication. While this holds true for intraperitoneal perforations or scope related perforations, the majority of retroperitoneal perforations can be managed conservatively. We have observed that completion of the primary biliary procedure for which ERCP was intended improves outcome, but there is no published literature to support this.

We aimed to study the epidemiology of ERCP related perforation and to evaluate the effect of completion of the intended biliary procedure on the outcome of this complication.

Materials and methods

In total, 11 500 ERCPs were performed between January 2007 and April 2012 in the Department of Gastroenterology at the GB Pant Institute of Postgraduate Medical Education and Research in New Delhi, India. ERCP records were evaluated for the occurrence of procedure related perforations.

Case records for 171 (1.5 %) patients diagnosed with ERCP related perforations were reviewed retrospectively. Diagnosis of ERCP related perforation was made on endoscopic, radiological or surgical evidence. We analyzed the risk factors associated with poor outcomes in these patients. The parameters analyzed included demographic characteristics, clinical characteristics, laboratory parameters, and completion of intended biliary procedure. Mortality was considered to be a poor outcome.

Completion of primary biliary procedure was defined as "completing the primary aim for which ERCP was planned," e. g. removal of stone in choledocholithiasis or placement of stent to facilitate biliary drainage.

Management protocol

All patients diagnosed as having perforations were managed with nothing by mouth (NPO) for 72 hours, intravenous antibiotics (a combination of third generation cephalosporins, fluoroquinolone with or without metronidazole), and intravenous fluids. If a perforation was detected during the procedure, then every effort was made to quickly complete the biliary procedure if possible. The procedure was left incomplete only if the common bile duct (CBD) was not cannulated at all. All patients were monitored for vital signs every 2 hours, abdominal signs every 6 hours, and abdominal girth measurement every 12 hours. Laboratory investigations were carried out as required. Patients with no abdominal signs, and having normal bowel sounds were allowed oral liquids after 72 hours which was gradually escalated to normal diet within the next 24 hours. Patients having deterioration with this management or the appearance of new abdominal signs were scheduled for surgery.

Patients with evidence of intraperitoneal perforation (defined as air under the diaphragm on abdominal radiograph or CT scan) were scheduled for surgery without trial of conservative management.

Surgical management included peritoneal lavage with feeding jejunostomy along with duodenotomy and primary repair of the perforation.

Statistical analysis

Statistical analyses were performed using SPSS version 16.0 for Windows. Results were expressed as the mean ± standard deviation (SD) for quantitative variables and as percentages for categorical variables. Categorical variables were compared using the Chi-squared test. Continuous variables were compared by unpaired Student's *t* test for variables with a normal distribution and the Mann-Whitney *U* test for variables without a normal distribution. *P* values of 0.05 or less were considered statistically significant. All parameters with statistical significance as described were subjected to multivariate analysis using logistic regression and results expressed as odds ratio (OR) with 95 % confidence interval (95 %CI).

Results

A total of 11 500 patients (7000 females) underwent therapeutic ERCP during the study period. Indications for ERCP were benign disease in 7000 (60.9 %) and malignant disease in 4500 (39.1 %). In total, 60.9 % (n = 7000) of all patients undergoing ERCPs were female. Of the 11 500 patients, 171 (1.5 %) were diagnosed as having ERCP related perforations.

The mean age of patients with ERCP related perforations was 47.2 ± 15.2 years (6 – 90 years). Amongst the patients with ERCP related perforations, 139 (81.3 %) were female. Mean hospital stay was 14 ± 6 days. The majority of patients (n = 113, 66.1 %) were more than 40 years of age. Most of the perforations (n = 135, 79 %) were detected during the procedure. The majority 129 (75.4 %) were related to use of the NKP technique. The primary procedure was completed in 100 (58.5 %) patients. Of these 100 patients, only two underwent surgery and two patients died as a result of multiorgan failure. Of the 71 patients in whom the primary procedure was not completed, surgery was needed in six patients and 10 patients did not survive.

The majority of patients were managed conservatively (n = 164, 96 %). Although 159 patients recovered, 12 patients did not survive. Among these 12 patients, eight had evidence of ongoing cholangitis. On univariate analysis, poor outcome factors were female gender ($P < 0.001$), age > 40 years ($P < 0.001$), benign etiology of biliary disease ($P < 0.001$), and use of the NKP technique ($P < 0.001$), while good prognostic factors included detection of perforation during the procedure ($P = 0.001$), completion of the primary biliary procedure ($P < 0.001$), conservative management ($P < 0.001$), and shorter hospital stay ($P = 0.005$) (▶ **Table 1**). On multivariate analysis (OR (95 %CI)), length of hospital stay (0.8 [0.7 – 0.9]) ($P = 0.014$), completion of biliary procedure for primary disease (5.5 [1.1 – 28.4]) ($P = 0.04$), and conservative management (19.1 [2.3 – 157.9]) ($P = 0.006$) were the only factors associated with a favorable outcome (▶ **Table 2**).

▶ **Table 1** Univariate analysis factors associated with poor or favorable outcome.

Variable	Survival (n = 159)	Death (n = 12)	*P* value
Female gender, n (%)	131 (82.4)	8 (66.7)	< 0.001
Age > 40 years, n (%)	101 (63.5)	9 (75)	< 0.001
Benign etiology, n (%)	111 (69.8)	6 (50)	< 0.001
Detection during procedure, n (%)	124 (78)	11 (91.7)	0.001
Completion of intended biliary procedure, n (%)	98 (61.6)	2 (16.7)	< 0.001
Needle knife precut, n (%)	120 (75.5)	9 (75)	< 0.001
Surgical management, n (%)	4 (2.5)	3 (25)	0.18
Hospital stay, mean ± SD, days	16.3 ± 5.7	11.6 ± 5.4	0.005

▶ **Table 2** Multivariate analysis factors associated with poor or favorable outcome.

Variable	*P* value	OR (95 %CI)
Female gender	0.324	0.484 (0.114 – 2.045)
Benign etiology	0.14	2.8 (0.7 – 11.9)
Completion of intended biliary procedure	0.04	5.5 (1.1 – 28.4)
Conservative management	0.006	19.1 (2.3 – 157.9)
Hospital stay	0.014	0.8 (0.7 – 0.9)

Discussion

This study is the largest in terms of management of ERCP related perforations. We found the ERCP related perforation rate to be around 1.5 % which is slightly higher than in the reported literature [1 – 5, 8]. Most of our patients undergoing ERCP were females and perforation was relatively more common in females compared to males. Age more than 40 years, use of NKP technique, and benign nature of underlying disease were other significant risk factors for ERCP related perforations. We also found that completion of intended biliary procedure had a profound impact on outcome of this complication.

Mortality and morbidity in this study were comparable to that reported by Howard et al. [9]. Our patients had an average length of hospital stay of 14 ± 6 days vs 8.5 days, and the mortality rate was 7 % in our study compared to 5 % in the study by Howard et al. Detection rate of perforations during the procedure was 79 % in our study compared to 91 % in the study by Howard et al. If a perforation is not recognized or suspected during ERCP, it would be difficult to make an early diagnosis (i. e. within 12 hours) [11, 12]. The perforation is usually diagnosed with an abdominal radiograph or CT scan. The diagnosis is especially likely to be delayed if the patient has concurrent elevated lipase, and the pain is attributed to ERCP-induced pancreatitis.

Dunham et al. [13] advocated repeat ERCP after perforation to ensure that residual CBD stones and blood clots from sphincterotomy are cleared so that bile flows into the duodenum rather than into the retroperitoneum. However, they were against placing a biliary stent because they felt that the presence of the foreign body might prevent healing of the perforation; however, Howard et al. placed biliary stents or naso-biliary tubes in 20 out of 22 patients with ERCP related perforations. In our study, 100 out of 171 (58.5 %) patients had completion of the biliary procedure. Only two patients with completed intended biliary procedure had poor outcomes compared to 10 out of 71 in whom the procedure was not completed ($P < 0.001$).

Although our study is retrospective, the uniform criteria for diagnosis and the standardized management protocol followed make it robust. Some endoscopists [14, 15] prefer early surgery for all ERCP associated perforations. With increasing experience in treating this uncommon but potentially lethal complication, there is increasing evidence that most perforations can be managed without surgery [13, 16, 17]. In our study, only 4 % (7 of 171) required surgery while the rest were all managed conservatively.

Conclusions

ERCP related perforation is uncommon. The majority can be managed conservatively. Mortality is uncommon and completion of the intended biliary procedure lowers the risk of mortality.

Competing interests

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

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