

# Post-Endoscopic Retrograde Cholangio-pancreatography Complications at Dr. Cipto Mangunkusumo General National Hospital

*Rolan Sitompul\**, *Achmad Fauzi\*\**, *Dadang Makmun\*\**,  
*Murdani Abdullah\*\**, *Ari Fahrial Syam\*\**, *Marcellus Simadibrata\*\**

\*Department of Internal Medicine, Krakatau Medika Hospital, Cilegon

\*\* Division of Gastroenterology, Department of Internal Medicine, Faculty of Medicine University of Indonesia/Dr. Cipto Mangunkusumo General National Hospital, Jakarta

## ABSTRACT

**Background:** This study retrospectively evaluated post-endoscopic retrograde cholangio-pancreatography (ERCP) complications at Cipto Mangunkusumo hospital in order to improve management of a subsequent prospective study of post-ERCP complications.

**Method:** The indications, findings, diagnostic or therapeutic procedure, cannulation, devices used during the procedure, and complications of patients treated consecutively with ERCP between January 2004 and November 2008 were evaluated retrospectively.

**Results:** Of 176 ERCP patients who were initially evaluated, 38% had undergone diagnostic ERCP and 62% therapeutic ERCP. The median age of the patients was 49 years (range 18–80 years); 95 (53.9%) were male. Only 54 of these 176 procedures could be evaluated for post-ERCP complications. A computed tomographic abdominal scan or magnetic resonance cholangio-pancreatography was performed in 23 (42.6%) patients and a biliary sphincterotomy in 14 (25.9%) patients. The overall complication rate was 33.3%: 14.8% after diagnostic ERCP and 18.5% after therapeutic ERCP. The complications after diagnostic ERCP were pancreatitis in 3 (15%) patients, cholangitis in 3 (15%) patients, hemorrhage in 1 (5%) patient, pancreatitis and hemorrhage in 1 (5%) patient; the complications after therapeutic ERCP were pancreatitis in 6 (17.6%) patients, cholangitis in 3 (8.8%) patients, hemorrhage in none, and concomitant pancreatitis with hemorrhage in 1 (2.9%) patient. No significant difference was observed between the complication rates and the type of ERCP performed.

**Conclusion:** There were no differences in the complications after diagnostic and therapeutic ERCP. As our study shows the post-ERCP complication rate to be higher than those of other large retrospective and prospective studies, we must evaluate it in a prospective study.

**Keywords:** post-ERCP, complications, therapeutic ERCP, diagnostic ERCP

## INTRODUCTION

Endoscopic retrograde cholangiopancreatography (ERCP) was first reported in 1968 and was soon considered a safe and direct technique for evaluating biliary and pancreatic diseases. It is now a commonly performed endoscopic procedure. ERCP has evolved

from a diagnostic procedure to an almost exclusively therapeutic procedure. Other imaging techniques, such as ultrasonography, computed tomography (CT), magnetic resonance imaging, endoscopic ultrasonography, and intraoperative cholangiography, provide diagnostic information that allows the selection of patients for therapeutic ERCP.<sup>1,2</sup>

At Cipto Mangunkusumo hospital, several studies of ERCP procedures have been performed since 1987. In 1987, a review of 520 patients was conducted, and in 1991, Lesmana et al reported 34 patients who had undergone parentoscopic endoprosthesis procedures

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Correspondence:  
Rolan Sitompul  
Department of Internal Medicine  
Krakatau Medika Hospital  
Jl. Semang Raya Cilegon Indonesia  
Phone: +62-254-330461 Fax: +62-254-37410  
E-mail: rianoffaj@yahoo.co.id

and 84 patients who had undergone endoscopic sphincterotomy and stone extraction. Clinical descriptions of 24 patients with obstructive jaundice from August 1989 to August 1990 were reported by Waspodo.<sup>3,4,5</sup>

Because ERCP has since evolved from a diagnostic to a therapeutic procedure, a prospective study of the complications observed after these ERCP procedures is required. Preparatory to such a study, we performed a retrospective study of post-ERCP complications that had occurred between January 2004 and November 2008 to evaluate any differences between the diagnostic and therapeutic procedures and to improve the management of the subsequent prospective study.

## METHOD

A retrospective study was conducted at the Cipto Mangunkusumo hospital for the period from January 2004 to November 2008. In total, 199 consecutive ERCPs were performed during the study period; 176 of these could be evaluated, and 54 of the procedures met the criteria for inclusion in the evaluation of post-ERCP complications. Data on the patients' characteristics, ERCP indications and findings, cannulation, period of hospitalization, and complications were collected retrospectively. These data were entered into a database for subsequent processing and analysis.

Post-ERCP complications were defined as any adverse effects related to the ERCP that prolonged the patient's hospitalization or required the readmission of a previously discharged patient.<sup>6</sup> Acute pancreatitis was defined as the new onset of abdominal pain, with an elevated amylase level at least three times higher than the upper limit of the normal range for more than 24 hours after the procedure, requiring hospitalization for more than one night.

The grading system used for the major complications of ERCP and endoscopic sphincterotomy was:<sup>6,7</sup> (1) mild: serum amylase at least three times the normal level for more than 24 hours after the procedure, or the readmission of the patient or prolongation of the planned hospital stay by 2–3 days; (2) moderate: hospitalization of 4–10 days; (3) severe: hospitalization for more than 10 days, haemorrhagic pancreatitis, phlegmon or pseudocyst, or intervention (percutaneous drainage or surgery).

Bleeding was defined as clinical evidence of haemorrhage, with a reduction in haemoglobin of more than 2 g/dL or the need for a blood transfusion. Cholangitis was defined as a temperature higher than 38 °C for more than 24 hours that was considered to have a biliary etiology.<sup>6,7</sup> Any intensive-care-unit admission after the procedure was graded as a severe

complication. ERCP was defined as therapeutic when an endoscopic sphincterotomy, pre-cut sphincterotomy, drainage, stricture dilatation, stent exchange, sphincter of Oddi manometry, or biliary stone removal was performed at the same time, singly or in combination.<sup>6,7</sup>

The statistical analysis was performed using SPSS version 10.0. The diagnostic and therapeutic ERCP complications were compared using the  $\chi^2$  test or Fisher's exact test. All tests of significance were two-tailed and  $p < 0.05$  was considered significant.

## RESULTS

In total, 199 ERCPs were performed during the study period, of which 176 were initially evaluated. The median age of the patients was 49 years (range 18–80 years); 95 (53.9%) were male. The ethnic distribution was 71 (40.3%) Javanese patients, 28 (15.9%) Betawinese patients, 23 (13.1%) Sundanese patients, 19 (10.8%) Batak patients, 11 (6.3%) Minangkabau patients, 7 (3.9%) patients from Sulawesi (Buginese, Makassarese or Torajas), and 17 (9.7%) patients from other ethnic groups. The indications for ERCP were presented in figure 1.

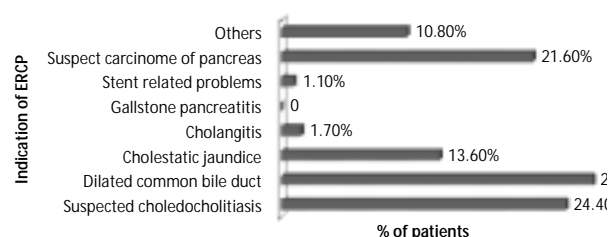


Figure 1. Indications for ERCP in 176 patients

Therapeutic ERCP was performed in 109 (62%) patients and diagnostic ERCP in 67 (38%) patients. ERCP failed in 18 (10.2%) patients because of unsuccessful cannulation. Failure of cannulation was predominantly caused by a mass in the papilla vateri. Endoscopic sphincterotomy (EST) was performed in 48 (44.1%) patients undergoing ERCP (table 1).

Table 1. Therapeutic procedures in 109 patients

Type of procedure	n	%
EST	9	8.3
EST and stone extraction	27	24.8
EST and stone extraction and stent	6	5.5
EST and biliary stent	4	3.7
EST and stricture dilatation	1	0.9
NBD and EST dilatation	1	0.9
Biliary stent/stent removal	36	33
Dilatation and stent	2	1.8
Biopsy and stent	8	7.3
Biopsy	15	13.8
<b>Total</b>	<b>109</b>	<b>100</b>

EST: endoscopic sphincterotomy; NBD: naso-biliary drain

Of the 176 patients who underwent ERCP procedures, only 54 could be evaluated for post-ERCP complications (table 2). Of these patients, 29 (53.7%) were male. Their median age was 47 years (range 26-80 years). Twenty-three (13%) patients had been referred from other hospitals. A CT abdominal scan or magnetic resonance cholangiopancreatography (MRCP) was performed in 23 (42.6%) patients.

**Table 2. Major complications in 54 patients: comparison of diagnostic and therapeutic ERCPs**

Complication	ERCP		p
	Diagnostic n = 20 (%)	Therapeutic n = 34 (%)	
Pancreatitis	3 (15)	6 (17.6)	1.00
Cholangitis	3 (15)	3 (8.8)	0.66
Haemorrhage	1 (5)	0	0.37
Pancreatitis and haemorrhage	1 (5)	1 (2.9)	1.00
Total	8 (40)	10 (29.4)	

Prophylactic antibiotics were given to 75% of patients, usually second-generation cephalosporin. Eleven (20.4%) patients had co-morbidities such as diabetes mellitus (eight patients), ischaemic heart disease (one patient), atrial fibrillation (one patient), and renal impairment (one patient); 23 (42.6%) patients had co-morbidities such as anemia of iron-deficiency, hypokalemia, hypoalbuminemia, hypertension, pulmonary obstructive disease, and others; 20 (37%) patients had no co-morbidity. Only one patient was taking anti-platelet drugs for an underlying disease.

The mean duration of the chief complaint requiring hospitalization was  $30.6 \pm 29.3$  days (median 25.5, range 1-120 days). The period of hospitalization until the ERCP procedure was  $11.5 \pm 8.5$  days (median 10, range 1-42 days). Adverse event while under anaesthesia were not well reported. Table 2 shows the major complications in the 54 patients and a comparison of the complications after diagnostic and therapeutic ERCPs. Table 4 shows the types of procedures performed in the 34 patients.

**Table 3. Grades of pancreatitis complications**

Pancreatitis	ERCP		Total
	Diagnostic	Therapeutic	
Mild	3	1	4
Moderate	2	1	3
Severe	1	1	2
Total	6	3	9

**Table 4. Therapeutic procedures in 34 patients**

Type of procedure	n	%
Endoscopic sphincterotomy	2	5.9
EST and stone extraction	9	26.5
EST, stone extraction, and stent	2	5.9
EST and stricture dilatation	1	2.9
Biliary stenting/stent removal	18	52.9
Dilatation and stenting	1	2.9
Biopsy	1	2.9
Total	34	100

## DISCUSSION

ERCP has evolved from a purely diagnostic procedure to a therapeutic procedure with the introduction of non-invasive investigative tools such as MRCP. Most of the ERCP procedures examined in this study were therapeutic (62%). In 1990, Wasposito et al reported that the duration of the chief complaint requiring hospitalization was 2.7 weeks for stone diseases and 3.9 weeks for malignancies. The period of hospitalization until definitive therapy was 20 days for stone diseases and 18.4 days for malignancies.<sup>5</sup>

The post-ERCP complication rate in the present series of patients was higher than those of other studies; at 33.3%, the overall complication rate higher than that of a prospective Singaporean study 9.8%, the study of Lesmana 10%, and other studies 6.6-8.7%.<sup>3,6,7,8</sup> However, as this finding refers to only 54 (30.7%) of 176 ERCP procedures, a prospective study is required. As mentioned above, the duration of the chief complaint and the period of hospitalization before definitive therapy did not change greatly between 1990 and this study, in the future definitive therapy must be done earlier.

There was no significant difference in the complication rates of the diagnostic and therapeutic ERCPs. This finding is consistent with those of a retrospective survey in the USA by Male et al<sup>6</sup> and a prospective study in Singapore by Ong et al,<sup>6</sup> but is in contrast to those of British and Italian studies in which therapeutic ERCP was associated with 3-4 fold higher complication rates.<sup>6</sup>

The reported incidence of post-ERCP pancreatitis ranges from 0% to 40%, with the reported incidence in most prospective series ranging from 1.8% to 7.2%.<sup>7,8,9</sup> This variation is probably attributable to differences in the definition of pancreatitis, the methods of data collection, and the indications for ERCP. In the present study, acute pancreatitis was the most common complication (16.6% of patients). Another two patients had mild pancreatitis with concomitant hemorrhage. Four (7.4%) cases of pancreatitis were mild, three (5.5%) were moderate, and two (3.7%) were severe. These incidences are

higher than those of two large prospective studies reported by Freeman et al and Loperfido et al.<sup>7,8</sup> In these two studies, which considered the therapeutic procedure only, the pancreatitis complication rates were 5.4% and 1.6%, respectively. In a prospective study, Cheng et al reported that pancreatitis accounted for 15.1% of post ERCP complications.<sup>10</sup> In a study undertaken in Singapore, in which both diagnostic and therapeutic procedures were considered, pancreatitis occurred in 5.4% of patients: mild in 2.3%, moderate in 2.8%, and severe in 0.4%.<sup>6</sup>

In this study, the risk of pancreatitis was similar after diagnostic and therapeutic ERCP. This is consistent with the findings of the prospective Singaporean study of Ong et al.<sup>6</sup> The risk factors identified for procedure-related pancreatitis included those related to patient characteristics, such as younger age, suspected dysfunction of the sphincter of Oddi, a history of ERCP-related pancreatitis, and recurrent pancreatitis, and factors related to the endoscopic technique, such as pancreatic duct opacification, small bile duct, multiple cannulation attempts or difficult cannulation, development of abdominal pain during the procedure, pre-cut sphincterotomy, and pancreatic-duct brushing for cytology.<sup>6,9,10,11,12</sup>

The incidence of post-ERCP haemorrhage in a systematic survey of prospective studies was 1.34%.<sup>13</sup> Study by Ong et al, showed the incidence of hemorrhage was only 0.8%.<sup>6</sup> The reported incidence of hemorrhage after sphincterotomy ranges from 0.76% to 2%.<sup>1</sup> In our study, procedure-related haemorrhage occurred in three (5.5%) patients, two after diagnostic ERCP and one after sphincterotomy and stenting procedures.

The rate of post-ERCP cholangitis was 0.7–1.0% in several studies.<sup>1,13</sup> The rate of cholangitis seems to have been slightly higher (2.3%) in the study by Ong et al, although routine antibiotics were given before the procedure. In this study, cholangitis occurred in six (11.1%) patients, all of whom had been given second-generation cephalosporin as the prophylactic antibiotic. Two of them died of severe cholangitis. Of these two patients, ERCP had demonstrated cholangiocarcinoma and Klatskin tumor. Two patients underwent sphincterotomy. Of these two patients, ERCP showed multiple stones in the common bile duct (CBD) and Klatskin tumor. Another two patients underwent diagnostic ERCPs: one patient was diagnosed with suspected carcinoma in the head of the pancreas and the other with total obstruction of the CBD, with dilatation and irregularity of the main pancreatic duct (MPD). Mallory et al and Freeman et al presumed that the risk factors for post-ERCP cholangitis were failed or incomplete biliary drainage, a percutaneous procedure, or malignant jaundice.<sup>1,15</sup> Four of our

patients had malignant jaundice, which might have contributed to incomplete biliary drainage and might have precipitated cholangitis.

In this study, three (5.5%) patients died from procedure-related causes: severe cholangitis in two patients and hemorrhage in one patient. The overall mortality rate after diagnostic ERCP is roughly 0.2% in general. The death rate after therapeutic ERCP is twice as high (0.4–0.49%).<sup>1</sup> A recent survey of prospective studies reported a death rate of 0.33% after the ERCP procedure.<sup>13</sup>

One patient who died from hemorrhage was a 53-year-old man. A CT-scan showed biliary cirrhosis and a liver biopsy revealed chronic hepatitis; he was negative for hepatitis B surface antigen and hepatitis C virus. His serum  $\alpha$ -fetoprotein level was 3.9 ng/mL, total serum bilirubin was 22.3 mg/dL, albumin was 3.3 g/dL, globulin was 2.4 g/dL, prothrombin time (PT) was 30.4 (control = 12.7), and activated partial thromboplastin time (APTT) was 75.4 (control = 36.5). This was corrected with fresh frozen plasma and an injection of vitamin K. Before ERCP, his PT was 10.2 (control = 13.2) and his APTT was 34 (control = 36.5). ERCP revealed total obstruction of the distal CBD, a normal MPD, and unsuccessful cannulation with wire, because the wire was always directed to the pancreatic duct. The patient died four days after the procedure.

The risk factors for hemorrhage identified by multivariate analysis included coagulopathy at the time of the examination, the use of anti-coagulants within 72 hours of the sphincterotomy, the presence of acute cholangitis or papillary stenosis, the use of pre-cut sphincterotomy, and the inexperience of the endoscopist.<sup>1,6</sup>

Cholangitis was suggested as the cause of death in a 44-year-old man who had undergone ERCP with an indication of dilated CBD. ERCP revealed stenosis/stricture of the distal CBD with proximal dilatation, IHBD dilatation, and a non-enlarged MPD, and he was diagnosed with cholangiocarcinoma. Seven days after the procedure, he suffered from sepsis and low blood pressure, and was unconscious for four days. His family then discharged him from hospital without permission.

The other death was of a 51-year-old woman with abdominal ultrasonography CT scan suggestive of carcinoma in the head of the pancreas and liver metastasis. Anemia and hypoalbuminemia were comorbidities. ERCP was performed twice. During the first procedure, the CBD was stented. The diagnosis was Klatskin tumour, with a differential diagnosis of carcinoma of the head of the pancreas and cholangiocarcinoma. A second ERCP, performed three months later. The result was migration of the stent to the proximal CBD and a plastic stent was



inserted beside the first stent, with the end of the stent in the right IHBD, and bile with pus was expelled from the stent. Seven days after the procedure, the patient's temperature was high and she became somnolent; she died 11 days after the procedure from severe cholangitis. Because this was a retrospective study, many ERCP procedures had been evaluated incompletely and a long time ago, and some factors related to the endoscopic technique could not be investigated. All these factors should be considered in our forthcoming prospective study.

## CONCLUSION

There were no differences in the complications after diagnostic and therapeutic ERCP. Our study showed that the post-ERCP complication rate was higher than those of other large retrospective or prospective studies, but because only 30.7% of procedures could be evaluated, a prospective study is required for a more complete evaluation.

## REFERENCES

1. Mallery JS, Baron TH, Dominitz JA, et al. Complications of ERCP. Standards of Practice Committee. American Society for Gastrointestinal Endoscopy. *Gastrointest Endosc* 2003;57: 633–8.
2. Adler DG, Baron TH, Davila RE, et al. The role of ERCP in diseases of the biliary tract and pancreas. American Society for Gastrointestinal Endoscopy. *Gastrointest Endosc* 2005;62:1-8.
3. Lesmana LA. Endoscopic retrograde cholangiopancreatography (ERCP) diagnostic and therapeutic in surgical icteric patients. The Symposium on the Management of Icterus. Faculty of Medicine University of Sriwijaya. Palembang 1991 Sept 14.
4. Lesmana LA. Non-operative therapy in elderly biliary obstructive patients. The Anniversary of Jakarta Hospital, Indonesia. Jakarta 1991 Sept 16.
5. Waspodo AS, Budi Husodo U, Lesmana LA, Akbar N, Sulaiman A, Noer MS. Clinical picture of obstructive jaundice in Internal Medicine Department Cipto Mangunkusumo Hospital/Faculty of Medicine, University of Indonesia. *Konkernas PPHI-PGI-PEGI*. Surakarta 1990 Dec 1–2.
6. Ong TZ, Khor JL, Selamat DS, et al. Complications of endoscopic retrograde cholangiography in the post-MRCP era: A tertiary center experience. *World J Gastroenterol* 2005;11:5209–19.
7. Al-Amri SM. Post ERCP complication [cited 2008 Sept 3]. Available from URL: <http://www.faculty.ksu.edu.sa/Al-Amri/Publications/POST%20ERCP%20COMPLICATION.ppt>.
8. Freeman ML, Nelson DB, Sherman S, et al. Complications of endoscopic biliary sphincterotomy. *N Eng J Med* 1996;335:909–18.
9. Cooper ST, Slivka A. Incidence, risk factors, and prevention of post-ERCP pancreatitis. *Gastroenterol Clin North Am* 2007;36:259–76.
10. Cheng CL, Sherman S, Watkins JL, et al. Risk factors for post-ERCP pancreatitis: a prospective multicenter study. *Am J Gastroenterol* 2006;101:139–47.
11. Mehta SN, Pavone E, Barkun JS, et al. Predictors of post-ERCP complications in patients with suspected choledocholithiasis. *Endoscopy* 1998;30:457–63.
12. Vandervoort J, Soetikno RM, Tham TC, et al. Risk factors for complications after performance of ERCP. *Gastrointest Endosc* 2002;56:652–6.
13. Andriulli A, Loperfido S, Napolitano G, Niro G, Valvano MR, Spirito F, Pilotto A, Forlano R. Incidence rates of post-ERCP complications: a systematic survey of prospective studies. *Am J Gastroenterol* 2007;102:1781–8.
14. Lal D, Lane M, Wong P. Complications of endoscopic retrograde cholangiopancreatography. *JNZ Med Assoc* 2003;116:1177.
15. Freeman ML. Cholangitis: emergency management [cited 2009 March 27]. American Society for gastrointestinal Endoscopy. Digestive Disease Week 2004. ASGE. Available from URL: [http://www.ddw.org/userssets/document/PDF/session\\_handsouts/2004/books/Tuesday/Tues0830Freeman.pdf](http://www.ddw.org/userssets/document/PDF/session_handsouts/2004/books/Tuesday/Tues0830Freeman.pdf).