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Original Article

Predictive factors for severe complications following therapeutic endoscopic retrograde cholangiopancreatography in patients aged 80 years or older

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Abstract: Because of increasing in severe complications following therapeutic endoscopic retrograde cholangiopancreatography (ERCP) in old age, special considerations are needed for elderly patients regarding ERCP management. 121 patients aged or over 80 treated with ERCP between December 2010 and December 2014 was enrolled in this study. For prediction of severe complications, three types of factors were investigated: chronic concomitant diseases, ASA (American Society of Anesthesiologists) scores, and ERCP related. Factors predicting severe complications following therapeutic ERCP were clarified. Multivariate logistic regression indicated that multiple procedures was an independent risk factor for severe complications in elderly patients (odds ratio [OR] 3.26, 95% confidence interval [95% CI] 0.59-18.06). Elderly patients need special consideration for pre- and post-ERCP management to avoid multiple procedures related severe complications.

Keywords: Elderly patients, endoscopic retrograde cholangiopancreatography, risk factor, severe complication, multiple procedures

Introduction

Life expectancy is increasing throughout most of the world. With the proportion of old age increasing [1], old patients undergoing ERCP will rise. Whereas ERCP-related complications have been shown to be similar between the elderly and the young patients [2, 3], elderly patients were at an increased risk of morbidity and mortality compared to their younger counterparts [4]. Postoperative morbidity and mortality in the elderly are likely associated with several comorbidities, type of intervention, hospital volume of ERCP procedures, higher American Society of Anesthesiologists (ASA) status, and geriatric syndromes such as frailty and delirium. It is crucial that factors predicting severity of complications are evaluated, to improve the quality of ERCP outcomes for elderly patients.

Patients and methods

Patients

This was a retrospective cohort study, using a retrospectively completed database of 121 consecutive patients aged or over 80, referred to the Beijing Military General Hospital with indications for ERCP, between December 2010 and December 2014. This study was approved by the institutional review board of Beijing Military General Hospital. Written informed consent was obtained from all patients.

Exclusion and inclusion criteria

Inclusion criteria were the presence of: (i) Patients more than 80 years of age or older; and (ii) Patients failure of biliary drainage caused by various reasons including unresect-

Table 1. Characteristics of Patients

Background	n (%)
Age, mean ± SD (range), years	83.65±3.45 (80-95)
Sex (M/F) (%)	67 (55.37%)/54 (44.63%)
Comorbidities, n (%)	
Diabetes mellitus	23 (19.01)
Cardiovascular disease	52 (42.98)
Cerebrovascular disease	24 (19.83)
Respiratory disease	13 (10.74)
Autoimmune disease	3 (2.48)
Nephropathy	2 (1.65)
Malignant tumor	4 (3.31)
Cirrhosis of the liver	1 (0.83)
ASA scores, n (%)	
1 G	44 (36.36)
2 G	42 (34.71)
3 G	31 (25.62)
4 G	4 (3.31)
Grade of difficulty, n (%)	
1 G	0 (0)
2 G	23 (19.01)
3 G	14 (11.57)
4 G	73 (60.33)
5 G	11 (9.09)
Diverticulum, n (%)	
No	85 (70.25)
Para	27 (22.31)
Inside	9 (7.44)
Biliary duct diameter (< 14/≥ 14 mm)	58 (47.93)/63 (52.07)
Benign or malignant, n (%)	
Benign	91 (75.21)
Malignant	30 (24.79)
ERCP procedures, n (%)	
One procedure	72 (59.5)
Multiple procedures	49 (40.5)

able biliary tumors, choledocolithiasis, and stenosis, etc. Exclusion criteria were the presence of: (i) Patients who were known to be more suitable or required for surgeries, such as those with resectable malignancy; and (ii) Patients had a poor general physical status (i.e. ASA ≥ 5) and thus may not tolerate ERCP.

Patient preparation and sedation

For the therapeutic ERCP, conscious sedation with intravenously administered diazepam 2.5-5.0 mg and pethidine 25-50 mg were administered.

Therapeutic ERCP procedures

All ERCP procedures were done by experienced endoscopists who carried out > 200 ERCP procedures per year. The procedures were performed with Side-viewing duodenoscopes (TJF-240/260V, Olympus). The precut technique was carried out in difficult case of biliary cannulation. Endoscopic sphincterotomy was carried out if necessary. Endoscopic papillary balloon dilation (EPBD) using a dilator balloon (COOK) was carried out in patients who required anti-thrombotic drugs or a stricture in the pancreatobiliary system. Endoscopic mechanical lithotripsy (EML) was carried out in patients with stones more than 12 mm in dimension. Standard techniques, such as basket or extraction balloon or both were used for bile duct stone removal. Patients with pancreatobiliary stricture were biopsied during the procedure. After the procedure, stents or nasobiliary catheters were used as appropriate for duct drainage. Most of the treatments were carried out for up to 30 min after inserting an endoscope. All the patients were hospitalized before the procedure. In the postprocedure recovery period, an endoscopy nurse written the clinical observation and then patients were hospitalized for additional 72 h to assess any post-ERCP complications.

Variables investigated

Complications that occurred within 30 days after the procedure were defined as procedure related complications. Post-ERCP severities of the complications were defined according to Cotton's criteria [5], we added cardiovascular and pulmonary diseases as procedure-related complications [4]. Definitions of severe complications were as follows:

1. Pancreatitis (which required hospitalization for more than 10 d; pseudocyst, or intervention); 2. Bleeding (transfusion of 5 units or more or angiographic or surgical intervention); 3. Perforation (medical treatment for more than

Table 2. Clinic feature based on patients with or without severe complications

Background	With complications	Without complications
Age (years)	82.92 (80-84)	83.73 (80-95)
Gender (M/F) (%) male	6 (50.00)	61 (55.96)
Comorbidities, n (%)		
Diabetes mellitus	1 (8.33)	21 (19.27)
Cardiovascular disease	6 (50)	46 (42.20)
Cerebrovascular disease	5 (41.67)	19 (17.43)
Respiratory disease	2 (16.67)	11 (10.09)
Autoimmune disease	1 (8.33)	2 (1.83)
Nephropathy	0 (0)	2 (1.83)
Malignant tumor	0 (0)	4 (3.67)
Cirrhosis of the liver	0 (0)	1 (0.92)
ASA scores		
Grade 1	0 (0)	44 (28.57)
Grade 2	2 (16.67)	40 (36.70)
Grade 3	8 (66.67)	23 (21.10)
Grade 4	2 (16.67)	2 (1.83)
Grade of difficulty		
Grade 1	0 (0)	0 (0)
Grade 2	0 (0)	23 (21.10)
Grade 3	1 (8.33)	13 (11.93)
Grade 4	8 (66.67)	65 (59.63)
Grade 5	3 (25)	8 (7.34)
Diverticulum		
No	10 (83.33)	75 (73.53)
Para	1 (8.33)	26 (23.85)
Inside	1 (8.33)	8 (7.34)
Biliary duct diameter		
< 14 mm	4 (33.33)	54 (49.54)
≥ 14 mm	8 (66.67)	55 (50.46)
Benign or malignant		
Benign	7 (58.33)	84 (77.06)
ERCP procedures		
One procedure	3 (25)	69 (63.3)
Multiple procedures	9 (75)	40 (36.7)

10 d or percutaneous or surgical intervention); 4. Infection (Septic shock or surgery); 5. Cardiovascular-respiratory diseases (died from heart attack or respiratory disease).

When a patient suffered with several complications, we used the most severe complication for grading. Procedure-related death was regarded as death after a procedure with complications or incomplete endoscopic treatment within 48 h, death probably linked to the procedure was regarded as death between the second and seventh day after a procedure [4].

Factors predicting moderate to severe complications

The following factors were considered to be potentially predictive of severe complications:

1. Age; 2. Gender; 3. Chronic concomitant diseases; 4. ASA scores; 5. Grade of difficulty; 6. Diverticulum; 7. Biliary duct diameter; 8. Benign or malignant; 9. One or multiple procedures.

Elderly patients with chronic concomitant diseases have increased risk of infection, and associated with delayed recovery and subsequent multiple organ dysfunctions [6, 7]. Post-procedure complications are associated with higher American Society of Anesthesiologists (ASA) status [8], multiple comorbidities and some geriatric syndromes, which may result in a decreased capacity to cope with the intervention [4]. Comorbidities were mainly classified as follows: Diabetes mellitus, cardiovascular disease, Cerebrovascular disease (previous stroke), Respiratory diseases (chronic obstructive pulmonary disease, asthma bronchiale), Autoimmune disease, Nephropathy, Malignant tumor and Cirrhosis of the liver.

Procedural difficulty was classified for 5 degrees according to Schutzetal [9]. A successful cannulation with clearance of the stones and satisfied drainage was defined as a successful procedure. Patients who were unsuccessfully treated or incomplete extraction of bile duct stones were scheduled for a further attempt at stone clearance during hospitalization, and the times of treatment sessions were written down (repeat ERCP within one month). Number of stones and stone diameter were

Table 3. Factors for severe complications: univariate and multivariate analysis

	Univariate		Multivariate	
Background	OR (95% CI)	*P value**	OR (95% CI)	*P value**
Age (years)	0.92 (0.76, 1.13)	0.437		
Gender				
Male	1		1	
Female	1.27 (0.39, 4.19)	0.694		
Comorbidities				
Diabetes mellitus	0.38 (0.05, 3.12)	0.368	0.19 (0.01, 2.77)	0.222
Cardiovascular disease	1.37 (0.42, 4.52)	0.606	0.53 (0.10, 2.92)	0.464
Cerebro disease	3.38 (0.97, 11.81)	0.056	0.25 (0.03, 1.89)	0.177
Respiratory disease	1.78 (0.35, 9.20)	0.490	0.11 (0.01, 1.65)	0.110
Autoimmune disease	4.86 (0.41, 58.04)	0.211	14.48 (0.50, 422.80)	0.121
Nephropathy	0.00 (0.00)	0.999	0.00 (0.00)	0.999
Malignant tumor	0.00 (0.00)	0.999	0.00 (0.00)	0.999
Cirrhosis of the liver	0.00 (0.00)	1.000	0.00 (0.00)	1.000
ASA scores		0.057		0.071
Grade 1	1		1	
Grade 2	0.00 (0.00)	0.998	0.00 (0.00)	0.998
Grade 3	0.00 (0.00)	0.997	0.00 (0.00)	0.997
Grade 4	0.00 (0.00)	0.997	0.00 (0.00)	0.997
Grade of difficulty		0.471		
Grade 2	1		1	
Grade 3	0.00 (0.00)	0.998		
Grade 4	0.00 (0.00)	0.998		
Grade 5	0.00 (0.00)	0.998		
Diverticulum		0.511		
No	1		1	
Para	0.29 (0.04, 2.36)	0.247		
Inside	0.29 (0.04, 2.36)	0.954		
Biliary duct diameter				
< 14 mm	1		1	
≥ 14 mm	1.33 (0.04, 2.36)	0.648		
Benign or malignant				
Benign	1		1	
Malignant	2.07 (0.40, 4.43)	0.246		
ERCP procedures				
One procedure	1		1	
Multiple procedures	5.18 (1.32, 20.23)	0.018	3.26 (0.59, 18.06)	0.035

OR, odds ratio; 95% CI, 95% confidence interval; *Logistic regression analysis.

classified according to the presence of ≥ 2 stones, stones of ≥ 10 mm. Biliary duct diameter were classified as ≥ 14 mm or not.

Statistical analysis

The statistical analysis was conducted with SPSS 15.0 software (SPSS Inc, Chicago, IL, USA). Risk factors for severe complications were analyzed using logistic regression. Characteristics with $P < 0.2$ were included in the multivariate regression models. Risk is presented as odds ratios (ORs) with 95 per cent confidence intervals (c.i.). All test results were two-tailed, and statistical significance was defined as $P < 0.05$.

Results

Clinical presentations

Table 1 was the characteristics of 121 patients. All severe complications are summarized as below. Two patients (1.6%) experienced severe pancreatitis, and recovered with conservative treatment. Three patients (2.5%) developed cholangitis, one of them (an 82-year-old male patient) suffered severe cholangitis with septic shock, and treated with 3 times of ERCP, but died after 20 days. One patient (0.8%) experienced venous bleeding, and required hypertonic saline-epinephrine solution local injection to control the bleeding. Four patients (3.3%) who had cardiopulmonary dysfunction, three (2.5%) were died because of severe complication. Two patients (1.6%) suffered systemic infection, all were died.

Table 2 provides demographic information and clinic feature based on patients with or without severe complications.

Factors predicting moderate to severe complications: univariate and multivariate analysis

Table 3 summarizes the results of the univariate and multivariate analysis for factors predicting severe complications. The univariate logistic regression model indicated that Comorbidities (Cerebrovascular disease) (OR: 3.38, 95% CI: 0.97, 11.81, P=0.056), ASA scores (P < 0.1) and Multiple procedures (OR: 5.18, 95% CI: 1.32, 20.23, P=0.018) were associated with severe complications. Multivariate logistic regression indicated that only multiple procedures (OR: 3.26, 95% CI: 0.59, 18.05, P=0.035) were associated with severe complications.

Discussion

ERCP is currently a good method of choice to save the lives of patients with biliary and pancreatic diseases with high operative risks [6, 7, 10]. However, due to the unsuccessful remove of gallbladder stones, most patients will suffer a recovery of common bile duct stones. ERCP can remove the bile duct stones, but elderly patients because of long-term bedridden, difficulty in defecation, or loss of function of Oddi's sphincter after Endoscopic sphincterotomy (EST), resulting in biliary pneumatosis and reflux cholangitis, which can increase the risk of stone recurrence [11].

Although literatures support the safety and effective of ERCP for patients aged 80 or older [2, 3, 12], a previous study found an increased risk of complications after ERCP in patients with older age and higher ASA fitness score [4]. Older age (> 80 years) was probably related to increased severity of complications in the present study. It may be as a result of immune system competence declines with age, leading to increased risks of morbidity and mortality. Additionally, postoperative complications in older age are associated with higher American Society of Anesthesiologists (ASA) status, comorbidities, and geriatric syndromes. All may result in a decreased capacity to cope with biliary disease and intervention. Our study found that multiple procedures were associated with severe complications in elderly patients. These results indicated that therapeutic ERCP for elderly patients should based on their own characteristics and avoid multiple procedures to reduce the incidence of serious complications.

There were some limitations in our study. First, this was a retrospective design which may lead to bias. Second, this study was not a multicenter study, and all data were from our single center. Third, we did not consider the effect of operator experience. The relationship between annual ERCP volume and severe complications has been reported [4]. Our hospital might be a high-volume center with ERCP volume of over 400 procedures per year, the operator-related factors may not have been associated with severe complications in the present study.

We collected a total of 2000 cases of therapeutic ERCP in our endoscopic center in 4 years. Through data analysis, we found that old age was probably associated with the same complication rate to young patients but increased the severity. Rather, the incidence rate of elderly patients receiving 2 or more ERCP procedures were significantly higher (40.5%; **Table 1**). When clinicians respond elderly patients, multiple procedures should be avoided in order to minimize the incidence of serious complications.

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Disclosure of conflict of interest

None.

Abbreviations

ERCP, endoscopic retrograde cholangiopancreatography; ASA, american society of anesthesiologists; EPBD, endoscopic papillary balloon dilation; EML, endoscopic mechanical lithotripsy; EST, endoscopic sphincterotomy.

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