Risk Factors for Post Endoscopic Retrograde Cholangiopancreatography Cholangitis

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Background: *Cholangitis is the one of complications in post endoscopic retrograde cholangiopancreatography (post-ERCP). Few studies investigated risk factors for post-ERCP cholangitis and the results showed different outcomes.*
Objective: *The aim of the study was to determine the contributing risk factors for post-ERCP cholangitis.*
Material and Method: *The medical records of patients who underwent ERCP from January 2013 to December 2015 were retrospectively reviewed. We excluded patients who had cholangitis before ERCP. All patients received intravenous prophylaxis antibiotic before the procedure. Demographic data, interested factors and result were collected. Univariate and multivariate analysis were used to identify risk factor for post-ERCP cholangitis.*
Results: *227 patients enrolled where 204 (89.9%) of them were receiving therapeutic procedure. 156 (68.7%) patients were performed by high experience endoscopists (performing >50 ERCPs per year). The success rate was 87.7%. Post-ERCP cholangitis occurred in 20 (8.8%) patients as a result of therapeutic procedures. By univariate analysis, 8 variables were identified. They were male sex, age >60 year, no epigastric pain, albumin <2.5 gm/dL, bile duct cancer, common bile duct stones, change and remove bile duct stent. Multivariate analysis showed that age >60 year, albumin <2.5 gm/dL and remove bile duct stent were significantly associated with post-ERCP cholangitis.*
Conclusion: *Age >60 year, albumin <2.5 gm/dL and remove bile duct stent are three major risk factors for post-ERCP cholangitis.*

Keywords: *Risk factor, Post-ERCP cholangitis, Endoscopic retrograde cholangiopancreatography*

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Endoscopic retrograde cholangiopancreatography (ERCP) is used for diagnostic and therapeutic pancreaticobiliary diseases, such as common bile duct stone, bile duct tumor, pancreatic tumor or iatrogenic common bile duct injury. Nevertheless, ERCP requires high experience endoscopist and the complication rates are higher than other endoscopy procedures.

There are many serious complications followed ERCP, such aspancreatitis, cholangitis, bleeding and duodenal perforation. The high incidence of post-ERCP pancreatitis resulted in extensive studies and reportswhile other complications were not widely stated.

The incidence of cholangitis is 0.5-5%[1] and mortality rate is 4.5-8%[2,3]. There are few studies about risk factors for post-ERCP cholangitis and the results showed different outcomes. The divergent outcomes may result from small number of patients and different population and methods. Therefore, this studyintended to determine the risk factors for post-ERCP cholangitis.

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Material and Method

The medical records of patients who underwent ERCP at Her Royal Highness Princess Maha Chakri Sirindhorn Medical Center, Srinakharinwirot University from January 2013 to December 2015 were retrospectively reviewed. We excluded patients who had cholangitis before ERCP. All patients received intravenous prophylaxis antibiotic before the procedure and used general anesthesia with endotracheal tube. Our hospital had 5 endoscopists (2 high experience endoscopists). All procedures which were performed by low experience endoscopists held under the supervision of high experience endoscopists. Demographic data and factors of interest were collected. Patient-related variables were gender, age, epigastric pain, liver function test and indication for

ERCP (diagnosis by US, CT scan or MRI). Procedure-related variables were experiences of endoscopists, detail of ERCP procedures, operative time and post-ERCP cholangitis. The ERCP procedures were done with standard technique.

Definitions

Diagnostic ERCP was defined as the study of x-ray pictures obtained from injecting x-ray contrast dye into bile or pancreatic ducts for diagnosing abnormality of bile or pancreatic ducts.

Therapeutic ERCP was defined as diagnostic ERCP with additional procedure, such as sphincterotomy, stone extraction or stent placement.

Success ERCP was defined as the cannulation of the bile duct or pancreatic duct and obtaining a cholangiogram or pancreatogram[4].

Post-ERCP cholangitis was defined as clinical of right upper quadrant pain, jaundice and a body temperature >38°C for 24-48 hr after ERCP without evidence of other concomitant infections.

High experience endoscopists was defined as performing >50 ERCPs per year[5].

Statistical analysis

The sample size was calculated based on the incidence rate of post-ERCP cholangitis. The result was 10-20 participants per outcome variables. As there were 10 outcome variables in the literature reviews, therefore, the total number of sample size was 200 persons. Data are presented as mean, SD, and percent. For potential risk factors were assessed using univariate analysis with Chi-squared test for categorical variables. Variables with a *p*-value <0.05 in the univariate analysis were all included in a forward stepwise multiple logistic regression model to identify the independent risk factor for post-ERCP cholangitis. An odds ratio with a 95% confidence interval that did not include unity was considered significant. Data were analyzed using the SPSS (version 23) software (Statistical Procedures for Social Sciences; Chicago, Illinois, USA).

Results

A total of 227 patients enrolled into the study. Patient characteristics are shown in Table 1. There were more female than male and the majority of patients were presented with epigastricpain. Choledocholithiasis was the most common indication for ERCP. The other indications were gall bladder cancer, Sump's syndrome, Mirizzi's syndrome, choledochal cyst, pancreatic fistula, pancreatic stone and pancreatic pseudocyst. 68.7% of patients were performed by high experience endoscopists. The procedure was more of the therapeutic ERCP where sphincterotomy was performed the most. The procedure resulted in high success rate (87.7%). Cause of fail ERCP was the ampulla of Vater not be reached or cannulated. Post-ERCP cholangitis occurred in 20 (8.8%) patients as a result of therapeutic procedures. Eight patients died, 3 from cholangitis, 2 from hospital-acquired pneumonia, the others from urinary tract infection, multi-organ failure and pulmonary embolism.

Table 1. Demographic data (n = 227)

Variable	
Patient-related variables	
Male (%)	110 (48.4)
Age (mean ± SD, year)	58.9±17.4
Epigastric pain (%)	140 (61.7)
Jaundice; TB >2.5 mg/dL (%)	75 (33)
Alb <2.5 gm/dL (%)	14 (6.6)
Indication for ERCP	
Choledocholithiasis (%)	139 (61.2)
Bile duct cancer (%)	21 (9.25)
Post-op biliary injury (%)	21 (9.25)
Benign biliary stricture (%)	12 (5.3)
Gallstones pancreatitis (%)	11 (4.8)
Pancreatic tumor (%)	8 (3.5)
Other* (%)	15 (6.6)
Procedure-related variables	
High experience endoscopists (%)	156 (68.7)
Therapeutic ERCP procedure (%)	204 (89.9)
Biliary sphincterotomy (%)	170 (74.9)
Stone extraction (%)	95 (41.8)
1st place bile duct stent (%)	52 (22.9)
Change bile duct stent (%)	14 (6.2)
Remove bile duct stent (%)	13 (5.7)
Operative time (mean ± SD, minute)	61.1±38.2
Success ERCP (%)	199 (87.7)

* Other-gall bladder cancer, Sump's syndrome, Mirizzi's syndrome, choledochal cyst, pancreatic fistula, pancreatic stone and pancreatic pseudocyst.

Univariate analysis

In the univariate analysis, 8 variables were statistically significantly associated with a risk of post-ERCP cholangitis (Table 2). The patient-related factors included male sex, age >60 year, no epigastric pain, albumin <2.5 gm/dL, bile duct cancer and common bile duct stones. Others are procedure-related factors which consisted of change and remove bile duct stent.

Multivariate analysis

Three risk factors were found to be significant in the multivariate logistic regression analysis (Table 3). Two were characteristics of the patients (age >60 year, alb <2.5 gm/dL) and one was procedure-related (remove bile duct stent).

Discussion

The overall incidence of post-ERCP cholangitis varies in prior studies between 0.5-5%. Our study reported that post-ERCP cholangitis was 8.8%. This incidence was rather higher than the average. There could be due to lower number of ERCP cases performed each year (average of 100 patients per year). In a prospective multicenter study by Loperfido[6], they showed that small center which performed ERCP less than 200 patients per year was a risk factor in post-ERCP cholangitis.

In our study, 8 variables were statistically significantly in univariate analysis. However, in multivariate analysis, we found only 3 variables that were significant. They were age, serum albumin and remove bile duct stent. The authors' study is the first to reveal that removal of bile duct stent was a risk factor in post-ERCP cholangitis, whereas other studies demonstrated that adding of the bile duct stent contributed to cholangitis[7-9]. Removal of bile duct stent could lead to infection due to the spreading of bacteria

Table 2. Univariate analysis of risk factors for post-ERCP cholangitis

Variables	Post-ERCP cholangitis incidence (%)		
	With variable	Without variable	*p*-value
Patient-related variables			
Significant			
Male sex	14/110 (12.7%)	6/117 (5.1%)	0.044
Age >60 year	15/108 (13.9%)	5/119 (4.2%)	0.010
No epigastric pain	15/87 (17.2%)	5/140 (3.6%)	<0.001
Alb <2.5 gm/dL	6/12 (50%)	14/215 (6.5%)	<0.001
Bile duct cancer	7/21 (33.3%)	13/206 (6.3%)	<0.001
Common bile duct stones	7/139 (5.0%)	13/88 (14.7%)	0.012
Not significant			
Jaundice	10/75 (13.3%)	10/152 (6.6%)	0.091
Post-surgery biliary leakage or stricture	3/21 (14.3%)	17/206 (8.3%)	0.353
Procedure-related variables			
Significant			
Change bile duct stent	4/14 (28.5%)	16/213 (7.5%)	0.007
Remove bile duct stent	4/13 (30.7%)	16/214 (7.5%)	0.004
Not significant			
Low experience endoscopists (≤2 ERCP/week)	7/71 (9.9%)	13/156 (8.3%)	0.707
Failed ERCP	2/28 (7.1%)	18/199 (9.0%)	0.739
Biliary sphincterotomy	15/170 (8.8%)	5/57 (8.8%)	0.991
Bile duct brush cytology	1/7 (14.3%)	19/220 (8.6%)	0.604
Common bile duct stones extraction	5/95 (5.3%)	15/132 (11.4%)	0.110
1st place bile duct stent	6/52 (11.5%)	14/175 (8%)	0.429
Operative time >60 min	6/79 (7.6%)	14/148 (9.5%)	0.637

Table 3. Significant risk factors for post-ERCP cholangitis by multivariate analysis

Risk factor	Adjusted OR	95% CI	*p*-value
Age >60 year	4.85	1.37, 17.18	0.014
Alb <2.5 gm/dL	12.37	2.26, 67.72	0.004
Remove bile duct stent	11.89	2.00, 70.73	0.006

in stent during the procedure. Supported this notion, Gianfranco's study[10] showed that there was microbial colonization in polyethylene stent. Since we did not have data about hemoculture or stent culture to confirm our hypothesis regarding infection due to stent, future research is required.

Age was the risk factor for complications in ERCP. This study was similar to results shown in other previous studies[6-8,11-13]. Those studies demonstrated the younger age as a significant risk factor in post-ERCP pancreatitis. In contrast, our study show age >60 years old was a risk factor in post-ERCP cholangitis which conform with Masci's study[13] who reported age >60 years old was significant risk factor in any complications. Podnos's study[14] reported that elderly lose physiologic reserves, gaining concomitant systemic illness, resulting in worse outcome, as compared to the younger population. ERCP may induce ascending infection, leading to cholangitis in the elderly due to their poor systemic response to infection.

There was no information available about serum albumin in post-ERCP cholangitis. This study showed hypoalbuminemia (alb <2.5 gm/dL) was also a risk factor. This may be explained by malnutrition impaired cell-mediated immunity and resistance to infection[15].

Results from this study could benefit the endoscopist for reducing the risk of complications after ERCP procedure. Before ERCP, hypoalbuminemia patient should improve nutrition status. In post-operative, high risk patients; those with age more than 60 years, low level of albumin and bile duct stent removal, should be closely monitored.

The study has a limitation as the patients came from a single center, resulting in less diversity of the data and conditions. Future studies with larger samples drawn from diverse communities are needed for generalization of the results to the global population.

Conclusion

Age >60 year, albumin <2.5 gm/dL and remove bile duct stent are three major risk factors for post-ERCP cholangitis.

What is already known on this topic?

The incidence and risk factors of post-ERCP pancreatitis resulted in extensive studies and reports while other complications were not widely stated.

What this study adds?

This study determined the contributing risk factors for post-ERCP cholangitis.The results assist endoscopists to reduce the complications and modified the associated risk factors.

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Potential conflicts of interest

None.

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ปัจจัยเสี่ยงที่ทำให้เกิดภาวะติดเชื้อในท่อน้ำดีหลังจากการทำ Endoscopic retrograde cholangiopancreatography

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ภูมิหลัง: *การติดเชื้อในท่อน้ำดีเป็นหนึ่งในภาวะแทรกซ้อนหลังจากการทำ Endoscopicretrograde cholangiopancreatography (ERCP) อย่างไรก็ตาม งานวิจัยที่ศึกษาเกี่ยวกับปัจจัยเสี่ยงที่ทำให้เกิดการติดเชื้อในท่อน้ำดีหลังจากทำ ERCP มีค่อนข้างน้อย และปัจจัยเสี่ยงแต่ละงานวิจัยก็ไม่เหมือนมัน ดังนั้นทางผู้วิจัยจึงทำการศึกษาเกี่ยวกับปัจจัยเสี่ยงที่ทำให้เกิดภาวะติดเชื้อในท่อน้ำดีหลังจากการทำ ERCP*

วัสดุและวิธีการ: *เป็นการศึกษาเชิงพรรณนาโดยเก็บข้อมูลย้อนหลังจากเวชระเบียนของผู้ป่วยที่ได้ทำ ERCP ที่โรงพยาบาลศูนย์การแพทย์สมเด็จพระเทพรัตนราชสุดาฯ สยามบรมราชกุมารี มหาวิทยาลัยศรีนครินทรวิโรฒ ตั้งแต่เดือนมกราคม พ.ศ. 2556 ถึง เดือนธันวาคม พ.ศ. 2558 โดยใช้เกณฑ์คัดออกคือ ผู้ป่วยที่มีภาวะติดเชื้อในท่อน้ำดีก่อนการทำหัตถการ ผู้ป่วยทุกรายได้รับยาฆ่าเชื้อเพื่อป้องการการติดเชื้อก่อนทำหัตถการ ใช้การวิเคราะห์ข้อมูลตัวแปรตัวเดียว และการวิเคราะห์ข้อมูลพหุตัวแปรในการหาปัจจัยเสี่ยงที่ทำให้เกิดภาวะติดเชื้อในท่อน้ำดีหลังจากการทำ ERCP*

ผลการศึกษา: *มีจำนวนผู้ป่วยในการศึกษานี้ 227 ราย ผู้ป่วยที่ได้ทำ ERCP ร่วมกับการรักษาจำนวน 204 ราย (ร้อยละ 89.9) มีผู้ป่วยจำนวน 156 ราย (ร้อยละ 68.7) ทำโดยศัลยแพทย์ที่มีประสบการณ์ (ทำมากกว่า 50 รายต่อปี) มีอัตราการประสบความสำเร็จในการทำคิดเป็นร้อยละ 87.7 และพบภาวะติดเชื้อในท่อน้ำดีหลังจากการทำ ERCP จำนวน 20 ราย (ร้อยละ 8.8) โดยเป็นผลมาจากการทำ ERCP ร่วมกับการรักษา จากการวิเคราะห์ข้อมูลตัวแปรตัวเดียวพบ 8 ปัจจัย คือ เพศชาย อายุมากกว่า 60 ปี ไม่มีอาการปวดท้อง ค่า albumin น้อยกว่า 2.5 กรัมต่อเดซิลิตร มะเร็งในท่อน้ำดี นิ่วในท่อน้ำดี การเปลี่ยนและการถอด stent ในท่อน้ำดี เมื่อนำไปวิเคราะห์ข้อมูลพหุตัวแปร พบปัจจัยคือ อายุที่มากกว่า 60 ปี ค่า albumin ที่น้อยกว่า 2.5 กรัมต่อเดซิลิตร และการถอด stent ในท่อน้ำดีออก*

สรุป: *อายุที่มากกว่า 60 ปี ค่า albumin ที่น้อยกว่า 2.5 กรัมต่อเดซิลิตร และการถอด stent ในท่อน้ำดีออก เป็นปัจจัยเสี่ยงที่ทำให้เกิดภาวะติดเชื้อในท่อน้ำดีหลังจากการทำ ERCP*