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Original Article

Outcomes of Acute Cholangitis in Maharat Nakhon Ratchasima Hospital: A Retrospective Review

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Abstract

Introduction: Acute cholangitis is a common biliary tract infection which has a high mortality rate, especially in severe cholangitis. The recommended treatments are emergent or urgent biliary drainage. The therapeutic procedure of choice is endoscopic retrograde cholangiopancreatography (ERCP). The second choice is percutaneous biliary drainage (PTBD) and surgical biliary decompression. Due to the limited resources for ERCP and radiologists that may perform PTBD in the Maharat Nakhon Ratchasima Hospital (MNRH), the aim of this study was to review the outcomes of cholangitis treatment and factors associated to mortality in MNRH.

Meterials and Methods: This study reviewed medical records of all patients who were newly diagnosed with acute cholangitis at Maharat Nakhon Ratchasima Hospital between January 1st, 2017 and December 31st, 2017. Logistic regression was used to analyze factors associated with mortality and effect size was reported as odds ratio with 95% confidence interval. A *p*-value less than 0.05 was considered as statistically significant.

Results: The medical records review of 250 acute cholangitis patients indicated that the overall mortality was 11.2% (almost all of whom had severe acute cholangitis). The overall mortality rates of patients who were treated by minimally invasive biliary drainage, antibiotics alone, or open surgical drainage were 4.6%, 10.7% and 31.6% respectively. Independent factors associated with mortality were severe acute cholangitis (OR= 61.20; 95% CI: 7.84 to 478; $p < 0.01$), surgical drainage (OR= 6.60; 95% CI 1.30 to 33.48; $p = 0.02$), and non-stone etiology (OR= 4.07; 95% CI 1.28 to 12.94; $p = 0.02$).

Conclusion: Minimally invasive biliary drainage should be a procedure of choice for biliary drainage in acute cholangitis due to its lower mortality compared to open surgical drainage. Open surgical drainage should be reserved when other preferred methods are not available.

Keyword: Cholangitis

Introduction

Acute cholangitis is a common disease and usually diagnosed by clinical characteristics described as Charcot's triad of fever, right upper quadrant abdominal pain, and jaundice. In severe cases, patients have additional clinical symptoms of an altered mental status and hemodynamic instability, known as Reynold's pentad[1]. Although Charcot's triad has high specificity, it has low sensitivity to diagnose cholangitis[2]. Currently, the diagnostic criteria for the management of acute cholangitis is described in the Tokyo Guideline of 2018 (TG18) and was proposed during an international consensus meeting.

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According to the TG18, patients with cholangitis should be classified into mild, moderate, and severe acute cholangitis[3]. In mild acute cholangitis, biliary drainage is needed if the patient does not respond to initial antibiotics treatment. For moderate and severe acute cholangitis, urgent or emergent endoscopic biliary drainage (EBD) or percutaneous transhepatic biliary drainage (PTBD) is necessary along with antibiotics treatment and organ function support[3]. Open surgical biliary drainage is associated with higher morbidity and mortality when compared with endoscopic or percutaneous biliary drainage. Therefore, open surgical drainage is performed less often.

At Maharat Nakhon Ratchasima hospital (MNRH), however, endoscopic biliary drainage was available for only 2 days a week and only one radiointerventionist was available who could perform PTBD during the weekdays. Therefore, most urgent biliary drainages were surgical drainages or PTBD performed by a surgeon. These circumstances may have had an influence on mortality and the outcome of treatment compared to what is reported in other studies. This study aims to review types of treatments, mortality rate, and factors associated with mortality.

Meterials and Methods

After recieving approval by the institutional review board of MNRH, medical records of all patients over 18 years of age, who were newly diagnosed with acute cholangitis using ICD-10 code K803 and K830 in the MNRH department of surgery during January 1st, 2017 to December 31st, 2017 were reviewed. Diagnosis and severity classification using diagnostic criteria and severity classification of cholangitis according to TG18 were used. Patients were included if they were 18-years or older, and had suspected or definite diagnosis of acute cholangitis according to TG18. Patients who were diagnosed with cholangitis prior to the study period were excluded. The patient's age, sex, etiology of acute cholangitis, severity of cholangitis, treatment methods, underlying diseases, and discharge status were reviewed. Mortality in this study was in-hospital mortality which was defined by the patient's status at discharge.

Endoscopic biliary drainage was performed using side viewing endoscope. Anesthetic procedure included sedation with Midazolam and Pethidine or general anesthesia depending on the patient's condition. Ten-centimeter biliary stents of 7 F or 10 F were used as needed. Endoscopic sphincterotomy was not done in severe cholangitis. Common bile duct stones were removed by balloon extraction in some patients if appropriate. Percutaneous transhepatic biliary drainage (PTBD) was done by the surgeon or radiointerventionist under ultrasound guidance. The procedure was performed under local anesthesia or under general anesthesia as appropriate. An 8-10 F pigtail drainage catheter was used as external biliary drainage catheter. Both these procedures were referred to as minimally invasive biliary drainage (MIBD).

Surgical drainage was performed via a right subcostal incision. Bile was drained using a T-tube via a choledochotomy. A cholecystectomy was also performed on some patients as appropriate. Intraoperative T-tube cholangiography and choledochoscopy were not routinely performed. Common bile duct stones were removed only if they were seen at the choledochotomy site.

Organ failure/dysfunction was defined for separate organs. Cardiovascular dysfunction was defined as a systolic blood pressure < 90 mmHg or requiring the use of norepinephrine or dopamine to keep the blood pressure normalized. Neurological dysfunction was defined as a disturbance of consciousness. Respiratory dysfunction was defined as a PaO2/FiO2 ratio < 300, or the need for endotracheal tube (ETT) intubation due to respiratory failure if PaO2/FiO2 ratio was not recorded. Renal dysfunction was defined as a serum creatinine level > 2.0 mg/dL. Hepatic dysfunction was defined as a PT-INR > 1.50. Hematological dysfunction was defined as a platelet count < 100,000mm^3. Acute cholangitis patients with at least one organ dysfunction were categorized as having severe cholangitis.

The R studio program was for statistical analysis in the present study. The mean and standard deviation or median and interquartile range were used to summarize continuous data with as appropriate. Proportion and percentage were used to summarize categorical data. Comparison between 2 groups of continuous data was done through an independent t-test or Wilcoxon rank sum test where appropriate. Comparison of categorical data was done by Chi-squared test or Fisher's exact test where appropriate. Univariate logistic regression was used to analyze factors associated with mortality and effect size was reported as a crude odds ratio with a 95% confidence interval. Factors that have a *p*-value < 0.2 in univariate logistic regression will stay in the

multivariate logistic regression model to analyze their association with mortality and the adjusted odds ratio with 95% confidence interval was reported. A *p*-value of less than 0.05 was considered statistically significant.

Results

From January 1st, 2017 to December 31st, 2017, there were 250 patients diagnosed with acute cholangitis and 28 (11.2%) of whom died during hospital admission. The mean age of patients was 66.8 years. The most common comorbid diseases were hypertension (HT) and diabetes mellitus (DM). Of the 250 patients with acute cholangitis, 88 (36%) were diagnoses with severe cholangitis. Approximately 70% of patients were referred from other hospitals. The mortality rates for patients undergoing MIBD, given antibiotics only, and who underwent open surgical biliary drainage were 4.6%, 10.7% and 31.6%. respectively.

The most common cause of acute cholangitis was biliary tract stones (63.2%). Other causes included malignant obstruction and benign biliary stricture. Treatment was categorized into 3 groups: 1) antibiotics alone, 2) minimally invasive biliary drainage (MIBD), which included endoscopic biliary drainage (EBD) or percutaneous transhepatic biliary drainage (PTBD), and 3) open surgical biliary drainage, which included T-tube insertion with or without cholecystectomy. Patient characteristics are shown in Table 1.

Of the 250 patients, 25.2% (63 of 250) received biliary drainage through either MIBD or open surgery.

Table 1 Patient characteristics (n = 250)

Characteristics	Alive (n=222) Summary n (%)	Dead (n=28) Summary n (%)	*p*-value
Women	109 (49.09)	12 (42.85)	0.67
Age, years: mean (SD)	66.51 (16.91)	69.18 (14.74)	0.38
Comorbidity			
Diabetic Mellitus	38 (17.17)	7 (25)	0.45
Hypertension	77 (34.68)	14 (50)	0.17
Chronic kidney disease	15 (6.76)	6 (21.43)	0.02
Ischemic heart disease	19 (8.56)	6 (21.43)	0.04
Organ failure/dysfunction			
Cardiovascular	25 (11.26)	16 (57.14)	< 0.01
Neurological	14 (6.31)	19 (67.86)	< 0.01
Renal	22 (9.91)	12 (42.86)	< 0.01
Respiratory	27 (12.16)	20 (71.43)	< 0.01
Hepatic	23 (10.36)	17 (60.14)	< 0.01
Hematologic	13 (5.86)	4 (14.29)	0.11
Severity			< 0.01
Mild	19 (8.56)	0	
Moderate	142 (63.96)	1 (3.57)	
Severe	61 (27.48)	27 (96.43)	
Cause of acute cholangitis			0.01
Stone	146 (65.77)	12 (42.86)	
Malignancy	37 (16.67)	9 (32.14)	
Benign stricture	14 (6.31)	0	
Other	25 (11.26)	7 (25)	
Treatment of acute cholangitis			0.07
Antibiotics alone	167 (75.23)	20 (71.43)	
Minimally invasive biliary drainage	42 (18.92)	2 (7.14)	
Surgical drainage	13 (5.86)	6 (21.43)	
Referred from other hospital (%)	157 (70.72)	21 (75)	0.80

There were 44 (17.6%) patients treated by MIBD (38 were EBD and 6 were PTBD). Surgical drainage was performed in 19 patients (7.6%): 2 for mild cholangitis, 8 for moderate cholangitis, and 9 for severe cholangitis. Sixteen of these patients also had an additional cholecystectomy. For the 88 patients in the severe cholangitis group, 65 (73.9%) were treated by ATB alone, 14 (15.9%) by MIBD, and 9 (10.2%) by surgical biliary drainage. The mortality rate of severe cholangitis for those treated by ATB alone, MIBD, and surgical drainage were 30.3%, 14.3%, and 55.6%, respectively.

The results of univariable and multivariable logistic regression analysis are shown in Tables 2 and 3. Independent factors associated with mortality included severe cholangitis, OR, 61.20 (95% CI 7.84 to 478), surgical drainage, OR, 6.60 (95% CI 1.30 to 33.48), and non-stone etiology, OR, 4.07 (95% CI 1.28 to 12.94).

Discussion

Before the endoscopic era, treatment of acute cholangitis was either with antibiotics alone or with open surgical biliary drainage. Treatment with antibiotics only was associated with a high mortality, which was occasionally up to 100%[4,5]. Surgical treatment also had a high mortality rate that ranged between 6.5% to 40%[4,6–8]. A randomized controlled trial in 1992 demonstrated that patients who underwent endoscopic drainage had significantly lower morbidity and mortality compared to the surgery group[9]. Since then, endoscopic biliary drainage has played a major role in the treatment of acute cholangitis. However, in the MNRH surgery department endoscopic or percutaneous biliary drainage was not available twenty four hours a day, or even seven days a week. This study gave a slightly different picture of cholangitis treatment and outcomes.

In the present study, the overall mortality rate of cholangitis was 11.2%. Almost all deaths were in patients with severe acute cholangitis. The mortality rates by severity were 0%, 0.7% and 30.7% in mild, moderate and severe cholangitis, respectively. The most common

Table 2 Univariable analysis of factors associated with mortality

Factors	Crude OR (95% CI)	*p*-value
Sex (female VS male)	0.78 (0.35, 1.72)	0.53
Age	1.01 (0.99, 1.04)	0.42
Diabetic mellitus	1.61 (0.64, 4.07)	0.33
Hypertension	1.88 (0.85, 4.15)	0.12
Chronic kidney disease	3.76 (1.33, 10.69)	0.02
Ischemic heart disease	2.91 (12.05, 8.06)	0.05
Severe cholangitis	66.66 (8.87, 500.73)	< 0.01
Etiology of cholangitis (stone VS non-stone)	0.39 (0.18, 0.87)	0.02
Referred from other hospital	1.24 (0.5, 3.06)	0.63
Treatment (ATB only as reference category)		0.02
- MIBD	0.4 (0.09, 1.77)	0.23
- Srgicak drainage	3.85 (1.32, 11.27)	0.01

Table 3 Multivariable analysis of factors associated with mortality

Factors	Adjusted OR (95% CI)	*p*-value
Hypertension	2.61 (0.85, 7.96)	0.09
Chronic kidney disease	1.68 (0.46, 6.13)	0.43
Ischemic heart disease	3.23 (0.75, 13.92)	0.12
Severe cholangitis	61.20 (7.84, 477.92)	< 0.01
Non-stone etiology of cholangitis	4.07 (1.28, 12.94)	0.02
Treatment (ATB only as reference category)		
- MIBD	1.00 (0.18, 5.63)	0.99
- Surgical drainage	6.60 (1.30, 33.48)	0.02

cause of cholangitis was biliary tract stones, which was consistent with other studies[10,11]. The mortality according to the treatment methods was highest in the surgical drainage group, followed by antibiotics only group and MIBD group respectively. Independent factors associated with the mortality included severe cholangitis, non-stone etiologies, and open surgical drainage.

The overall mortality rate in the present study was slightly higher than that of other studies, which ranged between 2.7% and 10%[12–17], and almost all of the mortality cases had severe cholangitis (96.4%). The 30.7% mortality rate in severe cholangitis is significantly higher than that seen in a large international multi-center retrospective observational study in Japan and Taiwan, which reported the overall mortality rate in severe cholangitis to be 8.4%[11]. This was probably due to the limitations in our institute, which is the relative unavailability of EBD or PTBD. In severe cholangitis urgent EBD or PTBD should be performed as soon as the patient's condition permits[3]. But in our setting, surgical drainage was usually the only choice for urgent biliary drainage. The limited resources also explained the reason why only 17.6% of patietns were treated by EBD or PTBD.

Nineteen out of 250 cholangitis patients were treated by surgical drainage and the mortality rate was 31.6%. Choledochotomy with T-tube insertion without cholecystectomy or any attempt to remove common bile duct stones has been the procedure recommended[8,18]. In the present study cholecystectomy was added to almost all the operations. This may increase operative time, which may also resulted in the increase in morbidity and mortality.

The present study showed a high proportion of ATB only treatment (74.7%) which had an overall mortality of 10.7%. In patients with severe cholangitis who received ATB only, the mortality increased to nearly 30%. The high proportion of ATB only treatment was mainly because of the limited availability of EBD or PTBD, and also the patients' refusal to undergo surgery. The mortality rate of patients with severe acute cholangitis in the surgical group seemed to be higher than that in the ATB alone group. This may be because we recorded only in-hospital mortality. Patients in the ATB alone group who were discharged alive were not only those recovered from illness, but also those who refused biliary drainage and were subsequently referred to continue antibiotics back at the community hospital, where the final outcome was unknown.

Our study had several limitations. First, this was a retrospective observation study and accuracy of data was limited. Second, the outcome measure of the study was in-hospital mortality rate. Therefore, the actual mortality of severe cholangitis in the ATB alone group may be higher. The 30-day mortality may reflect a more accurate mortality rate.

Conclusion

Acute cholangitis is a common disease that is associated with high mortality, especially in severe acute cholangitis patients who did not received biliary drainage. Minimally invasive biliary drainage should be the treatment of choice. Due to the limited availability of ERCP or PTBD, surgeons may be needed to perform urgent PTBD. Surgical drainage should be used when other options of urgent biliary drainage are not available. The mortality rate of ATB alone treatment in the present study may have been underestimated.

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บทคัดย่อ

ผลการรักษาโรคท่อน้ำดีอักเสบเฉียบพลันในโรงพยาบาลมหาราชนครราชสีมา

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ความเป็นมา: ภาวะท่อน้ำดีอักเสบฉียบพลันเป็นการติดเชื้อที่มีอัตราการเสียชีวิตสูงโดยฉพาะในรายที่มีอาการรุนแรง การรักษาที่แนะนำคือการระบายน้ำดีที่ติดเชื้อฉุกเฉินหรือเร่งด่วนโดยการส่องกล้องทางเดินน้ำดี, การเจาะระบายน้ำดีผ่านตับ และสุดท้ายคือการผ่าตัดเปิดท่อน้ำดี โรงพยาบาลมหาราชนครราชสีมามีข้อจำกัดในการทำการส่องกล้องทางเดินน้ำดี และการเจาะระบายท่อน้ำดีผ่านตับในเวลาฉุกเฉิน การศึกษานี้มีวัตถุประสงค์เพื่อศึกษาผลการรักษา และปัจจัยที่เกี่ยวกับการเสียชีวิตของภาวะท่อน้ำดีอักเสียบเฉียบพลันในโรงพยาบาลมหาราชนครราชสีมา

วัสดุและวิธีการ: ศึกษาเวชระเบียนย้อนหลังของผู้ป่วยภาวะท่อน้ำดีอักเสบเฉียบพลันที่ได้รับการรักษาที่โรงพยาบาลมหาราชนครราชสีมาตั้งแต่วันที่ 1 มกราคม ถึง 31 ธันวาคม 2560 โดยศึกษาข้อมูลทั่วไป ความรุนแรงของภาวะท่อน้ำดีอักเสบ วิธีการรักษา และสถานะผู้ป่วยเมื่อสิ้นสุดการรักษา และวิเคราะห์ปัจจัยที่เกี่ยวข้องกับการเสียชีวิตด้วยการวิเคราะห์ถดถอยลอจิสติก และรายงานเป็นช่วงความเชื่อมั่น 95%

ผลการศึกษา: มีเวชระเบียนผู้ป่วยที่ได้รับการวินิจฉัยภาวะท่อน้ำดีอักเสบเฉียบพลัน 250 ราย อัตราการเสียชีวิตร้อยละ 11.2 โดยผู้ป่วยที่เสียชีวิตเกือบทั้งหมดเป็นกลุ่มที่มีอาการรุนแรง อัตราการเสียชีวิตแบ่งตามวิธีการรักษาด้วยการระบายท่อน้ำดีโดยการส่องกล้องหรือระบายท่อน้ำดีผ่านตับ, การให้ยาปฏิชีวนะอย่างเดียว และการผ่าตัดแบบเปิด เท่ากับร้อยละ 4.6, 10.7, และ 31.6 ตามลำดับ ปัจจัยที่มีผลต่อการเสียชีวิตคือ ภาวะท่อน้ำดีอักเสบเฉียบพลันรุนแรง (OR= 61.20; 95% CI 7.84 to 478; $p < 0.01$), การผ่าตัดเพื่อระบายน้ำดี (OR= 6.60; 95% CI 1.30 to 33.48; $p = 0.02$) และการอุดตันที่ไม่ได้เกิดจากนิ่วในทางเดินน้ำดี (OR= 4.07; 95% CI 1.28 to 12.94; $p = 0.02$)

สรุปผลการศึกษา: การระบายน้ำดีโดยวิธีการส่องกล้อง หรือเจาะระบายน้ำดีผ่านตับควรเป็นการรักษาหลักในภาวะท่อน้ำดีอักเสบ เนื่องจากมีอัตราการเสียชีวิตน้อยกว่าการผ่าตัดเพื่อระบายน้ำดี ซึ่งการผ่าตัดแบบเปิดควรเลือกใช้เมื่อไม่สามารถรักษาด้วยวิธีการอื่นได้