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***Retrospective Study***

**Efficacy and safety of emergency endoscopic retrograde cholangiopancreatography for acute cholangitis in the elderly**

Tohda G *et al*. Emergency ERCP for severe acute cholangitis

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**Abstract**

**AIM:** To investigate the efficacy and safety of emergency endoscopic retrograde cholangiopancreatography (ERCP) in elderly patients with acute cholangitis.

**METHODS:** From June 2008 to May 2016, emergency ERCPs were performed in 207 cases of acute cholangitis at our institution. Patients were classified as elderly if they were aged 80 years and older (*n =* 102); controls were under the age of 80 years (*n =* 105). The patients’ medical records were retrospectively reviewed for comorbidities, laboratory data, etiology of cholangitis (presence of biliary stones, biliary stricture and malignancy), details of the ERCP (therapeutic approaches, technical success rates, procedure duration), ERCP-related complications and mortality.

**RESULTS:** The frequency of comorbidities was higher in the elderly group than the control group (91.2% *vs* 67.6%). Periampullary diverticulum was observed in the elderly group at a higher frequency than the control group (24.5% *vs* 13.3%). Between the groups, there was no significant difference in the technical success rates (95.1% *vs* 95.2%) or endoscopic procedure durations. With regard to the frequency of ERCP-related complications, there was no significant difference between the two groups (6.9% *vs* 6.7%), except for a lower rate of post-ERCP pancreatitis in the elderly group than in the control group (1.0% *vs* 3.8%). Neither angiographic nor surgical intervention was required in any of the cases with ERCP-related complications. There was no mortality during the observational periods.

**CONCLUSION:** Emergency ERCP for acute cholangitis can be performed safely even in elderly patients aged 80 years and older.

**Key words:** Endoscopic retrograde cholangiopancreatography; Acute cholangitis; Elderly; Complication; Comorbidity

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**Core tip:** We retrospectively evaluated the efficacy and safety of emergency endoscopic retrograde cholangiopancreatography (ERCP) in elderly patients with acute cholangitis. Patients who have undergone emergency ERCPs were classified as elderly group aged 80 years and older (*n =* 102) or controls under the age of 80 years (*n =* 105). The frequency of comorbidities was higher in the elderly group than the control group. However, there was no significant difference in the technical success rates, endoscopic procedure durations and ERCP-related complications between the two groups. There was no mortality during the observational periods. Emergency ERCP for acute cholangitis can be performed safely even in elderly patients.

Tohda G, Ohtani M, Dochin M. Efficacy and safety of emergency endoscopic retrograde cholangiopancreatography for acute cholangitis in the elderly. *World J Gastroenterol* 2016; In press

**INTRODUCTION**

With the increase in life expectancy, pancreatic and biliary diseases have become common problems in the elderly. Endoscopic retrograde cholangiopancreatography (ERCP) has been established as an alternative treatment to surgery for patients with high operative risk[1]. However, ERCP also has higher rates of adverse events compared with the other types of gastrointestinal endoscopic procedures[2]. Complications of ERCP include pancreatitis, hemorrhage, perforation, cholangitis and cardiorespiratory problems[3]. Although previous studies have shown that ERCP can be safe and well tolerated even in the elderly[4-24], the management of elderly patients with acute cholangitis presents certain risks for endoscopists. These risks are attributable not only to acute cholangitis itself but also to the risks associated with the overall health of the patient and their concomitant medical disorders. The general state of a patient’s health plays an important role in determining the outcome of any invasive treatments. However, in cases of acute cholangitis, interventional ERCP is often required as an emergency procedure, so it is difficult to evaluate the patient’s overall clinical condition before the procedure. Because of various risks, there is a tendency for patients, family members and even physicians to adopt a conservative approach and avoid therapeutic ERCP for these cases. Because few studies have focused on the outcomes of emergency ERCP in elderly patients with acute cholangitis[22], we retrospectively evaluated the safety and efficacy of emergency ERCP for patients aged 80 years and older who presented with acute cholangitis.

**MATERIALS AND METHODS**

***Study design***

This was a retrospective review of patients with acute cholangitis at a single hospital. From June 2008 to May 2016, 207 cases of emergency ERCP were performed for acute cholangitis at our institution. Of these, 102 patients who were 80 years of age or above were classified into the elderly group, while 105 patients who were below the age of 80 years were classified as the control group. After obtaining ethical approval from the Institutional Review Board at our hospital, we conducted a retrospective review of medical records of patients who underwent emergency ERCP for acute cholangitis. Demographic characteristics, medical history (specifically comorbidities), clinical features, laboratory data, ERCP findings (*i.e*., periampullary diverticulum, presence of biliary stones, benign biliary stricture and malignant obstruction), details of ERCP procedures (*i.e*., therapeutic approaches, technical success rates, procedure duration), ERCP-related complications and mortality were evaluated. All of the patients involved in this study underwent emergency ERCP within 24 h of admission.

***Definition***

Acute cholangitis was diagnosed as clinical symptoms characterized by a fever, jaundice, and abdominal pain that thought to be a result of cholestasis and bacterial infection in the biliary tract. Laboratory data indicative of the presence of inflammation (*e.g.*, leukocytosis), biliary obstruction (*e.g.*, hyperbilirubinemia, elevation of biliary and liver enzymes), and imaging findings supporting the evidence of inflammation and biliary obstruction were also used for a more accurate diagnosis of acute cholangitis. Severity of acute cholangitis can range from mild to serious life-threatening levels. We classified acute cholangitis into three grades; mild (grade I), moderate (grade II), and severe (grade III), in accordance with the Tokyo Guidelines[25], which have since been widely used all over the world as the diagnostic criteria and a severity assessment of acute cholangitis. We performed emergency endoscopic biliary drainage in cases of severe acute cholangitis with at least one of the following conditions: either (1) shock; (2) mental confusion; or (3) a coagulation defect that was not attributable to the use of anticoagulants.

The presence of comorbidity was defined as the presence of one or more of the following conditions; hypertension, ischemic heart disease, chronic heart failure, arrhythmia, cerebrovascular disease, diabetes mellitus, chronic liver disease, chronic pulmonary disease, chronic renal failure, or malignancy. ERCP-related complications were defined according to the previously published criteria[3]. Bleeding after endoscopic sphincterotomy (EST) was classified into two types: (1) minor bleeding, defined as controllable by endoscopic hemostasis and no need for blood transfusion; or (2) major bleeding, defined as bleeding requiring a blood transfusion and/or angiographic or surgical intervention to control the hemorrhage. Post-ERCP pancreatitis was defined as abdominal pain with a concurrent rise in the serum amylase level after the endoscopic procedure. The primary aim of this study was to evaluate the safety and efficacy of emergency ERCP in patients with acute cholangitis. Therefore, we reviewed the data on these patients over a period of 30 d post-admission. Technical success of interventional ERCP was defined as the achievement of endoscopic biliary drainage with or without stone removal.

***Endoscopic procedure***

Before performing ERCP, informed consent was obtained from each patient and/or caregiver. All endoscopic procedures were performed by experienced endoscopists who had performed more than 500 cases of therapeutic ERCP with more than 15 years of experience. Moderate sedation was administered by gastroenterologists by giving intravenous injections of midazolam and pethidine hydrochloride. All of the patients underwent continuous monitoring by electrocardiogram and pulse oximetry and received 2 L/min of oxygen through a nasal cannula throughout the endoscopic procedure. During the procedure, the following events were considered cardiorespiratory suppression associated with sedation: (1) a decline in SpO2 to less than 90%; (2) heart rate less than 45 beats per min; or (3) systolic blood pressure below 80 mmHg. In case of EST, an electrosurgical generator with an automatic controlled cutout system (Endocut mode) was used. Plastic type biliary stents (7 Fr diameter) were routinely used for biliary drainage during the initial ERCP. To remove residual biliary stones, follow up ERCP was performed depending on each patient’s specific needs and medical condition.

***Statistical analysis***

We have confirmed that the sample size of each group in this study is sufficient in size to make a definite conclusion using power calculations. Various parameters were compared between the elderly and control groups. Continuous variables with normal distributions were compared by the two-sample *t*-test. The Mann-Whitney *U* test was used for the comparison of continuous variables with skewed distributions. The chi-square test or Fisher’s exact test was used for categorical variables as appropriate. *P* values of 0.05 or less were considered statistically significant. All statistical analyses were performed using the EZR[26] (Saitama Medical Center, Jichi Medical University, Saitama, Japan, version 1.32), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria). More precisely, it is a modified version of R commander that was designed to add statistical functions frequently used in biostatistics.

**RESULT**

The clinical data of the patients involved in this study are presented in Table 1. Between the elderly and control groups, patients in the elderly group showed a significantly lower level of serum albumin and platelet, a higher level of aspartate transaminase (AST), and a higher stage of American Society of Anesthesiology (ASA) classification. With regard to the presence of comorbidities (Table 2), the elderly group had a significantly higher prevalence of hypertension, ischemic heart disease, cerebrovascular disease, dementia, chronic obstructive pulmonary disease, and malignancy other than a primary biliary and pancreatic lesion. Periampullary diverticulum was also highly observed in the elderly group. The etiology of each case of acute cholangitis is shown in Table 3. In both groups, common bile stones were the most frequent etiology of acute cholangitis. The frequency of malignant obstruction was significantly higher in the elderly group than the control group.

Procedural details of the therapeutic ERCPs are described in Table 4. Endoscopic biliary drainage by insertion of a biliary stent was successful in 95.1% of elderly patients and 95.2% of control patients. Between the groups, there was no significant difference in the endoscopic procedure durations. Second ERCPs were performed approximately 1 wk after the initial ERCP in 87.3% (89 out of 102 cases) of elderly patients and 97.1% (102 out of 105 cases) of control patients. EST was carried out in 67.6% of the elderly group and 82.9% of the control group. For cases with a prior intake of Warfarin, vitamin K was given to the patients before EST. Complete clearance of biliary stones was achieved in 81.5% of the elderly group and in 93.1% of the control group.

The frequency of ERCP-related complications was 6.9% in the elderly group, while it was 6.7% in the control group (Table 5). There was no significant difference between the two groups, except for a lower rate of post-ERCP pancreatitis in the elderly group. All cases of bleeding from the EST site were mild, and neither blood transfusion nor angiographic/surgical intervention was required in any of the reviewed cases. In this study, all of the ERCP-related complications were mild and none of the patients required surgical intervention. During the procedures, a few cases of cardiorespiratory suppression related to sedation were observed (Table 6). All patients with hypoxemia responded immediately to an increase in concentration of administered oxygen (5 L/min). Hypotension and bradycardia were also corrected immediately using intravenous saline solution or atropine injections. Finally, no patient required mask ventilation, endotracheal intubation, or any resuscitative treatment. The frequency of cardiorespiratory suppression during the procedures was similar between the elderly and control groups.

Transient aggravation of cholangitis was observed in 3 cases of patients who underwent endoscopic biliary drainage. However, these patients gradually recovered after the endoscopic procedure. Ten patients with unsuccessful endoscopic biliary drainage received percutaneous transhepatic biliary drainage (PTCD) as an alternative treatment. Finally, all cases with septic condition by severe acute cholangitis achieved source control *via* endoscopic biliary drainage (*n =* 197) or PTCD (*n =* 10), and procedure-related mortality was not observed in either group. The median duration of hospitalization periods was significantly longer in the elderly group than in the control group (20 d *vs* 15 d) because many elderly patients required rehabilitation periods for improvement of their overall health and other conditions.

**DISCUSSION**

With the progressive increase in the elderly population, the frequency of pancreatic and biliary diseases has increased. Among this population, bile duct stones often cause clinical problems, such as acute cholangitis. Because of the increasing degree of morbidity that accompanies the aging process, urgent treatments are required for elderly patients with severe infectious conditions. Elderly patients with acute cholangitis are sometimes critically ill, so emergency interventions are necessary. However, physicians and patients’ family members tend to be reluctant to consent to surgical treatments because elderly patients can be at a higher risk of developing complications from surgical procedures. ERCP is an established procedure for pancreatic and biliary diseases. With a rise in life expectancy, the demand for ERCP in the elderly has been increasing. It has been reported that the rates of ERCP-related complications or mortality in the elderly are comparable with those of younger patients[4-24], but there are few reports of emergency ERCP for elderly patients with acute cholangitis[22]. The primary aim of this study was to evaluate the outcomes of emergency ERCP in the elderly with acute cholangitis.

In this study, we performed aggressive endoscopic approaches for elderly patients with acute cholangitis. They received urgent biliary drainage by an endoscopic biliary stent insertion, and the removal of bile duct stones with EST was considered in accordance with the patients’ general conditions. Biliary drainage with complete stone removal at the time of the first procedure is desirable for patients. However, such an interventional approach is not feasible in all cases, often due to severe biliary infection and/or coagulopathy. In this study, biliary drainage by stent insertion with or without EST was performed as an initial treatment, and repeat ERCPs for the extraction of residual biliary stones were considered as indicated when the patients’ clinical conditions were improved. As a result, the ERCP-related complication rate in our study was comparable with that of previous studies, even in elderly patients with serious condition by acute cholangitis.

Several studies have shown that there is no relationship between coexisting medical conditions and ERCP-related complications[27], except for cases with underlying liver cirrhosis[28]. Other studies have reported that an elderly age with concomitant medical illness is associated with a higher mortality in cases of acute cholangitis[29]. In this study, complication rates of ERCP in the elderly group was similar to those of previous reports[4-24], and there was no relationship between comorbidities and ERCP-related complications. It has also been reported that the risk of sedation-related adverse events during ERCP increases in the elderly[6,7]. However, our study showed that there was no difference in the frequency of cardiorespiratory suppression between the elderly and control groups because we use fewer sedative agents with lower initial and cumulative doses in the elderly groups.

In our institution, all cases of emergency ERCP were carried out by two endoscopists who had previously performed more than 500 cases of therapeutic ERCPs. During the study period, which spanned 8 years, endoscopists used different types of ERCP devices. However, we believe that a bias caused by endoscopic accessories, including a catheter and guidewire, would be negligibly small. Before reviewing the data retrospectively, we estimated that technical success rate of ERCP in the elderly population would be less than that in younger patients due to anatomical factors, such as the presence of periampullary diverticulum and/or difficult bile duct stones with impaction. However, there was no statistically differences in the technical success rate of ERCP between the elderly and control groups.

In conclusion, emergency ERCP for acute cholangitis is a safe and effective procedure in elderly patients over 80 years of age. Advanced age is not a contraindication to ERCP, even in cases with acute cholangitis. To perform urgent ERCP safely in these cases, informed consent, adequate monitoring during the procedure, prompt detection and management of ERCP-related complications are crucial. We believe that our study can be informative in deciding whether ERCP is the best treatment in elderly patients with acute cholangitis. These results can be utilized in discussions with patients and their families through the informed consent process. The primary aim of this study was to evaluate the outcomes of emergency ERCP for elderly patients with acute cholangitis. Therefore, all patient data were reviewed for short observational periods of 30 d. Due to this limitation, the low complication rates observed in this study may not hold true because patients could have had more late complications that were not captured in our study. Prospective studies with long-term follow-up periods will be required to confirm the efficacy and safety of emergency ERCP in elderly patients with acute cholangitis.

**COMMENTS**

***Background***

Previous studies have shown that endoscopic retrograde cholangiopancreatography (ERCP) can be safe and well tolerated, even in the elderly. However, the management of elderly patients with acute cholangitis presents certain risks, which are attributable not only to acute cholangitis itself but also to the risks associated with patients’ overall health conditions. Therefore, there is a limited data on the outcome of emergency ERCP in elderly patients with acute cholangitis.

***Research frontiers***

Prior reports described interventional ERCPs as a useful tool for the treatment of biliary diseases. However, only few prior reports evaluated the emergency ERCP for acute cholangitis in the elderly because of high-risks. This study contributes to clarify the efficacy and safety of emergency ERCP for severe acute cholangitis especially in the elderly.

***Innovations and breakthroughs***

Severe acute cholangitis is a potentially life-threatening condition, and biliary drainage should be considered as soon as possible to improve the general condition of patients. In this study, emergency ERCP for acute cholangitis could be performed safely even in the elderly, and all cases receiving interventional ERCPs were improved. The results presented emphasize the efficacy and safety of emergency ERCP for severe acute cholangitis even in the elderly patients.

***Applications***

This study suggests that emergency interventional ERCP could be a less-invasive and effective treatment for acute cholangitis even in elderly patients in spite of their high frequency of concomitant medical disorders.

***Terminology***

Interventional ERCP: endoscopic treatments such as a biliary drainage by stent insertion, endoscopic sphincterotomy with or without stone removal.

***Peer-review***

The author of this paper evaluated that emergency ERCP could be performed safely for severe acute cholangitis even in the elderly. Further clinical trials in a large population will be valuable.

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Grade A (Excellent): 0

Grade B (Very good): B, B, B

Grade C (Good): 0

Grade D (Fair): 0

Grade E (Poor): 0

Table 1 Clinical characteristics and laboratory data of enrolled patients

|  |  |  |  |
| --- | --- | --- | --- |
|  | Age ≥ 80 years  (*n =* 102) | Age < 80 years  (*n =* 105) | *P* value |
| Age (yr) | 85 (81-92) | 67 (58-75) | < 0.05 |
| Sex |  |  |  |
| Male | 41 (40.2) | 62 (59.0) | < 0.05 |
| Female | 61 (59.8) | 43 (41.0) |  |
| Fever (centigrade) | 39.0 (38.5-39.3) | 38.9 (38.7-39.4) | NS |
| WBC (103/L) | 12.8 (10.4-15.2) | 12.5 (10.7-14.6) | NS |
| Platelet (103/L) | 132 (105-180) | 171 (130-231) | < 0.05 |
| Albumin (g/dL) | 2.9 (2.6-3.3) | 3.6 (3.4-4.0) | < 0.05 |
| Bilirubin (mg/dL) | 4.3 (3.1-6.0) | 4.2 (2.8-6.7) | NS |
| AST (U/L) | 229 (150-418) | 182 (141-256) | < 0.05 |
| ALT (U/L) | 195 (128-277) | 197 (144-303) | N |
| ALP (U/L) | 798 (576-1154) | 811 (510-1175) | NS |
| γ-GTP (U/L) | 336 (256-451) | 350 (249-548) | NS |
| ASA |  |  |  |
| class 2 | 34 (33.3) | 59 (56.2) | < 0.05 |
| class 3 | 67 (65.7) | 45 (42.9) |  |
| class 4 | 1 (1.0) | 1 (1.0) |  |

Continuous variables are expressed as median (interquartile range; IQR), categorical variables are expressed as *n* (%). WBC: White blood cells; AST: Aspartate transaminase; ALT: Alanine transaminase; ALP: Alkaline phosphatase; γ-GTP: γ-glutamyl transpeptidase; ASA: American Society of Anesthesiology; NS: Not significant.

Table 2 Comorbidities of patients with acute cholangitis *n* (%)

|  |  |  |  |
| --- | --- | --- | --- |
|  | Age ≥ 80 years  (*n =* 102) | Age < 80 years  (*n =* 105) | *P* value |
| Comorbidity | 93 (91.2) | 71 (67.6) | < 0.05 |
| Hypertension | 80 (78.4) | 53 (50.5) | < 0.05 |
| Ischemic heart disease | 40 (39.2) | 18 (17.1) | < 0.05 |
| Chronic heart failure | 8 (7.8) | 6 (5.7) | NS |
| Arrhythmia | 17 (16.7) | 14 (13.3) | NS |
| Cerebrovascular disease | 30 (29.4) | 10 (9.5) | < 0.05 |
| Dementia | 23 (22.5) | 4 (3.8) | < 0.05 |
| Diabetes mellitus | 21 (20.6) | 19 (18.1) | NS |
| Chronic liver disease | 9 (8.8) | 8 (7.6) | NS |
| Liver cirrhosis | 3 (2.9) | 3 (2.9) | NS |
| COPD/Asthma | 15 (14.7) | 7 (6.7) | < 0.05 |
| Chronic renal failure | 5 (4.9) | 4 (3.8) | NS |
| Malignancy1 | 8 (7.8) | 3 (2.9) | < 0.05 |
| Periampullary diverticulum | 25 (24.5) | 14 (13.3) | < 0.05 |

1Malignancy other than a primary biliary and pancreatic lesion. COPD: Chronic obstructive pulmonary disease; NS: Not significant.

Table 3 Etiology of acute cholangitis *n* (%)

|  |  |  |  |
| --- | --- | --- | --- |
|  | Age ≥ 80 years  (*n =* 102) | Age < 80 years  (*n =* 105) | *P* value |
| CBD stone | 65 (63.7) | 72 (68.6) | NS |
| Gallstone cholecystitis | 2 (2.0) | 4 (3.8) | NS |
| Pancreatitis | 1 (1.0) | 2 (1.9) | NS |
| Malignant obstruction | 31 (30.4) | 23 (21.9) | < 0.05 |
| Pancreatic cancer | 4 (3.9) | 5 (4.8) | NS |
| Biliary cancer | 21 (20.6) | 11 (10.5) | < 0.05 |
| GB cancer | 3 (2.9) | 4 (3.8) | NS |
| Other cause1 | 3 (2.9) | 3 (2.9) | NS |
| Benign stricture | 3 (2.9) | 4 (3.8) | NS |

1Biliary obstruction caused by metastatic lymph node(s). CBD: Common bile duct; GB: Gall bladder; NS: Not significant.

Table 4 Procedural details of endoscopic retrograde cholangiopancreatography *n* (%)

|  |  |  |  |
| --- | --- | --- | --- |
|  | Age ≥ 80 years  (*n =* 102) | Age < 80 years  (*n =* 105) | *P* value |
| Details of the procedure |  |  |  |
| Biliary stent insertion | 97 (95.1) | 100 (95.2) | NS |
| Endoscopic sphincterotomy | 69 (67.6) | 87 (82.9) | < 0.05 |
| Complete stone removal | 53/651 (81.5) | 67/722 (93.1) | < 0.05 |
| Technical success3 | 97 (95.1) | 100 (95.2) | NS |
| Procedures time (min), mean ± SD | 37.6 ± 8.1 | 40.1 ± 7.7 | NS |
| Failed cannulation | 5 (4.9) | 5 (4.8) | NS |

Number of patients with biliary stones in the elderly1 and in the control2 groups, 3technical success is defined as an endoscopic biliary drainage at an initial ERCP. ERCP: Endoscopic retrograde cholangiopancreatography; NS: Not significant.

Table 5 Endoscopic retrograde cholangiopancreatography-related complications *n* (%)

|  |  |  |  |
| --- | --- | --- | --- |
|  | Age ≥ 80 years  (*n =* 102) | Age < 80 years  (*n =* 105) | *P* value |
| Total | 7 (6.9) | 7 (6.7) | NS |
| Bleeding after EST | 3 (2.9) | 2 (1.9) | NS |
| Post-ERCP pancreatitis | 1 (1.0) | 4 (3.8) | < 0.05 |
| Aggravation of cholangitis | 2 (2.0) | 1 (1.0) | NS |
| Aspiration pneumonia | 1 (1.0) | 1 (1.0) | NS |
| Mortality | 0 | 0 | NA |

ERCP: Endoscopic retrograde cholangiopancreatography; EST: Endoscopic sphincterotomy; NS: not significant; NA: Not available.

Table 6 Cardiorespiratory suppression during endoscopic retrograde cholangiopancreatography under moderate sedation *n* (%)

|  |  |  |  |
| --- | --- | --- | --- |
|  | Age ≥ 80 years  (*n =* 102) | Age < 80 years  (*n =* 105) | *P* value |
| Total | 9 (8.8) | 8 (7.6) | NS |
| Hypoxemia | 2 (2.0) | 2 (1.9) | NS |
| Bradycardia | 4 (3.9) | 4 (3.8) | NS |
| Hypotension | 5 (4.9) | 4 (3.8) | NS |

Hypoxemia: Peripheral oxygen saturation (SpO2) below 90%; Bradycardia: Heart rate less than 45 beats per minutes; Hypotension: Systolic blood pressure below 80 mmHg; ERCP: Endoscopic retrograde cholangiopancreatography; NS: not significant.