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

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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
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[1]. Although previous studies have shown that ERCP can be safe and well tolerated even in the elderly[3,4,5], 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[6], we retrospectively evaluated the safety and efficacy of emergency ERCP for patients aged 80 years and older who presented with acute cholangitis.

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.

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., periampillary 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
the achievement of endoscopic biliary drainage with or without stone removal.

Technical success of interventional ERCP was defined as the achievement of endoscopic biliary drainage with or without stone removal.

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| Age (yr) | ≥ 80 yr (n = 102) | < 80 yr (n = 105) | P value |
|----------|-----------------|-----------------|--------|
| 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 (10^3/L) | 12.8 (10.4-15.2) | 12.5 (10.7-14.6) | NS     |
| Platelet (10^3/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) | NS     |
| 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)       | 34.5 (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 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.

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[26]. 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 χ² 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 used in biostatistics.

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

| Comorbidity                      | \( \geq 80 \text{ yr} \) \( n=102 \) | \( < 80 \text{ yr} \) \( n=105 \) | \( P \) 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           |
| Malignancy                      | 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 \( n \) (%)

| Etiology                        | \( \geq 80 \text{ yr} \) \( n=102 \) | \( < 80 \text{ yr} \) \( n=105 \) | \( P \) 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 cause                     | 3 (2.9)                             | 3 (2.9)                          | NS           |
| Benign stricture                | 3 (2.9)                             | 3 (2.9)                          | NS           |

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

| Details of the procedure         | \( \geq 80 \text{yr} \) \( n=102 \) | \( < 80 \text{yr} \) \( n=105 \) | \( P \) value |
|---------------------------------|-------------------------------------|----------------------------------|--------------|
| Biliary stent insertion         | 97 (95.1)                           | 100 (95.2)                       | NS           |
| Endoscopic sphincterotomy       | 69 (67.6)                           | 87 (82.9)                        | < 0.05       |
| Complete stone removal          | 53/65 (81.5)                        | 67/72 (93.1)                     | < 0.05       |
| Technical success               | 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. Technical 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 \( n \) (%)

| Complication                  | \( \geq 80 \text{ yr} \) \( n=102 \) | \( < 80 \text{ yr} \) \( n=105 \) | \( P \) 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.

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

| Age \( \geq 80 \text{ yr} \) \( (n = 102) \) | Age < 80 yr \( (n = 105) \) | \( P \) 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 65 beats per minute; Hypotension: Systolic blood pressure below 80 mmHg; ERCP: Endoscopic retrograde cholangiopancreatography; NS: Not significant.

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 \( (20 \text{ d vs } 15 \text{ d}) \) 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\(^{[25]}\). 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 concomitant 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 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-risk 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.

**REFERENCES**

1. Siegel JH, Kasmim FE. Biliary tract diseases in the elderly: management and outcomes. Gut 1997; 41: 433-435 [PMID: 9391238 DOI: 10.1136/gut.41.4.433]

2. Andriulli A, Loperfido S, Napolitano G, Niro G, Valvino MR, Spirito F, Pilotta A, Forlano R. Incidence rates of post-ERCP complications: a systematic survey of prospective studies. Am J Gastroenterol 2007; 102: 1781-1788 [PMID: 17509029 DOI: 10.1111/j.1572-0241.2007.01279.x]

3. Anderson MA, Fisher L, Jain R, Evans JA, Appalaneni V, Ben-Menachem T, Cash BD, Decker GA, Early DS, Fanelli BD, Fisher DA, Fukami N, Hwang JH, Ikenberry SO, Jue TL, Khan KM, Kirsnyk ML, Malpas PM, Maple JT, Sharaf RN, Shergill AK, Dominitz JA. Complications of ERCP. Gastrointest Endosc 2012; 75: 467-473 [PMID: 22341094 DOI: 10.1016/j.gie.2011.07.010]

4. García CJ, Lopez OA, Islan S, Othman M, Jia Y, Mulla ZD, Zuckermand M. Endoscopic Retrograde Cholangiopancreatography in the Elderly. Am J Med Sci 2016; 351: 84-90 [PMID: 26802762 DOI: 10.1016/j.amjms.2015.10.003]

5. Ye X, Huai J, Sun X. Effectiveness and safety of biliary stenting in the management of difficult common bile duct stones in elderly patients. Turk J Gastroenterol 2016; 27: 30-36 [PMID: 26674978 DOI: 10.5152/tjg.2015.150305]

6. Finkelmeier F, Tal A, Ajuauou M, Filman M, Zeuzem S, Waidmann O, Albert J. ERCP in elderly patients: increased risk of sedation adverse events but low frequency of post-ERCP pancreatitis. Gastrointest Endosc 2015; 82: 1051-1059 [PMID: 26089104 DOI: 10.1016/j.gie.2015.04.032]

7. Day LW, Lin L, Somsouk M. Adverse events in older patients undergoing ERCP: a systematic review and meta-analysis. Endosc Int Open 2014; 2: E28-E36 [PMID: 26134610 DOI: 10.1055/s-0034-1365281]

8. Behlil B, Ayfer S, Seygin V, Altay K, Mustafa C, Cem C, Bilge O, Fatih A, Emrah A, Zafer B, Kadir A, Belkis U. Safety of endoscopic retrograde cholangiopancreatography in patients 80 years of age and older. Prz Gastroenterol 2014; 9: 227-231 [PMID: 25276254 DOI: 10.1114/pg.2014.45105]

9. Yun DY, Han J, Oh JS, Park KW, Shin IH, Kim HG. Is endoscopic retrograde cholangiopancreatography safe in patients 90 years of age and older? Gut Liver 2014; 8: 552-556 [PMID: 25228977 DOI: 10.5009/gnl13310]

10. Katsinelos P, Kountouras J, Chatzimavroudis G, Zavos C, Terzoudis S, Pilipilidis I, Paroutoglou G. Outpatient therapeutic endoscopic retrograde cholangiopancreatography is safe in patients aged 80 years and older. Endoscopy 2011; 43: 128-133 [PMID: 21108173 DOI: 10.1055/s-0034-1255934]

11. Ali M, Ward M, Staley D, Duerksen DR. A retrospective study of the safety and efficacy of ERCP in octogenarians. Dig Dis Sci 2011; 56: 586-590 [PMID: 20585982 DOI: 10.1007/s10620-010-1304-4]

12. Obana T, Fujita N, Noda Y, Kobayashi G, Ito K, Horaguchi J, Koshita S, Kanno Y, Yamashita Y, Kato Y, Ogawa T. Efficacy and safety of therapeutic ERCP for the elderly with choledocholithiasis: comparison with younger patients. Intern Med 2010; 49: 1935-1941 [PMID: 20847495 DOI: 10.2169/internalmedicine.49.3660]

13. Lukens FJ, Howell DA, Upender S, Sheth SG, Jafri SM. ERCP in the very elderly: outcomes among patients older than eighty. Dig Dis Sci 2010; 55: 847-851 [PMID: 19337836 DOI: 10.1007/s10620-009-0784-6]

14. Hu KC, Chang WH, Chu CH, Wang HY, Lin SC, Wang TE, Shih SC. Findings and risk factors of early mortality of endoscopic retrograde cholangiopancreatography in different cohorts of elderly patients. J Am Geriatr Soc 2009; 57: 1839-1843 [PMID: 19744170 DOI: 10.1111/j.1532-5415.2009.02477.x]

15. Talar-Wojnarowska R, Szule G, Wóźniak B, Panzek M, Malecka-Panas E. Assessment of frequency and safety of endoscopic retrograde cholangiopancreatography in patients over 80 years of age. Pol Arch Med Wewn 2009; 119: 136-140 [PMID: 19514642]

16. Riphaus A, Stergiou N, Wehmann T. ERCP in octogenarians: a safe and efficient investigation. Age Ageing 2008; 37: 595-599 [PMID: 18539605 DOI: 10.1093/ageing/afn119]

17. Fritz E, Kirchgatterer A, Hubner D, Aschl G, Hinterreiter M, Stadler B, Knoflach P. ERCP is safe and effective in patients 80 years of age and older compared with younger patients. Gastrointest Endosc 2006; 64: 899-905 [PMID: 17140895 DOI: 10.1016/j.gie.2005.05.010]

18. Katsinelos P, Paroutoglou G, Kountouras J, Zavos C, Beltsis A, Tzovaras G. Efficacy and safety of therapeutic ERCP in patients 90 years of age and older. Gastrointest Endosc 2006; 63: 417-423 [PMID: 16500389 DOI: 10.1016/j.gie.2005.09.051]

19. Avila-Funes JA, Montaño-Loza A, Zepeda-Gómez S, Meza-Junco J, Melano-Carranza E, Valdivios-Andracia F, Valdivios-Díaz MA, Ponce de León-Rosas S. Endoscopic retrograde cholangiopancreatography in the elderly. Rev Invest Clin 2005; 57:
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20 Chong VH, Yim HB, Lim CC. Endoscopic retrograde cholangiopancreatography in the elderly: outcomes, safety and complications. *Singapore Med J* 2005; **46**: 621-626 [PMID: 16228093]

21 Köklü S, Parlak E, Yüksel O, Sahin B. Endoscopic retrograde cholangiopancreatography in the elderly: a prospective and comparative study. *Age Ageing* 2005; **34**: 572-577 [PMID: 16267181 DOI: 10.1093/ageing/afi180]

22 Hui CK, Liu CL, Lai KC, Chan SC, Hu WH, Wong WM, Cheung WW, Ng M, Yuen MF, Chan AO, Lo CM, Fan ST, Wong BC. Outcome of emergency ERCP for acute cholangitis in patients 90 years of age and older. *Aliment Pharmacol Ther* 2004; **19**: 1153-1158 [PMID: 15153168 DOI: 10.1111/j.1365-2036.2004.01962.x]

23 Mitchell RM, O’Connor F, Dickey W. Endoscopic retrograde cholangiopancreatography is safe and effective in patients 90 years of age and older. *J Clin Gastroenterol* 2003; **36**: 72-74 [PMID: 12488713]

24 Rodríguez-González FJ, Naranjo-Rodriguez A, Mata-Tapia I, Chicano-Gallardo M, Puente-Gutierrez JJ, López-Vallejos P, Hervás-Molina AJ, de Dios-Vega JF. ERCP in patients 90 years of age and older. *Gastrointest Endosc* 2003; **58**: 220-225 [PMID: 12872089 DOI: 10.1067/mge.2003.363]

25 Wada K, Takada T, Kawarada Y, Nimura Y, Miura F, Yoshida M, Mayumi T, Strasberg S, Pitt HA, Gadacz TR, Büchler MW, Belghiti J, de Santibanes E, Gouma DJ, Neuaus H, Dervenis C, Fan ST, Chen MF, Ker CG, Bornman PC, Hilvano SC, Kim SW, Liu KH, Kim MH. Diagnostic criteria and severity assessment of acute cholangitis: Tokyo Guidelines. *J Hepatobiliary Pancreat Surg* 2007; **14**: 52-58 [PMID: 17252297]

26 Kanda Y. Investigation of the freely available easy-to-use software ‘EZR’ for medical statistics. *Bone Marrow Transplant* 2013; **48**: 452-458 [PMID: 23208313 DOI: 10.1038/bmt.2012.244]

27 Freeman ML. Complications of endoscopic biliary sphincterotomy: a review. *Endoscopy* 1997; **29**: 288-297 [PMID: 9255535 DOI: 10.1055/s-2007-1004193]

28 Moreira VF, Arribas R, Sanroman AL, Meroño E, Larena C, Garcia M, Torres G. Choledocholithiasis in cirrhotic patients: is endoscopic sphincterotomy the safest choice? *Am J Gastroenterol* 1991; **86**: 1006-1010 [PMID: 1858736]

29 Lai EC, Mok FP, Tan ES, Lo CM, Fan ST, You KT, Wong J. Endoscopic biliary drainage for severe acute cholangitis. *N Engl J Med* 1992; **326**: 1582-1586 [PMID: 15842558 DOI: 10.1056/NEJM199206113262401]

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