Does Endoscopic Retrograde Cholangiopancreatography Carry Higher Risk for Patients 90 Years and Older? A Single-Institution Retrospective Study

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Background: Endoscopic retrograde cholangiography (ERCP) for patients aged ≥90 years is often required. The safety of ERCP for super-elderly patients is a major concern for gastrointestinal endoscopists. We retrospectively examined the safety of ERCP for super-elderly patients by comparison with patients in their 70s.

Material/Methods: We reviewed 66 patients aged ≥90 years (Group A) and 43 patients in their 70s (Group B) who underwent ERCP in our institution from January 2012 to October 2019. Data were collected on patients' backgrounds, corresponding procedures, and clinical outcomes, including adverse events.

Results: Patients in Group A (mean age: 92.3±2.1 years) had significantly poorer performance status (median: 3 *vs.* 0; $P<0.001$) and American Society of Anesthesiologists classification (median: III *vs.* II; $P<0.001$) when compared to Group B (mean age: 75.1±2.7 years). Underlying cardiovascular, cerebrovascular, renal, and orthopedic comorbidity occurrence was significantly higher in Group A than in Group B (87.88% *vs.* 67.44%; $P=0.0094$). Group A comprised more patients with benign disease than Group B (90.91% *vs.* 76.74%; $P=0.040$). Group B comprised more patients with malignant disease (31.82% *vs.* 53.54%; $P=0.041$). Emergency ERCP was higher in Group A than in Group B (71.70% *vs.* 29.73%; $P<0.0001$). No significant between-group differences in adverse events (15.15% *vs.* 11.63%; $P=0.602$) and mortality rate (1.52% *vs.* 2.33%; $P=0.758$) were noted.

Conclusions: Indications for ERCP should not be determined simply based on the super-elderly age of patients. ERCP may not necessarily carry higher risks if endoscopists practice maximal caution against gastrointestinal perforation.

MeSH Keywords: Cholangiopancreatography, Endoscopic Retrograde • Comorbidity • Frail Elderly • Geriatrics • Mortality

Abbreviations: AE – adverse event; ERCP – endoscopic retrograde cholangiography; ASA – American Society of Anesthesiologists; AST – aspartate aminotransferase; ALT – alanine aminotransferase; CRP – C-reactive protein, N.S. – not significantly different; PS – performance status

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Background

Endoscopic retrograde cholangiography (ERCP) is a diagnostic and therapeutic procedure for biliary and pancreatic disorders. It is often indicated for cases of biliary obstruction caused by biliary stones or biliary/pancreatic malignancies. According to the 2020 World Population Prospects report by the United Nations, the global increase in life expectancy is contributing to a progressive increase in the proportion of the elderly population [1]. Accordingly, the number of endoscopic procedures using ERCP is increasing with technical advancements in endoscopic methods and instruments given the growing aging society in Japan.

ERCP is generally considered to be associated with more frequent adverse events (AEs) when compared to other gastrointestinal endoscopic procedures [2]. In current clinical practice, endoscopists may hesitate to perform endoscopic procedures, especially for super-elderly patients aged ≥90 years in the context of hepatobiliary-pancreatic disease, as these patients often have comorbidities and decreased physiological or psychological reserves. The feasibility of ERCP for aged patients has been discussed in previous reports [3]; however, evidence for its safety in the patients aged ≥90 years remains controversial. Nevertheless, it is generally believed that endoscopic procedures using ERCP play an essential role and are considered less invasive than surgical management under general anesthesia.

To date, the number of studies evaluating the performance and safety of therapeutic ERCP in patients aged 90 years or older is limited [4]. To confirm the feasibility of ERCP for super-elderly patients aged ≥90 years, we retrospectively evaluated the safety of ERCP by comparison with patients in their 70s, focusing on patients' backgrounds, hematological parameters, clinical outcomes, and adverse events, including ERCP-induced complications. Moreover, we reviewed previously reported cases and those presenting with gastrointestinal perforation by ERCP, and assessed the feasibility of ERCP for patients aged ≥90 years.

Material and Methods

Patients' characteristics

We retrospectively reviewed 66 super-elderly patients aged 90 years and older and 43 patients ages 70-79 years who underwent ERCP at the Department of Gastroenterology of Juntendo Urayasu Hospital (Chiba, Japan) from January 2012 to October 2019. As proposed by the Japan Gerontological Society and the Japan Geriatrics Society, we referred to patients aged 90 years or older as super-elderly. Patients were divided into 2 groups independent of previous treatments or procedures. Patients

who had undergone gastrectomy with Billroth-II reconstruction or Roux-en-Y reconstruction were excluded, as endoscopic access for duodenal papilla was impossible by side-viewing duodenoscopy. Super-elderly patients aged ≥90 years were classified as Group A and patients ages 70–79 years were classified as Group B. We compared patients' backgrounds (sex, age, performance status (PS) [5], American Society of Anesthesiologist classifications (ASA) [6], absence or presence of antiplatelet therapy, underlying comorbidities, and preoperative laboratory data) between the 2 groups. Comorbid disease was defined as a disease under ongoing medication on admission. Comorbidities were classified into 10 groups: psychiatric, neurogenic, respiratory, cardiovascular, renal, metabolic, cerebrovascular, orthopedic, and malignant diseases. Patients' backgrounds and demographic data of each group are shown in Table 1.

Endoscopic procedures

Prior to ERCP, written informed consent for ERCP was obtained from all patients or legally authorized representatives. The Institutional Review Board of our institution approved this study (approval number: 2020-004). Three experienced endoscopists who had performed 400 cases conducted ERCP. During each ERCP session, continuous careful monitoring of vital signs, such as systolic and diastolic blood pressure (mmHg), minimum oxygen saturation (%), heart rate (beat/minute), and blood temperature (°C), were monitored in all patients just prior to ERCP and on the following day. Patients were placed in the semiprone position or in the decubitus position for cases with difficult cannulation for the duodenal papilla. As premedication for ERCP, all patients were administered topical pharyngeal spray with 10% lidocaine and sedated by administration of sedative agents (0.02–0.03 mg/kg of flunitrazepam, 1–2 mg of midazolam, and 35 mg of pethidine hydrochloride as an initial dosage) as per the latest Japanese guidelines for sedation in gastroenterological endoscopy [7]. Additional flunitrazepam or midazolam (1 mg each) was administered if sedation was considered inadequate according to the discretion of the endoscopist. Flunitrazepam was discontinued given its halted production in Japan, and midazolam was used instead. Duodenal relaxation was obtained by intravenous administration of butylscopolamine bromide as a first choice or glucagon (1–2 mg) as a second choice for patients with contraindications for scopolamine butylbromide such as heart disease, prostate hypertrophy, or glaucoma. ERCP was performed using standard duodenoscopy (TJF 240 or JF 260V; Olympus Optical Co., Ltd., Tokyo, Japan). Carbon dioxide (CO_2) gas was provided with a CO_2 regulator (Olympus Optical Co., Ltd., Tokyo, Japan) for insufflation for all cases. In terms of therapeutic strategies, endoscopic sphincterotomy (EST) was predominantly selected for bile drainage or removal of choledocholithiasis. A standard papillotomy knife was used for EST (Olympus Optical Co., Ltd,

Table 1. Patients' backgrounds and demographic data.

		Group A (n=66)		Group B (n=43)		p-Value
Gender	Male	18		18		0.152
	Female	48		25		
Age		92.27±2.10		75.11±2.86		*<0.001
PS	0:	4		28		
	1:	16		7		
	2:	12		4		
	3:	24		2		
	4:	10		2		
	Mean:	2.30±1.18		0.67±1.13		
	Median	3		0		*<0.001
ASA	I:	4		9		
	II:	21		25		
	III:	41		7		
	IV:	0		2		
	Median	III		II		*<0.001
Antiplatelet therapy	None:	41		39		
	Single:	19		3		
	Dual:	6		1		
	Intake percentage:	25	(39.68%)	4	(9.3%)	*0.030
Comorbidities	1) Psychiatric	5	(7.58%)	2	(4.65%)	0.535
	2) Neurogenic	0	(0.00%)	2	(4.65%)	0.052
	3) Malignancy	6	(9.09%)	10	(23.26%)	*0.046
	4) Respiratory	0	(0.00%)	1	(2.33%)	0.213
	5) Cardiovascular	44	(66.67%)	12	(27.91%)	*<0.001
	6) Renal	7	(10.61%)	0	(0.00%)	*0.027
	7) Metabolic	12	(18.18%)	10	(23.81%)	0.439
	8) Celebrovascular	12	(18.18%)	2	(4.65%)	*0.039
	9) Orthopedic	6	(9.09%)	0	(0.00%)	*0.042
	10) Others	2	(3.03%)	2	(4.65%)	0.660
	Total	58	(87.88%)	29	(67.44%)	*0.0094
Laboratory data	1) Amylase	84.87	(U/L)	257.55	(U/L)	*0.002
	2) CRP	6.829	(mg/dL)	3.451	(mg/dL)	*0.005
	3) WBC	9050	(/m³)	7034	(/m³)	0.193
	4) T-Bil	3.04	(mg/dL)	3.01	(mg/dL)	0.889
	5) D-Bil	2.625	(mg/dL)	2.44	(mg/dL)	0.556
	6) AST	132.54	(U/L)	105.02	(U/L)	0.349
	7) ALT	112.7	(U/L)	78.71	(U/L)	0.096

* Positive for significant difference.

Table 2. Breakdown of target disease and corresponding procedures by ERCP.

	Group A (n=66)		Group B (n=43)		p-Value
Target disease					
Malignant	21	(31.8%)	23	(53.5%)	
Benign	40	(60.6%)	20	(46.5%)	
Combined	5	(7.6%)	0	(0.0%)	*0.015
Corresponding procedures					
Post EST	19	(28.8%)	3	(7.0%)	
EST	9	(13.6%)	10	(23.3%)	
EPBD	6	(9.1%)	3	(7.0%)	
EST plus EPBD	0	(0.0%)	1	(2.3%)	
EST plus EPLBD	5	(7.6%)	3	(7.0%)	
Others	27	(40.9%)	23	(53.4%)	*0.044

* Positive for significant difference.

Tokyo, Japan). Patients with previously performed EST (post-EST) were included in the study. EST with large balloon dilatation (EPLBD) was selected in cases with large choledocholithiasis preoperatively estimated to exceed 12 mm. In EPLBD, Giga® was applied as an exclusive kit (Century Medical, Inc, Tokyo, Japan). Endoscopic papillary balloon dilatation (EPBD) was selected instead of EST for patients receiving antiplatelet therapy. Multi-Stage ExPander® for EPBD was applied as a kit (Medi-Globe., GmbH, Achenmühle, Germany). Procedures were combined in a timely manner. For cases with unexpected bleeding, a single antiplatelet drug was administered. In cases where multiple antiplatelet therapy was administered, only a single antiplatelet drug was continued. In the present study, heparin substitution for antiplatelet drugs was not used.

Clinical parameters and outcomes

Patients' background data (sex, age, PS, ASA, absence or presence of antiplatelet therapy, underlying comorbidities, and preoperative laboratory data) are presented in Table 1. Data on serum levels of hepatobiliary and pancreatic enzymes, total or direct bilirubin (mg/dL), aspartic acid aminotransferase (AST) (U/L), alanine aminotransferase (ALT) (U/L), amylase (U/L), white blood cell (WBC/mm^3), and CRP (mg/dL) were collected. We classified indicative causes for ERCP into benign or malignant diseases, or a combination of both. Therapeutic alternatives were classified into previously performed EST (Post-EST), EST, EPBD, and EST plus EPLBD according to alternatives for duodenal papilla. The breakdown of target diseases indicative for ERCP and corresponding therapeutic procedures for duodenal papilla by ERCP in both groups are presented in Table 2. Therapeutic outcomes, including total procedure time (minutes), emergency rate (%), intraoperative minimum oxygen saturation (%), percentage of oxygen administration requirement (%), and maximal oxygen supplement (L/min), were evaluated. Total dosages of administered sedative agents were calculated according to the type of sedative agent (flunitrazepam/midazolam).

Technical success was defined as cases for which endoscopists considered the scheduled purpose of ERCP had been obtained, regardless of adverse events. Total hospitalization days were defined as the duration (days) from admission day to discharge. Urgent ERCP was defined as ERCP for cases for which poor outcomes were predicted without an urgent procedure within 24 h. We evaluated the necessity of urgent ERCP for biliary drainage based on the presence of septic shock with systolic blood pressure <90 mmHg or high-grade fever greater than 39°C. Comparisons of these parameters between groups are shown in Table 3.

The occurrence of ERCP-induced adverse events such as acute cholangitis or cholecystitis, post-ERCP pancreatitis, tube trouble, immediate or delayed gastrointestinal bleeding and perforation, bleeding, respiratory events such as aspiration pneumonia, cardiovascular events, and hyperamylasemia in both groups was evaluated. Concerning the definitions of AEs, patients with oxygen saturation <90% were administered nasal oxygen. Immediate bleeding was defined as oozing requiring a hemostatic approach during endoscopy. Delayed bleeding was defined as a decrease in hemoglobin >3 g/dL. Respiratory disorders were defined as patients' respiratory discomfort indicating oxygen saturation < 90% followed by radiographic demonstration by computed tomography (CT). Acute cholecystitis was defined based on wall thickening and enlargement of the gallbladder. Cholangitis was defined as continuous high-grade fever more than 39°C with elevated hepatobiliary enzymes at required additional intervention. Acute post-ERCP pancreatitis was defined as worsening of abdominal pain with elevation

Table 3. Therapeutic outcomes by ERCP.

	Group A (n=66)		Group B (n=43)		*p*-Value
Procedure time	37.22±2.52	(min)	34.02±3.12	(min)	0.435
Emergency rate	71.70	(%)	29.73	(%)	*<0.0001
Oxygen – administration	64.2	(%)	67.44	(%)	0.1851
Minimum oxygen saturation	90.07±0.425	(%)	91.619±0.425	(%)	*0.009
Maxima oxygen supplement	2.272±2.29	(L/min)	1.581±1.467	(L/min)	0.092
Doses of sedative agents					
Flunitrazepam	8.37±4.33	(mg)	N/A	(mg)	N/A
Midazolam	4.346±2.30	(mg)	6.84±3.82	(mg)	*<0.001
Technical success	98.48	(%)	100	(%)	0.4174
Hospitalization	28.89±34.22	(days)	15.14±16.75	(days)	*0.002

* Positive for significant difference; N/A – not available.

Table 4. Incidence of adverse events related to ERCP.

	Group A (n=66)		Group B (n=43)		*p*-Value
Acute cholangitis/cholecystitis	1	(1.52%)	0	(0%)	0.417
Post – ERCP pancreatitis	2	(3.03%)	2	(4.65%)	0.660
Tube trouble	2	(3.03%)	0	(0%)	0.249
Gastrointestinal perforation	2	(3.03%)	0	(0%)	0.249
Bleeding	0	(0%)	0	(0%)	
Respiratory events	0	(0%)	0	(0%)	
Cardiovascular events	1	(1.52%)	1	(2.33%)	0.758
Others	2	(3.03%)	1	(2.33%)	0.826
Rate of AE	10	(15.15%)	5	(11.63%)	0.602
Mortality rate	1	(1.52%)	1	(2.33%)	0.758

of high levels of serum amylase followed by radiographic demonstration of peripancreatic effusion or swollen pancreas with pancreatic duct dilatation by CT. Gastrointestinal perforation was diagnosed by detecting perforation sites directly by endoscopy or extraintestinal air density via subsequent CT. Diagnosis of AEs and accompanying countermeasures were performed by consensus of the attending physicians. The final occurrence of AEs and mortality rate (%) were calculated and compared between groups (Table 4). Mortality was defined as ERCP-induced death within 30 days of ERCP.

Statistical analyses

Averages were compared between 2 groups using the paired *t* test. For non-parametric data, averages were compared among 3 or more groups using the Kruskal-Wallis test. Differences in frequency between groups were analyzed using the chi-square test. *P*<0.05 was considered statistically significant. JMP 14 statistical software (SAS Institute Japan) was used for all analyses.

Results

A total of 109 patients underwent ERCP in the present study. Patients were classified into 2 groups according to age: Group A comprised patients aged 90 years or older, and Group B comprised patients in their 70s. Sixty-six procedures for 39 patients in Group A and 43 procedures for 35 patients in Group B were examined in total. Patients' background and demographic data are shown in Table 1. Group A comprised 18 men and 48 women (mean age: 92.27±2.10 years; range: 90–97 years). Group B comprised 18 men and 25 women (mean age: 75.11±2.86 years; range: 70–79 years). Group B included significantly more patients with PS0, whereas Group A included

significantly more patients with PS1–4. The mean PS was significantly worse in Group A than in Group B (2.30±1.18 *vs.* 0.674±1.13, *P*<0.001). Patients with ASA I and II were only present in Group B, whereas patients with ASA III were present in Group A (*P*<0.0001). Only 2 patients with ASA IV were present in Group B; however, the median ASA was significantly worse in Group A than in Group B (III *vs.* II, *P*<0.001). Group A included significantly more patients with single or dual antiplatelet agents when compared to Group B (single/dual=19/6 [37.88%] *vs.* 3/1 [9.3%]; *P*=0.030). Group A included significantly more patients with cardiovascular disease (44/66 [66.67%] *vs.* 12/43 [27.9%]; *P*<0.0001), cerebrovascular disease (12/66 [18.18%] *vs.* 2/43 [4.65%]; *P*=0.039), renal disease (7/66 [10.61%] *vs.* 0/43 [0%]; *P*=0.027), and orthopedic disorders (6/66 [9.09%] *vs.* 0/43 [0%]; *P*=0.042). Group B included significantly more patients with a malignant disease (6/66 [9.09%] *vs.* 10/43 [23.26%]; *P*=0.0416). No significant differences between groups were observed in other comorbidities, including psychiatric disorders, neurogenic disorders, respiratory disease, and metabolic syndrome. Comorbidity occurrence was significantly higher in Group A than in Group B (58/66 [87.88%] *vs.* 29/43 [67.44%]; *P*=0.0094).

Prior to ERCP, serum levels of amylase were higher in Group B than in Group A (257.55 *vs.* 84.87 U/L; *P*=0.002). In contrast, serum levels of CRP were higher in Group A than in Group B (6.289 *vs.* 3.451 mg/dL; *P*=0.002). No significant differences between groups in hepatic function, including T-bil, D-bil, AST, ALT, and WBC, were noted (Table 1).

ERCP-indicative diseases were classified into 3 groups according to absence and/or presence of malignant diseases. Hepatobiliary malignancies, including metastatic liver carcinoma, hepatocellular or cholangiocellular carcinoma, carcinoma of ampulla of Vater, pancreatic carcinoma, and common bile duct carcinoma, were classified as malignant. Cholecystitis or cholangitis due to cholecystocholedocholithiasis, intraductal pancreatic mucinous neoplasm, chronic pancreatitis, narrowing of the pancreatic duct, dilatation of common bile duct, or Lemmel syndrome were classified as benign. Of 43 patients, 23 (53.5%) had more malignancies in Group B, and 40 of 66 (60.6%) patients had more benign disease in Group A. As such, the breakdown of target diseases for ERCP were significantly different (*P*=0.015) (Table 2). Corresponding ERCP procedures for each target disease were classified into 6 groups, as shown in Table 2. More cases with previously performed EST were identified in Group A than in Group B (19/66 [28.8%] *vs.* 2/43 [7.0%]). Each corresponding procedure differed in both groups (*P*=0.044) (Table 2).

Regarding therapeutic outcomes by ERCP, no significant difference between groups in ERCP procedure time was noted (37.22±2.52 *vs.* 34.02±3.12 min; *P*=0.435). The percentage of emergent ERCP was higher in Group A than in Group B (38/53

71.70 (%) *vs.* 11/37 29.73 (%); *P*=0.041). Higher doses of sedative agents (midazolam) were required in Group B than in Group A (Group A *vs.* Group B: 4.35±2.30 *vs.* 6.84±3.82 mg, respectively; *P*<0.001). No significant differences were noted in cases requiring oxygen administration between groups (Group A *vs.* Group B: 64.2 *vs.* 67.44%, respectively; *P*=0.185). Minimum oxygen saturation was significantly lower in Group A than in Group B (90.07±0.43 *vs.* 91.62±0.43%; *P*=0.009), with no significant difference in maximal oxygen supplement (2.27±2.29 *vs.* 1.58±1.47 L/min; p=0.092). Duration of hospital stay was longer for Group A than for Group B (28.89±34.22 *vs.* 15.14±16.75 days) (Table 3). No significant differences between groups were observed in the incidence of procedure-related adverse events, acute cholangitis/cholecystitis, post-ERCP pancreatitis, tube trouble, gastrointestinal perforation, bleeding, respiratory and cardiovascular events, occurrence of adverse events, and mortality rate.

In contrast, 2 cases of duodenal perforation occurred in Group A, which were treated non-surgically (Table 4). Previously reported cases with severe complications typified by gastrointestinal perforation by ERCP in super-elderly patients are summarized in Table 5. In summary, the data do not indicate that gastrointestinal perforation occurs more commonly in patients aged 90 years and older.

The present single-center retrospective study has several limitations. Several risk factors were not evaluated. Further, several patients who had undergone EST were counted twice or more, as having both stent occlusion and choledocholithiasis, so the same patients were included under different procedures.

Discussion

In the present study, we retrospectively investigated indications for ERCP in patients age ≥90 years compared with patients in their 70s in our single institution. Our data suggest that ERCP may not always carry a higher risk for super-elderly patients.

Physicians are generally cautious when performing medical procedures in super-elderly patients ≥90 years old in clinical settings. In particular, endoscopists often hesitate to perform endoscopic therapeutic procedures for patients ≥90 years because endoscopy is invasive and carries high risks of complications. In particular, older patients have a higher incidence of postoperative complications (26.1 *vs.* 12.0%, *P*<0.01) and higher mortality rate (9.2 *vs.* 2.7%, *P*<0.01) in biliary tract surgery when compared to younger patients [8]. Similarly, endoscopic procedures for hepatobiliary-pancreatic disorders often carry high risks, especially in the elderly [9]. Several studies have emphasized that super-elderly patients may tolerate laparoscopic procedures under general anesthesia in contrast to patients

Table 5. Previous reports focusing on gastrointestinal perforation by ERCP in super-elderly patients aged ≥90 years old.

Investigator	Years of study	Incidence			p-Value
		≥90 years	Controls	(years)	
Sugiyama M, et al.	2000	0/22	0/381	(78–89)	1.000
Rodrigues-Gonzales FR, et al.	2003	0/126	–		–
Hui CK, et al.	2004	1/64	0/165	(<90)	0.567
Katsinelos P et al.	2006	0/63	5/350	(78–89)	>0.50
Cariani G, et al.	2006	0/28	–		–
Gronroos JM, et al.	2010	0/35	–		–
Yun DY, et al.	2014	0/43	0/129	(<90)	1.000
Saito H, et al.	2019	0/126	2/569	(75–89)	1.000

aged 65 years and older. Super-elderly patients may benefit from avoiding unnecessary surgery in favor of ERCP [10]. Endoscopic procedures for the hepatobiliary-pancreatic tract may be less invasive than surgical procedures under general anesthesia, as super-elderly patients often have lower reserve and more co-morbidities. Therefore, potential benefits and risks of surgical procedures for super-elderly patients must be assessed carefully.

Physicians must consider the advantages and disadvantages of ERCP based on patient characteristics. In this regard, verifying the evidence for the feasibility and effectiveness of ERCP for patients over 90 years old is critical. Nevertheless, systematic studies on risks associated with ERCP in the super-elderly are lacking. Endoscopists are required to consider the character-istics of super-elderly patients before performing ERCP. The present study demonstrated that super-elderly patients who underwent ERCP had poor PS and ASA, with more underlying comorbidities, including cardiovascular, renal, metabolic, cere-brovascular, and orthopedic disorders. However, the incidence of ERCP-related adverse events was not significantly different between patients over 90 years and patients in their 70s. This is a crucial point which we would like to emphasize for endos-copists performing ERCP for super-elderly patients. Here, we report the incidence of ERCP-related adverse events of bleed-ing, cholecystitis/cholecystitis, respiratory disorders, cardio-vascular events, pancreatitis, gastrointestinal perforation, and mortality rate in reference to previous reports on ERCP for su-per-elderly patients ≥90 years. Total adverse events associated with ERCP in patients over 90 years old were not significantly different to those in the control group (rate of AE: 0–15.1%). Similarly, ERCP-associated mortality was not significantly dif-ferent between groups (mortality rate: 0–10%) [6,11–17], con-sistent with the results of the present study (mortality rate: 1.52% *vs.* 2.33%; *P*=0.758). It is noteworthy that the technical success rate was high in both groups (technical success rate: 98.48% *vs.* 100%; *P*=0.4174).

With regards to individual AEs, hemorrhage is a major con-cern for super-elderly patients. However, evidence for in-creased frequency of ERCP-induced hemorrhage is lacking, despite the larger number of super-elderly patients on anti-platelet therapy. The number of patients older than 90 years receiving treatment with antithrombotic agents was signifi-cantly higher than that for patients in their 70s. No post-ER-CP hemorrhage was observed in either group in the present study. In recent years, endoscopists are required to perform ERCP without discontinuation of antiplatelet agents because cerebrovascular or cardiovascular comorbidities themselves would be fatal. Although the incidence of hemorrhage in su-per-elderly patients did not increase even under treatment with antiplatelet agents, endoscopists should remain cogni-zant of potential ERCP-induced hemorrhage.

In this study, super-elderly patients were more often required to undergo urgent ERCP treatment when compared to control patients due to the predominance of benign target diseases such as choledocholithiasis or cholangitis. Takahashi et al. re-ported that benign diseases surpassed malignant diseases in patients aged ≥90 years who underwent ERCP [10]. This could be caused by hepatobiliary tract infections, which may be in-duced by decreased bile juice or gallbladder contractility. If biliary tract infections occur in super-elderly patients, clinical conditions may become progressively more severe. Therefore, certain hepatobiliary interventions are inevitable to avoid life-threatening bacterial cholangitis. Choledocholithiasis is an acute-onset disease that often triggers acute obstructive sup-purative cholangitis, which can have lethal consequences, es-pecially in super-elderly patients due to their poor physiolog-ical reserve. As such, urgent treatment will be required more often for patients of advanced age due to the higher incidence of acute cholangitis [12]. Yun et al. reported no significant dif-ferences in urgent ERCP between super-elderly patients and controls (41.9% *vs.* 40.4%; *P*=0.858) [16], Sugiyama et al. [6]

Table 6. Previous reports from 2000 onward on frequency of main adverse events and mortality rates of ERCP in super-elderly patients aged ≥90 years old.

Investigators	Year	Hemor-rhage	Acute cholangitis or cholecystitis	Respiratory disorders	Cardio-vascular disorders	Pancreatitis	Perforation	AEs	Mortality
		Super-elderly patients/controls (%)							
Sugiyama, et al. [5]	2000	0/2	5/1	0/0	0/0	0/2	0/0	5/7	0/0.3
Rodriguez-González, et al. [6]	2003	0.62/–	1.25/–	0/0	0/0	0/–	0/–	2.5/–	0.71/–
Hui, et al. [7]	2004	3.1/4.2	0/1.2	0/0	0/0	0/1.2	1.56/0	4.7/7.3	1.6/1.2
Katsinelos, et al. [8]	2006	6.3/1.7	0/0.9	0/1	0/0	0/3.4	0/1.4	6.3/8.3	1.6/0.6
Cariani, et al. [9]	2006	0/–	0/–	0/–	0/–	0/–	0/–	0/–	0/–
Grönroos, et al. [10]	2010	7.3/–	0/–	0/–	0/–	0/–	0/–	7.3/–	0/–
Yun, et al. [11]	2014	1/6	–/–	9/2	0/0	1/13*	0/0	5/22	1/0
Saito, et al. [12]	2019	2.4/0.7	1.6/1.9	0/0.2	0.8/0.2	1.6/3.7	0/0.4	7.7/9.5	0/2.3
Present study	2020	0/0	1.5/–	0/0	1.5/2.3	3.0/4.7	3.0/0	15.2/11.6	1.5/2.3

* Positive for significant difference; '–' – no description.

and Saito et al. [17] both described a higher percentage of urgent ERCP in super-elderly groups (32 vs. 15%; P<0.05, and 85.7 vs. 70.3%; P<0.001, respectively). These observations may be associated with a higher rate of urgent ERCP in super-elderly patients (71.70 vs. 29.73%; P<0.0001) based on the breakdown of target diseases for ERCP in the present study. Moreover, it should be noted that more patients in the super-elderly group (66 procedures for 39 patients) underwent ERCP twice or more than the group in their 70s (43 procedures for 35 patients). This is probably because fewer super-elderly patients had undergone curative surgical intervention than patients in their 70s with relation to physiological reserve power.

In super-elderly patients, respiratory disorders may occur with excessive sedation by sedative agents or ventilatory support due to septic circulatory impairment by cholangitis. The present study demonstrated that intraoperative doses of sedative agents in super-elderly patients undergoing ERCP were lower than those in patients in their 70s. Nevertheless, the minimal oxygen saturation during ERCP was significantly lower in super-elderly patients than in patients in their 70s. Recently, Takahashi et al. reported that the incidence of pneumonia was significantly different between patients ≥85 years old and controls (1/25 vs. 0/106, P=0.039) [10]. However, procedure-related respiratory disorders did not occur in either group in the present study. Sugiyama et al. reported that more prolonged ventilatory support was required in super-elderly patients, although pneumonia was induced not by endoscopic technique but by worsening target disease [6]. Hui et al. and Yun et al. reported that older patients required more ventilatory support; however, these cases were not associated with sedative agents, but were associated with severe cholangitis [12,16]. However, other studies listed in Table 6 did not report adverse respiratory events, suggesting that respiratory trouble may be caused by the severity grade of inflammatory target diseases as typified by acute cholangitis, rather than by sedative agents.

Cardiovascular disorders, although not specific to the ERCP procedure itself, remain important concerns. No significant differences in cardiovascular events between groups were noted, and their occurrence was rare. Pancreatitis is a complication pertinent to ERCP. The majority of previous reports have not found differences in the frequency of ERCP-pancreatitis. In contrast, Takahashi et al. reported that ERCP-pancreatitis occurred more often in patients ≥85 years old when compared to control patients (4 vs. 0%; P=0.039) [10]. Rodríguez-González et al. reported that ERCP-pancreatitis occurs less often in older patients than in younger patients due to pancreatic atrophy and decreased pancreatic enzymes associated with advanced age [6,16,18].

Acute cholangitis or cholecystitis is a rare but representative ERCP complication. Based on the references in Table 6, these conditions did not occur more frequently in super-elderly

patients when compared to control patients. Takahashi et al. reported that the frequency of cholangitis and cholecystitis in patients ≥85 years old and younger patients was not significantly different (12 *vs.* 4%; *P*=0.1) [10]. Similar findings were documented by Saito et al. (1.6 *vs.* 1.9%; *P*=1.0) [17]. The present data are compatible with past findings. These complications seem to be associated with primary target diseases, including cholangitis, rather than with ERCP-specific procedures, including pressured cholangiogram.

We encountered 2 cases of gastrointestinal perforations in the super-elderly group. Notably, the perforation occurred in 2 cases of super-elderly patients at the contralateral side of the duodenal papilla during extraction of the common bile duct stone. These 2 cases were managed conservatively by fasting and naso-gastric decompression, which resulted in prolonged hospital stay. Fortunately, surgical intervention was avoided. We speculate that these perforations occurred due to tissue fragility. Indeed, the aggregated data in Table 5 suggest that ERCP-induced gastrointestinal perforations do not occur more frequently in the super-elderly. Moreover, 2 perforation cases were classified into Stapfer type I using the standard classification system by Stapfer et al. [19]. Stapfer type I is defined as duodenal perforation in the lateral duodenal wall caused by the endoscope, which is the second most frequent perforation, responsible for 17.8% of total perforations according

to a systematic review on ERCP-related duodenal perforations by Cirocchi et al. [20]. Although we managed perforation cases without surgical intervention, Cirocchi et al. reported that 87% of Type I perforations were managed by surgery, and the remaining 13% were managed without surgery. Endoscopists should bear in mind that paying close attention to appropriate operation timing is important because postoperative mortality accounts for 20% of surgical treatment more than 24 hours later.

Conclusions

In conclusion, ERCP may not necessarily be avoided simply because patients are super-elderly. The present study suggests that endoscopists should consider the advantages and disadvantages for ERCP in patients ≥90 years old given their comorbidities. Therefore, ERCP should be performed, if necessary, as ERCP does not always carry high risks, even for patients over 90 years of age, but caution should be exercised in the peri-endoscopic period.

Conflicts of interest

None.

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