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Endoscopic retrograde cholangiopancreatography in super-elderly patients: Is it safe?

Çok yaşlı hastalarda endoskopik retrograd kolanjiyopankreatografi güvenli mi?

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Background and Aims: *There is no consensus, nor is there sufficient data, on the safety of endoscopic retrograde cholangiopancreatography in super-elderly patients. The demand for endoscopic retrograde cholangiopancreatography is increasing concurrently with the increasing human life expectancy. The aim of this study is, therefore, to assess the outcomes and safety of endoscopic retrograde cholangiopancreatography in super-elderly patients.* ***Materials and Methods:*** *The study sample consisted of 51 patients over 90 years of age who underwent endoscopic retrograde cholangiopancreatography between January 2014 and December 2018. Patients' demographic characteristics, indications, procedure-, and anesthesia- related adverse events, American Society of Anesthesiologists classification, the presence of comorbidities, and outcomes were analyzed. The Charlson Comorbidity Index was used to analyze comorbidity. A cutoff of Charlson Comorbidity Index ≥2 was used to identify patients on the basis of comorbidities.* ***Results:*** *The mean age of the 51 included participants was 91.86 (Standard Deviation = 2.42) years, and 16 of them were male. Bile duct stones were the most frequent indication (66.7%). Sphincterotomy was performed on 42 participants (82.4%). A stent was used in 17 participants (33.3%). The rate of difficult cannulation was 23.5%. Nine (17.6%) and 12 (24%) participants had minor procedure- and anesthesia-related adverse events, respectively. The mean procedure time was 35.16 (Standard Deviation = 6.65) minutes. Overall success was 86.3%. In-patient mortality was not seen.* ***Conclusion:*** *Therapeutic endoscopic retrograde cholangiopancreatography is a safe and effective treatment for pancreatobiliary disorders in super-elderly patients. Age ≥90 and a Charlson Comorbidity Index ≥2 are independently associated with increased morbidity in patients undergoing endoscopic retrograde cholangiopancreatography, which is successful and well tolerated. Endoscopic retrograde cholangiopancreatography should remain the treatment of choice for super-elderly patients.*

Keywords: *Endoscopic retrograde cholangiopancreatography, super-elderly patients, safety, adverse events, outcomes*

Giriş ve Amaç: *Çok yaşlı hastalarda, endoskopik retrograd kolanjiopankreatografinin güvenilirliği konusunda yeterli bilgi yoktur. Endoskopik retrograd kolanjiopankreatografi talebinde yaşam beklentisindeki artış ile birlikte bir artış vardır. Dolayısıyla bu çalışmanın amacı, çok yaşlı hastalardaki endoskopik retrograd kolanjiopankreatografinin sonuçlarını ve güvenilirliğini değerlendirmektir.* ***Gereç ve Yöntem:*** *Çalışmaya Ocak 2014 ile Aralık 2018 arasında endoskopik retrograd kolanjiopankreatografi uygulanan 90 yaş üstü 51 hasta dahil edildi. Demografik özellikler, endikasyonlar, işlem ve anestezi ile ilişkili yan etkiler, Amerikan Anesteziyologlar Derneği sınıflaması, eşlik eden komorbid hastalıklar ve sonuçları analiz edildi. Komorbiditeyi analiz etmek için Charlson Komorbidite İndeksi kullanıldı. Komorbidite ayrımı için Charlson Komorbidite İndeksi ≥ 2 sayısal tanımı kullanıldı.* ***Bulgular:*** *Dahil edilen 51 hastanın yaş ortalaması 91.86 (standart sapma = 2.42) yıl olup, 16'sı erkekti. En sık endikasyonu safra kanalı taşları oluşturuyordu (66.7%). Hastaların 42'sine sfinkteretomi yapıldı (82.4%). Stent ise hastaların 17'sine takıldı (33.3%). Zor kanülasyon oranı 23.5%'di. İşlem ile ilişkili 9 hastada (17.6%), anestezi ile ilgili 12 hastada (24%) minor yan etkiler görüldü. Ortalama işlem süresi 35.16 dakika (standart sapma = 6.65) olarak bulundu. İşlem başarı oranı ise 86.3%'di. Hastane içi mortalite görülmedi.* ***Sonuç:*** *Çok yaşlı hastalarda terapötik endoskopik retrograd kolanjiopankreatografi pankreatobiliyer hastalıklar için güvenilir ve etkili bir tedavi yöntemidir. Doksan yaş üzerinde olup, Charlson Komorbidite İndeksi ≥ 2 kriterleri başarılı endoskopik retrograd kolanjiopankreatografi işlemlerinde dahi bağımsız birer morbidite artışı göstergeleridir. Endoskopik retrograd kolanjiopankreatografi çok yaşlı hastalarda tercih edilen tedavi seçeneği olmalıdır.*

Anahtar kelimeler: *Endoskopik retrograd kolanjiopankreatografi, çok yaşlı hastalar, güvenilirlik, yan etkiler, sonuçlar*

INTRODUCTION

As the average human life expectancy rises, the number of people over 90 years of age in Turkey is increasing, resulting in a rapid increase in the number of elderly patients with pancreatobiliary disorders (1-3). Older patient age is associated with higher postoperative morbidity and mortality in patients with pancreatobiliary disorders. Postoperative mortality is 9.2% with a complication rate of 26.1% in elderly patients, suggesting that alternative endoscopic treatments for the management of biliary tract disorders are needed (1). There is, however, little information on the safety and outcome of endoscopic retrograde cholangiopancreatography (ERCP) in patients over 90 years of age. Super-elderly patients undergoing ERCP are at high risk for moderate-to-severe complications due to cardiovascular, pulmonary and neurological comorbidities (4). More data are needed on the performance of ERCP because super-elderly patients are a growing segment of the population, and an increasing number of them will undergo ERCP.

The aim of this study was, therefore, to retrospectively evaluate the success and complications of diagnostic and therapeutic ERCP.

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MATERIALS and METHODS

This study was approved by the Ethics Committee of Ümraniye Training and Research Hospital (B.10.1.TKH.4.34.H.GP0.01/49) and was conducted in accordance with the guidelines of the Declaration of Helsinki. The study sample consisted of 51 patients over 90 years of age who underwent ERCP between January 2014 and December 2018. Data collected from anesthesia and endoscopic records were analyzed.

All endoscopic procedures were performed by a team of four endoscopists and an anesthesiologist who had more than 10 years of experience. ERCP was performed using a standard duodenoscope, and therapeutic endoscopes were adjusted for all procedures.

Endoscopic sphincterotomy (EST) was performed for biliary stone removal, unless contraindications such as coagulopathy or thrombocytopenia were present. Endoscopic papillary balloon dilation was used when necessary. Standard techniques (mechanical lithotripsy, stone extraction baskets or balloons) were used to extract stones. Plastic stents were used for those with incomplete clearance of the bile duct or stones and those with benign or malignant strictures.

Ketamine was administered intravenously to achieve moderate sedation during the procedures. All patients received an induction dose of ketamine 0.5 mg/kg followed by continuous infusion of 10–15 mcg/kg/min. They also received 4 L oxygen through a nasal cannula. In the case of hypoxia, defined as blood oxygen saturation (SpO_2) <90%, the oxygen supply was increased to 10 L, and an airway or gastro-laryngeal mask was used when necessary. The Bispectral Index, which ranged from 60 to 80, was used to monitor pulse, O_2 saturation, non-invasive blood pressure, and depth of sedation every 5 minutes. The Charlson Comorbidity Index (CCI) was used to evaluate the severity of comorbidities. Patients were divided into three groups: mild (CCI ranging from 1 to 2), moderate (CCI ranging from 3 to 4), and severe (CCI ≥5) (Charlson et al. 1987). Success was defined as achievement of the goal set before the procedure. Difficult cannulation was defined as a cannulation time exceeding 30 minutes required to achieve successful cannulation.

Major adverse events were defined as bleeding requiring transfusion, perforations, cardiopulmonary events, and procedure- and/or sedation- related mortality. Minor adverse events were defined as minor post-procedural bleeding that did not require transfusion or any intervention, post-ERCP pancreatitis, mucosal injury, and fever.

Hypotension was defined as systolic blood pressure <90 mmHg, bradycardia <50 beats/min, tachycardia >120 beats/min, and hypoxemia peripheral oxygen saturation SpO_2 <90. Procedure time was defined as the time from insertion to complete removal of the endoscope. In-patient mortality was defined as death within 7 days of surgery.

Demographic aspects, indications, procedure-, and anesthesia- related adverse events, American Society of Anesthesiologists (ASA) classification, the presence of comorbidities, and outcomes were analyzed. The CCI was used to analyze comorbidity. A cutoff of CCI ≥2 was used to identify patients on the basis of comorbidities.

Statistical Analysis

Data were analyzed using SPSS 17.0 for Windows (Statistical Package for the Social Sciences) at a significance level of 0.05. Frequency analysis was used for nominal and ordinal parameters. Means and standard deviations were used for scale parameters. Mann-Whitney U and Chi-square tests were used for statistical analysis. Binary logistic regression analysis was used to assess the relationship between prognostic values for adverse effects.

RESULTS

Tables 1, 2, and 3 present the baseline characteristics of the cohort. In all, 68.6% of participants were female, and the median age was 91.86 (SD = 2.42) years. The indications were as follows: 1) Bile duct stones (66.7%), 2) cholangitis (23.5%), and 3-abnormal imaging/mass (9.8). Of all participants, 23.5% had minor anesthesia-related adverse events, 9.8% were ASA III, 86.3% ASA IV, and 3.9% were ASA V patients.

Of all participants, 82.4% underwent sphincterotomy, 33.3% had stents inserted, and 17.6% had minor procedure-related adverse events, which included minor bleeding, mucosal bleeding, fever, and post-ERCP pancreatitis. In all, 11.8% of procedures were urgent.

Only hypertension was significantly different ($p < 0.05$) (Table 2). Table 3 outlines the binary logistic regression analysis results for procedure- and anesthesia-related adverse events. Table 3 shows that procedure- and anesthesia-related adverse events did not differ by emergency procedure, age, or indication ($p > 0.05$).

Figure 1 shows the relation between anesthesia-related adverse events and the duration of the procedures. Anesthesia-related adverse events increased in direct proportion with the procedural duration.

Figure 2 shows the procedure-related adverse events. The duration of ERCP was longer in participants who did not have procedure-related adverse events.

Figure 3 shows the relationship between age, anesthesia, and adverse events. Anesthesia-related adverse events increased with age.

Tablo 1. Participants' demographic and clinic parameters

Parameters	Value
Age, mean ± SD	91.86±2.42
Male, n (%)	16 (31.4)
Sphincterotomy, n (%)	42 (82.4)
Stent, n (%)	17 (33.3)
Procedure-related adverse events, n (%)	9 (17.6)
Bleeding	4 (7.8)
Mucosal injury	2 (3.9)
Fever	2 (3.9)
Post-ERCP pancreatitis	1 (2.0)
Indications, n (%)	
Bile stone	34 (66.7)
Cholangitis	12 (23.5)
Abnormal imaging/Mass	5 (9.8)
Anesthesia-related adverse events	12 (23.5)
Atrial fibrillation	4 (7.8)
Respiratory depression	3 (5.9)
Hypotension	3 (5.9)
Apnea	2 (3.9)
Duration	35.16 ± 6.65
ASA Class, n (%)	
III	5 (9.8)
IV	44 (86.3)
V	2 (3.9)
Comorbidities, n (%)	
Coronary artery disease	4 (7.8)
Chronic obstructive pulmonary disease	12 (23.5)
Congestive heart failure	10 (19.6)
Diabetes Mellitus	25 (49.0)
Dementia	9 (17.6)
Cerebrovascular disease	2 (3.9)
Renal failure	6 (11.8)
Hypertension	44 (86.3)
Emergency procedure, n (%)	6 (11.8)
Success, n (%)	44 (86.3)
Second ERCP	4 (8.0)
Difficult cannulation	12 (23.5)
CCI >2	2 (3.9)

SD: Standart deviation, ERCP: Endoscopic retrograde cholangiopancreatography, ASA: American Society of Anesthesiologist, CCI: Charlson Comorbidity Index.

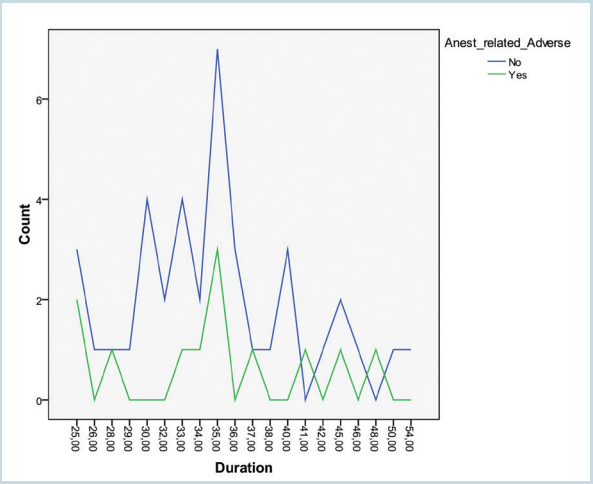

Figure 1. Anesthesia-related adverse events

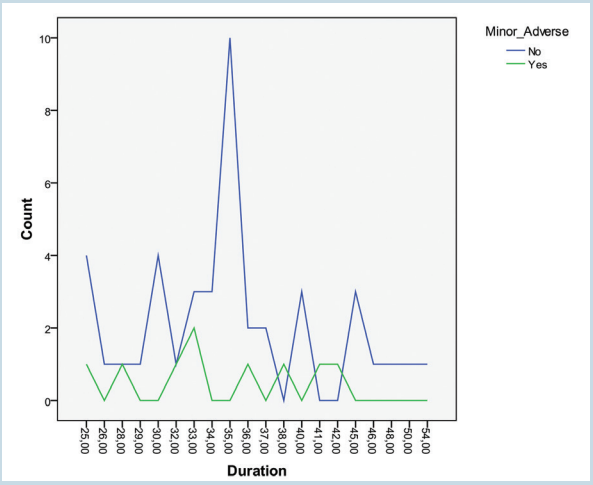

Figure 2. Procedure-related adverse events

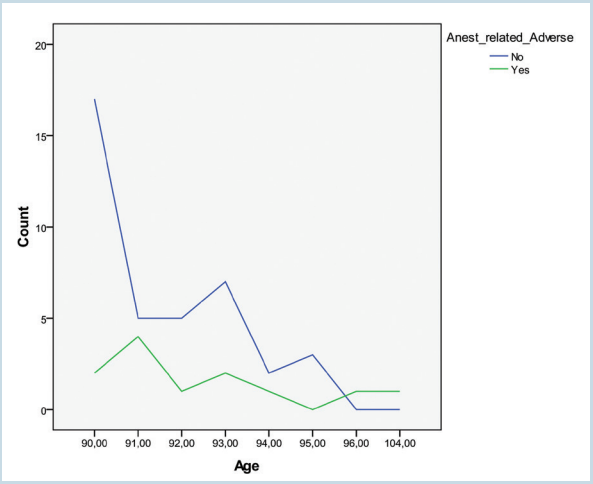

Figure 3. Age-dependent anesthesia-related adverse events

Tablo 2. Differences in demographic and clinic parameters between groups according to anesthesia-related adverse events

Parameters	Anesthesia-Related Adverse Events		p
	No	Yes	
Age, mean ± SD	91.51±1.67	93.00±3.88	0.172[a]
Male, n (%)	14 (35.9)	2 (16.7)	0.190[b]
Sphincterotomy, n (%)	33 (84.6)	9 (75.0)	0.459[b]
Stent, n (%)	12 (30.8)	5 (41.7)	0.489[b]
Procedure-related adverse events, n (%)	5 (12.8)	4 (33.3)	0.123[b]
Indications, n (%)			
Bile stone	26 (66.7)	8 (66.7)	
Cholangitis	8 (20.5)	4 (33.3)	0.195[b]
Abnormal imaging/Mass	5 (12.8)	-	
Duration	35.18±6.58	35.08±7.15	0.955[a]
ASA Class, n (%)	5 (12.8)	-	
III	32 (82.1)	12 (100.0)	<0.05
IV	2 (5.1)	-	
V			
Comorbidities, n (%)			
Coronary artery disease	4 (10.3)	-	N/A
Chronic obstructive pulmonary disease	7 (17.9)	5 (41.7)	0.104[b]
Congestive heart failure	6 (15.4)	4 (33.3)	0.190[b]
Diabetes Mellitus	21 (53.8)	4 (33.3)	0.214[c]
Dementia	6 (15.4)	3 (25.0)	0.459[b]
Cerebrovascular disease	2 (5.1)	-	N/A
Renal failure	5 (12.8)	1 (8.3)	0.663[b]
Hypertension	36 (92.3)	8 (66.7)	0.037[b]
Emergency procedure, n (%)	4 (10.3)	2 (16.7)	0.560[b]
Success, n (%)	33 (84.6)	11 (91.7)	0.515[b]

SD: Standart deviation. ASA: American Society of Anesthesiologist. a. Mann-Whitney U test, b. Chi-square with likelihood ratio, c. Chi-square test.

Tablo 3. Binary logistic regression analysis results for procedure- and anesthesia-related adverse events

	OR	Lower	Upper	p
Procedure-related Adverse Events				
Emergency procedure (1)	0.158	0.024	10.024	0.053
Age	0.947	0.640	10.403	0.787
Indication				0.743
Bile stone	20.253E8	0.000	.	0.999
Cholangitis	40.359E8	0.000	.	0.999
Anesthesia-related Adverse Events				
Emergency procedure (1)	0.600	0.089	40.039	0.599
Age	10.305	0.952	10.787	0.098
Indication				0.763
Bile stone	50.194E+08	0.000	.	0.999
Cholangitis	90.114E+08	0.000	.	0.999

DISCUSSION

Choledocholithiasis, biliary pancreatitis, malignancy, and obstructive jaundice occur frequently in the elderly, and malignancy and bile duct stones account for >70% of cases of jaundice in the population over 75 years of age (4,5). Abdominal surgeries are the most common in the elderly, and the mortality rate among them is 9.2% (1). However, ERCP reduces the need for surgery in super-elderly patients with pancreatobiliary disorders.

The number of patients over 90 years of age undergoing ERCP at our endoscopy center has recently increased with an increase in the aging population. There is a common belief that the higher the age, the higher the number of ERCP-related complications, depending on comorbidities; however, numerous studies suggest that this is not the case (6,7).

Our retrospective analysis showed that ERCP is an efficient and safe procedure for super-elderly patients. The incidence of minor procedure-related adverse events was 17.6%, despite comorbidities and higher ASA physical status scores. The incidence of anesthesia-related adverse events was 23.5%, most of which were transient cardiorespiratory problems that were medically treated.

This study brings forward two important findings. First, the incidence of procedure- and anesthesia-related adverse events during ERCP varies with age. Second, super-elderly patients are especially at risk of cardiopulmonary adverse events and bleeding (8). Super-elderly patients have twice the risk of bleeding compared with younger populations due to medication and the increased prevalence of coagulopathy. Our results are consistent with earlier findings. Yun et al. reported a success rate of 86%, an adverse event rate of 12%, and a mortality rate of 2% in patients over 90 years of age undergoing ERCP (9). Hui et al. reported on 30-day mortality in patients undergoing emergency ERCP for cholangitis and did not find a significant difference between elderly (7.8%) and younger populations (4.2%) (10).

Yang et al. (5) reported a complication rate ranging from 5% to 10% (mean: 6.04%) in elderly patients. Some studies reported a lower prevalence of post-ERCP pancreatitis in elderly patients than in younger patients (11). Only one of our participants had post-ERCP pancreatitis, which was conservatively treated. Yang et al. (5) found that the prevalence of post-ERCP pancreatitis in elderly and younger patients was 2.2% and 2.95%, respectively. Only one patient in the control group was diagnosed with moderate pancreatitis, while other patients were diagnosed with mild pancreatitis, which was conservatively treated.

Advanced age may be a protective factor against post-ERCP pancreatitis. A lower incidence of pancreatic trauma in elderly patients at the time of ERCP might be associated with age-related pathological changes in the pancreas. Pancreatic atrophy is commonly seen in elderly patients, and the pancreas may lose about 60 percent of its weight by 85 years of age (12). Bleeding was observed in 7.8% of our participants. The incidence of post-EST gastrointestinal hemorrhage ranges from 0.76% to 2%.

Some studies reported the same rate of bleeding in elderly (over 80 years of age) and young patients (8). All participants who experienced bleeding were treated successfully with adrenaline injections according to the guidelines of the European Association of Gastrointestinal Endoscopy and required no further interventions. We observed no perforation, which is a very rare but severe complication of ERCP, the prevalence of which ranges from 0.3% to 0.6%. The risk factors for perforation include Billroth II gastrectomy, dilation of the bile duct stricture, and endoscopic sphincterotomy (13).

The super-elderly group often required a second ERCP and a longer procedure, possibly due to more and larger bile stones. In our experience, most remaining stones should be removed by a second ERCP (14). Four of our participants underwent a second ERCP. If a patient with irretrievable stones undergoes a difficult procedure, we recommend that a temporary stent be placed or that ERCP be used a second time.

The type of sedation used is another important issue that should be considered when implementing ERCP in super-elderly patients. The use of moderate sedation has recently been reported as reliable. Sedation with ketamine prevents hypoxia and hypotension, which can occur frequently in elderly patients (2,15). Ketamine, a derivate of phencyclidine, with its rapid onset and short duration, provides a condition defined as dissociative anesthesia, which results in amnesia and analgesia with little or no cardiorespiratory depression (16-19).

Respiratory depression and hypotension were observed in three participants, and arrhythmia was observed in four participants. Apnea was observed in two participants and treated with airway interventions such as airway placement or bag mask respiration. All participants recovered quickly after the endoscope was removed. Careful preoperative evaluation and cooperation between anesthesiologists and gastroenterologists may also reduce the incidence of complications.

This study has several limitations. The major limitation is that this was a single-center study with a limited population. Post-discharge events were not collected. Therefore, improving the collection of perioperative clinical data and performing a multicenter study might be helpful in the future.

Complications in elderly patients are not different from those in young patients, although the former suffer from comorbid conditions and use antithrombotic drugs. Caution should be exercised when using ERCP in patients aged ≥90 years and those with a CCI ≥2.

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Conflict of Interest: *The authors declare no conflict of interest.*

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