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Technical success and adverse event rates after endoscopic retrograde cholangiopancreatography using deep sedation with propofol

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Abstract

Background With the increasing complexity and prolonged duration of endoscopic retrograde cholangiopancreatography (ERCP) procedures, sedation shifted from conscious sedation with benzodiazepines to deep sedation with propofol. We assessed the technical success and adverse event rates of ERCP with deep versus conscious sedation.

Methods Consecutive patients treated with ERCP in the University Medical Center Utrecht over a 7-year period (2010-2016) were screened for eligibility. Gastroenterologist-administered conscious sedation with midazolam was used from 2010-2013, whilst anesthesiology-administered deep sedation with propofol was used from 2013-2016. Data were retrospectively collected from electronic medical records. Outcomes were technical success and procedure-related adverse events within 30 days after ERCP. Associations of sedation type with outcomes were analyzed in univariable and multivariable analyses.

Results A total of 725 patients were included: 336 (46%) with conscious sedation and 389 (54%) with deep sedation. Technical success was significantly higher when propofol-based sedation was used (317 [82%] vs. 252 [75%], P=0.034). Adverse events also occurred significantly more often in the propofol group (77 [20%] vs. 38 [11%], P=0.002), due to higher rates of post-ERCP cholangitis (21 [5%] vs. 8 [2%], P=0.039), and post-ERCP pancreatitis (29 [7%] vs. 11 [3%], P=0.014). After adjustment, propofol-based sedation remained significantly associated with technical success and adverse events, with odds ratios of 1.53 (95% confidence interval [CI] 1.05-2.21) and 1.95 (95% CI 1.25-3.04), respectively.

Conclusion Propofol-based sedation resulted significantly more often in technical success of ERCP compared with midazolam-based sedation, but adverse events were almost twice as common, with higher rates of post-ERCP pancreatitis and cholangitis.

Keywords Endoscopic retrograde cholangiopancreatography, conscious sedation, deep sedation, biliary drainage, adverse events

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Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) was first described in 1968 as an imaging technique to visualize the biliary tract and pancreatic duct [1]. ERCP has evolved from a diagnostic tool to a therapeutic procedure for the management of a wide variety of pancreatobiliary diseases. Complex diseases are increasingly treated with ERCP instead of surgery or percutaneous transhepatic cholangiography (PTC), resulting in technically challenging ERCP procedures. Though less invasive than surgery or PTC, ERCP is also associated with adverse events (AEs), such as post-ERCP pancreatitis (PEP), cholangitis, bleeding, and perforation [2].

Benzodiazepines such as midazolam, either alone or in combination with opioids, are traditionally used for sedation during ERCP. Midazolam is well tolerated by patients and widely

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accepted in gastrointestinal endoscopy owing to its favorable safety profile. The increasing complexity and prolonged duration of ERCP required deeper levels of sedation and resulted in a shift to propofol-based deep sedation [3,4]. Deep sedation with propofol provides rapid onset and more constant levels of sedation. It improves patient comfort, cooperation and time to recovery [4]. Potential disadvantages of propofol are the lack of an antidote and the narrow therapeutic window. Although no significant difference in safety was found between the two sedation techniques [5], previous studies did not assess technical success (such as successful cannulation and complete drainage).

The aim of the current study is to compare the technical success and procedure-related AE rates of propofol-based deep sedation with midazolam-based conscious sedation in a large cohort of patients who underwent ERCP.

Patients and methods

Consecutive patients who underwent ERCP in the University Medical Center Utrecht between January 2010 and December 2016 were evaluated for eligibility. Exclusion criteria were: age below 18 years, American Society of Anesthesiologists (ASA) Class V, surgically altered gastrointestinal anatomy (such as Billroth II gastrectomy or pancreaticoduodenectomy with Roux-Y anastomosis), rendezvous procedures, ERCP performed under general anesthesia, resection of papilla adenomas, or unavailability of the patient file. We assessed the first ERCP procedures performed in our hospital within the abovementioned timeframe. This study was approved by the Institutional Medical Research Ethics Committee of the University Medical Center Utrecht (MREC number 19/239) and complied with the General Data Protection Regulation. This study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Guidelines [6].

Baseline patient and procedural characteristics were retrieved from the electronic patient record files and the endoscopy reports. Patient characteristics: age, sex, comorbidities, ASA classification, antithrombotic medication, previous cholecystectomy, previous ERCP performed before January 2010, previous papillotomy, presence of cholangitis, pancreatitis or cholecystitis. Laboratory measures before ERCP: bilirubin and C-reactive protein levels. ERCP characteristics: primary referral from other hospital, referral after failed ERCP, year of ERCP, type of ERCP (biliary or pancreatic), indication of ERCP, *a priori* degree of difficulty based on the classification of Schutz *et al* [7] (Appendix 1). Procedural characteristics: type of sedation, sedation success (defined as the ability to complete the ERCP without patient discomfort or agitation causing premature termination of the ERCP), precut sphincterotomy, sphincterotomy, bleeding per-procedurally, balloon dilation of the papilla, cannulation of common bile duct or pancreatic duct, presence of a stricture or of cholelithiasis, stent placement, rectal diclofenac prophylaxis, antibiotic prophylaxis.

Baseline patient and procedural data were retrospectively collected from electronic medical patient records by 1 researcher (either AMvdB, RT or MK). Outcomes were collected independently by 2 researchers (AMvdB and RT). Missing data were registered. Uncertainties and discrepancies were discussed with a third researcher (JK), and in cases of disagreement with a senior gastroenterologist and advanced endoscopist (FV).

Outcomes and definitions

Outcomes were retrieved from the electronic patient record files and endoscopy reports. The main outcomes were technical success and procedure-related AEs occurring within 30 days after ERCP. Technical success was defined as achievement of the procedural intention of ERCP (e.g., cannulation, drainage, stone removal, stent placement, change or removal). Partial technical success was defined as partial but not complete achievement of the procedural intention (e.g., stent placement with drainage, but failed stone extraction in case of choledocholithiasis; removal of some but not all stones; or drainage of some but not all intended ducts). Deep cannulation was considered successful if the bile duct was cannulated with the guidewire. In cases with acute cholangitis, defined as abdominal pain and cholestasis with a temperature >38°C or pus discharge during ERCP, achieving adequate drainage was considered as technical success.

We used the definitions and severity grading of the American Society for Gastrointestinal Endoscopy (ASGE) lexicon by Cotton *et al* [8]. The attribution of AEs to the procedure was judged as "possible", "probable" or "definite". If multiple AEs occurred in a patient, we registered them in order of occurrence. If referred patients were discharged or transferred back to a referring hospital and no further contact was sought within 30 days after ERCP, we considered patients free of AEs. Pre-existing acute cholangitis and biliary pancreatitis that persisted or worsened after ERCP were not considered AEs. Definitions of the baseline and procedural characteristics collected are provided in Appendix 2.

Procedures

All procedures and periprocedural care were performed in accordance with local guidelines at that time. Conscious sedation with midazolam and fentanyl, administered by the endoscopist, was the standard of care until January 2013. From January 2013 onward, deep sedation with propofol and alfentanil, administered by anesthesiologists, was implemented. Sedation groups are referred to as the "midazolam group" and the "propofol group".

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Statistical analysis

Data are presented as means and standard deviations (± SD) for continuous variables with normal distribution, and as medians with interquartile range (IQR) for continuous variables with a skewed distribution. Categorical variables are presented as absolute numbers and percentages. Categorical variables were compared for the midazolam group versus the propofol group using Pearson's chi-square test. The 2-sample *t*-test or Wilcoxon rank-sum was used for continuous variables, depending on the distribution. Univariable logistic regression analysis was performed to assess the association of type of sedation with technical success and AEs. In our multivariable analysis, we adjusted for predefined potential confounders that were selected based on expert opinion and previous literature in our multivariable analyses [2,9]. For the outcome technical success (yes vs. no or partial), we adjusted for sex, age (60 years or below vs. older than 60 years), ASA classification (1-2 vs. 3-4), degree of difficulty (grade 1 vs. grade 2 and 3), and indication of ERCP (benign biliary stricture, chronic pancreatitis/pancreatic duct pathology, leakage/trauma, malignancy, primary sclerosing cholangitis, lithiasis, stent change/removal, or other indication). For the outcome AEs, to minimize confounding by procedural characteristics, we further adjusted for precut sphincterotomy, sphincterotomy, pancreatic duct cannulation, and balloon dilation of the papilla. Effects are presented as odds ratios (OR) with 95% confidence intervals (CI). Results were considered statistically significant if the P-value was <0.05. Statistical analyses were performed using STATA version 15.1.

Results

In total, 1596 ERCPs were performed between January 2010 and December 2016. After the exclusion of 647 repeat ERCPs, 949 initial ERCPs were evaluated for eligibility. Subsequently, another 224 ERCPs were excluded for the reasons shown in Fig. 1, leaving 725 unique procedures, in which 336 (46%) patients were included in the midazolam group and 389 (54%) in the propofol group.

Patient and ERCP characteristics

Patient characteristics were comparable for the midazolam and propofol groups (Table 1). Mean age was approximately 60±15 years in both groups; 54% were males in the midazolam group and 50% in the propofol group (P=0.25). The presence of acute cholecystitis at presentation was significantly different, with 12 (4%) patients in the midazolam group versus 4 (1%) in the propofol group (P=0.02). As for the ERCP characteristics, the rates of ERCPs performed for biliary interventions (322 [96%] vs. 357 [92%], P=0.025) were significantly higher in the midazolam group compared with the propofol group. Sedation was significantly more often successful when propofol was used compared with midazolam (387 [99.5%] vs. 318 [94.6%], P<0.001). Balloon dilation of the papilla (22 [6%] vs. 4 [1%], P=0.002) and administration of diclofenac prophylaxis (241 [61%] vs. 21 [6%], P<0.001) occurred significantly more often in the propofol group (Table 2).

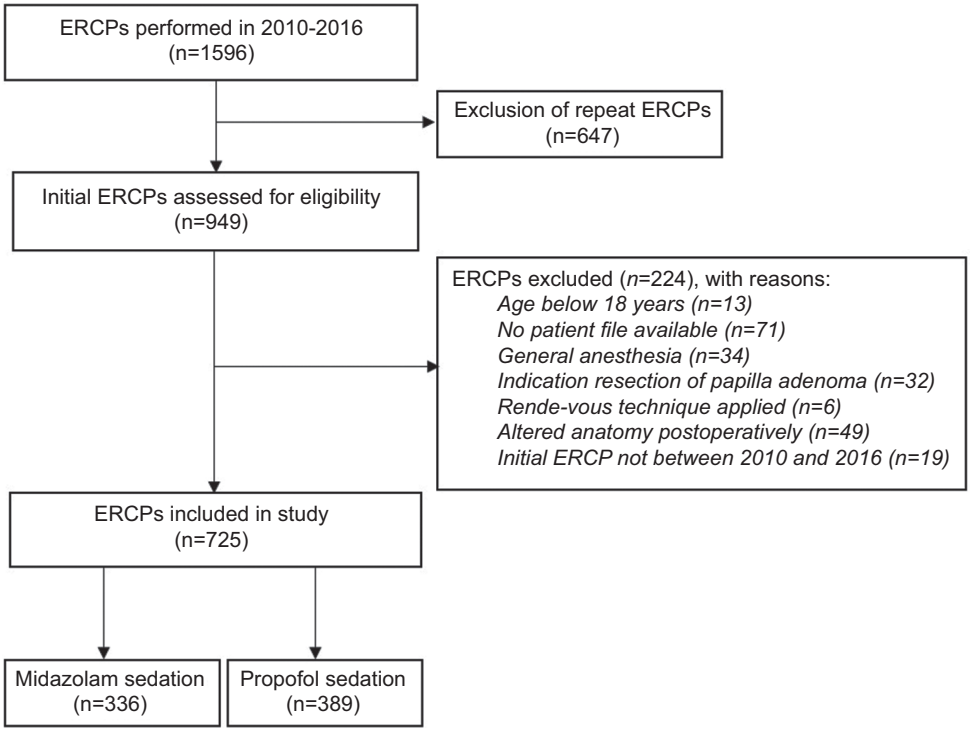

Figure 1 Selection process of included ERCPs
ERCP, endoscopic retrograde cholangiopancreatography

Table 1 Baseline characteristics of patients undergoing ERCP under midazolam or propofol sedation (n=725)

Characteristics	Midazolam	Propofol	P-value
	N=336	N=389	
Baseline characteristics			
Age, mean ± SD	60.0±15.8	60.8±15.0	0.49
Male sex, n (%)	181 (53.9)	193 (49.6)	0.25
Comorbidities, n (%)			
Liver disease	24 (7.1)	16 (4.1)	0.074
Kidney disease	20 (6.0)	33 (8.5)	0.19
Cardiovascular disease	91 (27.1)	96 (24.7)	0.46
Diabetes Mellitus	57 (17.0)	56 (14.4)	0.34
Pulmonary disease	31 (9.2)	30 (7.7)	0.46
Malignancy	179 (53.3)	215 (55.3)	0.59
ASA Classification, n (%)			0.20
1	14 (4.2)	23 (5.9)	
2	194 (57.7)	207 (53.2)	
3	126 (37.5)	151 (38.8)	
4	2 (0.6)	8 (2.1)	
Antiplatelet use, n (%)	62 (18.5)	68 (17.5)	0.73
Anticoagulant use, n (%)	34 (10.1)	40 (10.3)	0.94
Previous cholecystectomy, n (%)	60 (17.9)	91 (23.4)	0.067
Previous ERCP, n (%)	98 (29.3)	132 (33.9)	0.18
Previous sphincterotomy[1], n (%)	55 (17.1)	55 (14.4)	0.14
Stent *in situ*[2], n (%)	49 (14.7)	66 (17.1)	0.39
Acute pancreatitis, n (%)	15 (4.5)	14 (3.6)	0.55
Acute cholangitis, n (%)	74 (22.0)	64 (16.5)	0.057
Acute cholecystitis, n (%)	12 (3.6)	4 (1.0)	0.020
Bilirubin level in µmol/L, median (IQR)	79.5 (27-154)	74.5 (17-201)	0.6
C-reactive protein in mg/L, median (IQR)	43 (12-104)	38.5 (11-111)	0.64

[1]Unclear in 61 cases due to presence of a stent in the papilla and missing in 23 cases in whom the papilla was not reached or identified
[2]Missing in 5 cases
ERCP, endoscopic retrograde cholangiopancreatography; SD, standard deviation; ASA, American Society of Anesthesiologists

Outcomes

Technical success was achieved in 569 (78%) patients and was significantly more frequent in the propofol group than in the midazolam group (317 [81%] vs. 252 [75%], P=0.034). The rate of successful deep cannulation was also significantly higher in the propofol group than in the midazolam group (349 [90%] vs. 276 [82%], P=0.003).

Technical success was not or only partially achieved in 156 (22%) patients, for the following reasons: because ERCP was not possible due to a full stomach or a duodenal stenosis that could not be passed (n=17); cannulation failed (n=83); stone extraction failed (n=23); stent placement failed (n=24); or other reasons for not achieving technical success (n=9). Sedation was unsuccessful in 18 (12%) technically failed patients. Adverse events occurred in 115 (16%) patients and were significantly more common in the propofol group than in the midazolam group (77 [20%] vs. 38 [11%], P=0.002). In particular, rates of post-ERCP cholangitis (21 [5%] vs. 8 [2%], P=0.039) and PEP (29 [7%] vs. 11 [3%], P=0.014) were higher in patients with propofol. Perforation, bleeding, cardiopulmonary and other AEs did not differ significantly between the 2 groups (Table 3). The severity of AEs was classified as mild, moderate, severe or fatal in 41 (36%), 62 (54%), 9 (8%), and 3 (3%) patients, respectively. Eight (7%) patients experienced a second AE within 30 days, consisting of post-ERCP cholangitis (n=2), PEP (n=5) and perforation (n=1).

Association between type of sedation and procedural outcomes

Univariable analysis showed that sedation with propofol was significantly associated with technical success, with an OR of 1.47 (95% CI 1.03-2.09), and with AEs, with an OR of 1.94 (95% CI 1.27-2.94). After adjustment for potential confounders, propofol-based sedation remained significantly associated with technical success, with an OR of 1.53 (95% CI 1.05-2.21), and with AEs, with an OR of 1.95 (95% CI 1.25-3.04) (Table 4).

Discussion

We study investigated the technical success and adverse event rates in 725 patients treated with ERCP and sedated with either gastroenterologist-administrated conscious sedation with midazolam and fentanyl, or anesthesiologist-administrated deep sedation with propofol and alfentanil. Technical success was significantly higher with propofol-based sedation than with midazolam-based sedation. Propofol-based sedation was also associated with more AEs, especially PEP and post-ERCP cholangitis.

Previous randomized controlled trials (RCTs), originally designed to assess the safety of the two sedation types in patients

Table 2 Indication and procedural characteristics of patients undergoing ERCP with midazolam or propofol sedation

Characteristics	Midazolam (N=336)	Propofol (N=389)	P-value
ERCP indication characteristics			
Referral from other hospital, n (%)	56 (16.7)	76 (19.5)	0.32
Referral after failed ERCP[1]	22 (42)	41 (54)	0.16
Year of ERCP, n (%)			<0.001
2010	106 (31.5)	3 (0.8)	
2011	91 (27.1)	1 (0.3)	
2012	96 (28.6)	5 (1.3)	
2013	40 (11.9)	62 (15.9)	
2014	1 (0.3)	114 (29.3)	
2015	0 (0.0)	105 (27.0)	
2016	2 (0.6)	99 (25.4)	
Type of ERCP, n (%)			0.025
Biliary	322 (95.8)	357 (91.8)	
Pancreatic	14 (4.2)	32 (8.2)	
Indication of ERCP, n (%)			0.24
Benign biliary stricture	8 (2.4)	15 (3.9)	
Chronic pancreatitis/pancreatic	13 (3.9)	23 (5.9)	
pathology	20 (6.5)	31 (8.0)	
Leakage/trauma	140 (41.7)	162 (41.6)	
Malignancy	10 (3.0)	4 (1)	
Primary sclerosing cholangitis	132 (39.3)	135 (34.7)	
Lithiasis	6 (1.8)	11 (2.8)	
Stent change/removal	7 (2.1)	8 (2.1)	
Other			
Grade of difficulty, n (%)[2]			0.076
Grade 1	250 (74.4)	265 (68.1)	
Grade 2	68 (20.2)	88 (22.6)	
Grade 3	18 (5.4)	36 (9.3)	
Procedural characteristics			
Sedation success, n (%)	318 (94.6)	387 (99.5)	<0.001
Precut sphincterotomy, n (%)[3]	75 (23.4)	87 (22.8)	0.87
Sphincterotomy, n (%)[3]	170 (53.0)	201 (52.8)	0.96
Bleeding per-procedurally, n (%)[3]	24 (7.5)	24 (6.3)	0.54
Balloon dilation of the papilla, n (%)[3]	4 (1.2)	22 (5.8)	0.002
Cannulation of CBD, n (%)[3]	275 (85.7)	333 (87.4)	0.5
Cannulation of PD, n (%)[3,4]	99 (30.8)	124 (32.5)	0.63
Stricture present, n (%)[5]	135 (48.6)	178 (51.1)	0.52
Cholelithiasis present, n (%)[6]	88 (32.6)	97 (30.0)	0.50
Stent placed in CBD and/or PD, n (%)[5]	177 (63.9)	216 (61.4)	0.51
Diclofenac prophylaxis, n (%)	21 (6.3)	241 (62.0)	<0.001
Antibiotic prophylaxis, n (%)	161 (47.9)	162 (41.6)	0.09

[1]Missing in 3 cases;
[2]Based on the classification of Schutz *et al*;
[3]Missing in 23 cases in whom the papilla was not reached (n=17) or not identified (n=6);
[4]Intentional (n=33) and unintentional (n=190);
[5]In whom cannulation of CBD/PD succeeded (n=629);
[6]In whom cannulation of CBD succeeded (n=597)
ERCP, endoscopic retrograde cholangiopancreatography; CBD, common bile duct; PD, pancreatic duct

undergoing ERCP, showed no difference in cardiopulmonary AEs [10-13]. Rates of PEP were reported in two of these RCTs, with no significant difference between sedation types [10,11]. Low rates of perforation and post-sphincterotomy bleeding

were described in one RCT [10]. These RCTs were, however, not powered to detect differences in procedure-related outcomes [10,11]. No previous RCT assessed technical success by sedation type.

A retrospective study of 367 patients compared anesthesiologist-administered propofol sedation with historical controls who received endoscopist-administered sedation with benzodiazepines and opioids, and found comparable deep cannulation rates (95.2% vs. 94.4%, respectively, P=0.36) [14]. In contrast, a recently published Swedish nationwide registry study of 31,001 ERCP procedures reported a significantly higher deep cannulation rate with propofol-based sedation compared with midazolam-based sedation (89.0% vs. 86.8%, P<0.001), which is in line with the current results [15]. Sedation levels and patient cooperation have been reported to be superior with propofol-based sedation compared with traditional sedation with benzodiazepines (mostly midazolam) [4,16,17]. Tranquility of the deeply sedated and unconscious patient probably facilitates cannulation [15]. In addition, more cannulation attempts can be performed to strive for successful cannulation, with propofol-based sedation allowing longer procedure times [15].

Table 3 Outcomes of patients undergoing ERCP with midazolam or propofol sedation

Characteristics	Midazolam	Propofol	P-value
	N=336	N=389	
Technical success, n (%)			
Yes	252 (75.0)	317 (81.5)	0.034
Partial	14 (4.2)	19 (4.9)	0.64
No	70 (20.8)	53 (13.6)	0.010
Reasons for failure			
ERCP was not possible	13 (3.9)	4 (1.0)	0.012
Cannulation	47 (14.0)	36 (9.3)	0.046
CBD/PD failed			
Stone extraction failed	11 (3.3)	12 (3.1)	0.88
Stent placement failed	9 (2.7)	15 (3.9)	0.38
Other	4 (1.2)	5 (1.3)	0.91
Adverse events <30 days	38 (11.3)	77 (19.8)	0.002
Cholangitis	8 (2.4)	21 (5.4)	0.039
Post-ERCP pancreatitis	11 (3.3)	29 (7.5)	0.014
Perforation	4 (1.2)	6 (1.5)	0.69
Bleeding	3 (0.9)	4 (1.0)	0.85
Cardiopulmonary	2 (0.6)	7 (1.8)	0.14
Other[1]	10 (3.0)	10 (2.6)	0.74

[1]Consisting of subfebrile temperature (n=1) or fever without clear focus (n=5) after ERCP requiring prolonged admission, (suspected) stent dysfunction requiring repeat ERCP (n=11); cholecystitis after fully covered self-expanding metal stent placement in CBD (n=1); pseudocyst infection after stent placement in pancreatic duct in a patient with chronic pancreatitis (n=1); vomiting after ERCP requiring medical consultation at Emergency Department (n=1)

ERCP, endoscopic retrograde cholangiopancreatography; CBD, common bile duct; PD, pancreatic duct

Propofol is known for side-effects such as hypoventilation, hypotension and bradycardia. Although a trend has been reported, no significant increase of sedation-related cardiopulmonary AEs was found in patients undergoing advanced endoscopic procedures such as ERCP with propofol versus traditional sedation [4,5,16,18]. In line with the findings of these meta-analyses, we did not find a significant difference in cardiopulmonary AEs between midazolam and propofol-based sedation. However, procedure-related (endoscopic) AEs, such as pancreatitis, cholangitis, bleeding or perforation, were not reported in these previous studies.

PEP remains the most frequent AE of ERCP, with overall incidences varying from 3.5% to 9.7% [19,20]. The overall incidence of post-ERCP cholangitis is around 1% [19,21], though rates of around 20% have been reported in a selected group of patients with hilar cholangiocarcinoma [22]. This higher rate is presumably due to incomplete drainage of complex hilar strictures and opacified proximal bile ducts [22,23]. Whereas one would expect lower rates of these ERCP-related AEs with propofol sedation, as a result of improved cannulation rates, we observed higher overall rates of AEs, especially PEP and cholangitis. Most previous studies did not find significantly different overall endoscopic AE rates [3,14,15,24,25], PEP rates [10,14,25,26] or post-ERCP cholangitis rates [14,15] between propofol-based versus midazolam-based sedation. The Swedish registry mentioned above, however, reported a significantly higher rate of PEP and perforation of the gut in the propofol group than in the midazolam group [15]. It was suggested that this was due to the patient's deeply sedated and unconscious state allowing continued and more aggressive attempts in difficult cases.

Table 4 Associations of sedation type with technical success and adverse events

Sedation	Technical success[1]		Adverse events[2]	
	Univariable analysis	Multivariable analysis[3]	Univariable analysis	Multivariable analysis[4]
	OR (95%CI)	OR (95%CI)	OR (95%CI)	OR (95%CI)
Propofol (vs. midazolam)	1.47 (1.03-2.09)	1.53 (1.05-2.21)	1.94 (1.27-2.94)	1.95 (1.25-3.04)

[1]Technical success was defined as achievement of the procedural intention of ERCP (e.g., cannulation, drainage, stone removal, stent placement, change or removal)

[2]AEs (cholangitis, post-ERCP pancreatitis, perforation, bleeding and cardiopulmonary AEs) are defined according to the ASGE lexicon by Cotton *et al* [8]

[3]For technical success we adjusted for sex, age (≤60 years vs. >60 years), ASA classification (3-4 vs. 1-2), degree of difficulty (grade 1 vs. grade 2 and 3), and indication of ERCP (lithiasis vs. malignancy, benign biliary stricture, trauma/leakage, chronic pancreatitis/pancreatic duct pathology, primary sclerosing cholangitis, stent removal or change, other indication)

[4]We adjusted for the same variables as for technical success and we additionally adjusted for precut sphincterotomy, sphincterotomy and pancreatic duct cannulation

CI, confidence interval; OR, odds ratio; AEs, adverse events; ASGE, American Society for Gastrointestinal Endoscopy; ASA, American Society of Anesthesiologists

Procedure duration was also significantly longer in the propofol group [15]. Repeated and prolonged cannulation attempts with inadvertent manipulation and instrumentation of the papillary orifice and contrast filling of the pancreatic duct have been reported to be associated with higher AE rates [27-29]. The higher cholangitis rate in the propofol group might also be explained by the large proportion of malignant indications in our study, compared with previous studies. Effective drainage of malignant (especially complex hilar) strictures can be challenging, and cholangitis mostly develops in patients with malignant biliary obstruction or failed drainage [30]. In our tertiary referral center, 63 (8.7%) of our patients were treated after a failed ERCP elsewhere, and 41.7% of all ERCPs concerned malignant indications. This is in contrast with the previously mentioned Swedish registry covering approximately 90% of all ERCP procedures annually performed in Sweden, of which 15.2% concerned malignant indications, making it more representative of general clinical practice [15].

We included a large number of consecutive patients and obtained detailed information about the patients and the procedures performed. We defined "technical success" as achievement of the procedural intention of ERCP, to assess the desired treatment effect in relation to its specific indication. While most studies define technical success as successful cannulation of the common bile duct, this definition falls short when the aim is, for example, to remove a biliary stone or place a stent across a stenosis. Sedation type was determined by protocol change over time in almost all cases, minimizing bias by selection of patients based on patient characteristics or preference of the endoscopist. Crossover to the other sedation type occurred only in a small number of patients (Table 2).

This study had several limitations. Patients were retrospectively identified, and data were retrospectively collected from patient records. Increasing complexity of the procedures, as well as improvement of procedural techniques and healthcare over time, could have influenced outcomes. Quantitative measures for sedation success were not available. Procedure duration could not be collected retrospectively. We did not adjust for operator characteristics, such as endoscopists' experience, volume, and the contribution of a trainee, if present, since these data were not available. Patients were recruited from a single large tertiary referral center, possibly hampering generalizability to other centers. AEs might have been missed in patients who were immediately transferred back to the referring hospital.

Patients undergoing ERCP with propofol-based sedation have been previously reported to experience better comfort and faster recovery compared with midazolam-based sedation, without an increased risk of cardiopulmonary AEs [4,5,16]. In this study, we showed a benefit of propofol-based sedation in terms of technical success rates of ERCP. This result further supports the choice of sedation with propofol instead of midazolam when performing ERCP, in line with the current standard practice. After implementing new treatment strategies, however, it remains important to evaluate (safety) outcomes. The higher rates of PEP and post-ERCP cholangitis in patients deeply sedated with propofol stress the importance of taking into account ERCP-related risk factors for AEs, as provided in the European Society of Gastrointestinal Endoscopy guidelines [2]. Future studies should identify patients in whom propofol unacceptably increases the risk of AEs without improving technical success rates.

In conclusion, this study showed a higher rate of technical success, but also a higher rate of post-ERCP pancreatitis and cholangitis, in patients undergoing ERCP with propofol-based deep sedation compared with midazolam-based conscious sedation. Propofol sedation is probably preferable for patients undergoing ERCP procedures, but efforts are needed to decrease the higher rate of adverse events.

Summary Box

What is already known:

- Endoscopic retrograde cholangiopancreatography (ERCP) is associated with adverse events (AEs), such as post-ERCP pancreatitis (PEP), cholangitis, bleeding, and perforation
- The increasing complexity and prolonged duration of ERCP has required deeper levels of sedation and resulted in a shift of midazolam-based conscious sedation to propofol-based deep sedation
- Between midazolam-based conscious and propofol-based deep sedation, no significant difference in safety of sedation (i.e., cardiopulmonary AEs) was found. Data on differences in technical success and procedure-related AEs are scarce

What the new findings are:

- Technical success was achieved in 569 (78%) patients and adverse events occurred in 115 (16%) patients who underwent ERCP
- Propofol-based sedation resulted significantly more often in technical success of ERCP compared with midazolam-based sedation
- PEP and cholangitis were twice as common in patients undergoing ERCP with propofol-based deep sedation compared with midazolam-based conscious sedation

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Supplementary material

Appendix 1 Degree of difficulty based on the Schutz classification [7]

Degree of difficulty	Biliary procedures	Pancreatic procedures
Grade 1	– Diagnostic cholangiography – Biliary cytology – Stone extraction ≤10 mm – Dilation/stent placement/ nasobiliary drainage of extrahepatic strictures	– Diagnostic pancreatography – Pancreatic cytology
Grade 2	– Stone extraction >10 mm – Dilation/stent placement/ nasobiliary drainage of hilar tumors or benign intrahepatic strictures	– Minor papilla cannulation
Grade 3	– Intrahepatic bile duct stone removal – Bile duct stone removal using lithotripsy	– Therapeutic procedures including pseudocyst drainage

Appendix 2 Definitions of variables

Liver disease: Defined as chronic hepatitis B/C, inherited liver disease (e.g., cystic fibrosis), liver cirrhosis, autoimmune liver diseases (e.g., primary biliary cirrhosis, primary sclerosing cholangitis, autoimmune hepatitis). Hepatocellular carcinoma or hepatic metastases were not considered as liver disease but were registered as malignancy.
Kidney disease: Defined as glomerular disease, tubule-interstitial diseases or acute and chronic kidney failure.
Cardiovascular disease: Defined as cardiac failure, cardiomyopathy, coronary artery disease, peripheral arterial disease or cerebrovascular disease.
Pulmonary disease: Defined as lower respiratory tract infections, chronic obstructive respiratory disease (e.g., bronchitis, asthma or chronic obstructive pulmonary disease) or chronic restrictive respiratory disease.
Acute pancreatitis: Defined as (suspicion of) acute biliary pancreatitis, based on clinical presentation with typical upper abdominal pain and elevated lipase or amylase levels. Based on the ASGE lexicon by Cotton *et al* [8].
Acute cholangitis: Defined as (suspicion of) acute cholangitis, based on clinical presentation with abdominal pain and cholestasis with a temperature >38˚C or pus discharge during ERCP. Based on the ASGE lexicon by Cotton *et al* [8].
Acute cholecystitis: Defined as (suspicion of) acute cholecystitis, based on clinical presentation with typical right upper abdominal pain, temperature >38˚C and radiological imaging.
Referral from other hospital: Defined as patients referred for ERCP specifically, for example after failure or the absence of expertise in the local hospital.
Indication of ERCP: Defined as the pathology for which ERCP was indicated.
Grade of difficulty: Defined as the *a priori* degree of difficulty of ERCP procedures based on a modified classification of Schutz *et al* [7] (Appendix 1)
Sedation success: defined as being able to complete the ERCP without patient discomfort or agitation causing premature termination of the ERCP
Diclofenac prophylaxis: Defined as rectal diclofenac administered prior to or directly after ERCP
Antibiotic prophylaxis: Defined as broad spectrum antibiotics or antibiotics covering biliary pathogens prior to or directly after ERCP