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Original Article

Adverse events, success, and tolerability of biliary endoscopic retrograde cholangiopancreatography with conscious sedation vs anaesthesia: a multi-centre prospective study

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Abstract

Background and Aims: Endoscopic retrograde cholangiopancreatography (ERCP) is performed using anaesthesia or conscious sedation, though the effectiveness, adverse events (AEs), and tolerability of each approach remain unclear. Thus, we compared these approaches prospectively.

Methods: We performed a multi-centre prospective cohort study including patients with native papillae undergoing ERCP for biliary indications between 2018 and 2023. The primary outcome was sedation-related AEs, defined as sustained hypoxaemia or hypotension, unplanned mask ventilation or intubation, vasopressor or reversal agent use, cardiorespiratory arrest, or death. Secondary outcomes included other AEs, technical success measures, and patient-reported tolerability using a validated scale. Multivariable logistic regression was performed in addition to propensity score-matched analyses.

Results: At 8 centres, a total of 3174 first-time biliary ERCPs were performed, 433 (13.6%) employing anaesthesia. Nine sedation-related AEs occurred with conscious sedation (0.3%), while 2 (0.5%) occurred with anaesthesia (odds ratio, OR, 0.35, 0.07-2.37). Only 25 (0.9%) conscious sedation-supported ERCPs were aborted due to the inability to appropriately sedate patients. There were no significant differences in other AE rates, cannulation success, time, or attempts, use of pre-cut or needle-knife access methods, or inadvertent pancreatic duct cannulation. Odds of significant patient-reported intra-procedural awareness and discomfort were both higher with conscious sedation (ORs 16.19, 4.81-54.53, and 21.25, 4.44-101.61, respectively). Propensity score-matched analyses yielded no differences in any outcome compared with primary analyses.

Conclusions: Routine biliary ERCP is equally safe and effective with conscious sedation (vs anaesthesia). Given regional resource limitations, conscious sedation is justified as a primary option for routine biliary ERCP.

Key words: ERCP; AEs; performance and complications; sedation and monitoring.

Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) has several unique considerations when planning sedation that contribute to elevated risks of sedation-related adverse events (AEs).[1–7] Whereas anaesthetist-administered sedation for ERCP is common in certain regions,[8] endoscopist-directed conscious sedation remains the primary method of sedation for ERCP in others.[9] Anaesthetist-administered sedation involves either general endotracheal anaesthesia or deep sedation without an endotracheal tube (monitored anaesthesia care).

Studies directly comparing conscious sedation with anaesthesia during ERCP are scarce, varying widely in their designs and reaching conflicting conclusions regarding effectiveness and sedation-related AEs.[8–12] Furthermore, little is known regarding the sedation method as it relates to other common procedure-related AEs. Finally, relevant patient-reported experience measures in this field have been insufficiently studied to date,[13] representing another significant research gap.

The heterogenous nature and inconsistent findings of existing studies comparing anaesthetist-administered sedation and endoscopist-directed conscious sedation necessitate further study with data of higher granularity. Thus, by way of a large multi-centre prospective observational study, we aimed to compare these approaches during routine first-time biliary ERCP in terms of AEs, technical success, and patient-reported experiences.

Methods

Study design and settings

This was a multi-centre prospective study of patients undergoing ERCP at 8 centres in Canada and Europe. The study was registered (NCT05220774) with ethics approval at all participating centres, where ERCPs are performed using a combination of (endoscopist-directed) conscious sedation and anaesthesia-administered sedation, with the former approach supporting roughly 85% of ERCPs and the latter supporting the remaining 15% in pre-scheduled blocks during which patients deemed to require anaesthesia were primarily booked. However, a small proportion of patients requiring ERCP with no clear indications for anaesthesia are occasionally booked during these blocks, and the comparator group of this study comprised this small group.

Patients and variables

Patients undergoing ERCP between September 2018 and March 2023 were included if the following criteria were met. Inclusion criteria were (1) age ≥18 years, (2) any biliary indication, and (3) ability to provide informed consent. Exclusion criteria included *any* of: (1) prior ERCP, (2) any pancreatic indication, (3) planned cholangioscopy, (4) body mass index (BMI) ≥40, (5) abnormal or surgically altered upper gastrointestinal anatomy, (6) planned performance of >1 same-session endoscopic procedure, or (7) known history of difficult sedation or anaesthesia. All endoscopist-directed conscious sedation procedures were performed using combinations of fentanyl, midazolam, and/or diphenhydramine.

Patient- and procedure-related variables were captured via real-time observation by research assistants in addition to medical record review and patient interviews. Patients were also assessed using a patient-reported experience measure assessing intra and post-procedural tolerability that was previously validated in patients undergoing ERCP as well as colonoscopy and upper endoscopy.[14] All data were stored on a secure and encrypted data platform (REDCap, Vanderbilt University).[15]

Follow-up and outcomes

Thirty days after ERCP (+/– 5 days), research staff contacted patients using standardized scripts and performed medical record reviews.[16] The primary outcome was sedation-related AEs, defined as any of: oxygen saturation <85% for >60 seconds, requirement for mask ventilation or unplanned endotracheal intubation, intra-procedural use of one or more vasopressors or reversal agent(s), hypotension (defined as systolic blood pressure <90 mm Hg and requiring vasopressor treatment), cardiac and/or respiratory arrest, or death.[6,8] Secondary outcomes included other AEs, measures of technical success (cannulation success, time, and attempts, inadvertent pancreatic duct cannulation, rates of pre-cut methods (any use of the sphincterotome's cutting wire without established/confirmed deep biliary access—either via shallow suprapapillary pre-cut or a trans-pancreatic pre-cut) or needle-knife access (either needle-knife papillotomy or sphincterotomy), and overall ERCP procedure time from oesophageal intubation to extubation), and overall technical success by indication.[17,18] Within the definitions of technical success, a patient with a stone measuring up to 10 mm is expected to have this stone cleared, and ERCP would be deemed unsuccessful if a repeat procedure were booked. Finally, intra- and post-procedural patient tolerability was also a secondary outcome, with scores of >6/10 considered to represent poor tolerability.[14] Each potential AE was reviewed independently by 2 assessors blinded to the sedation method to ensure "definite" or "probable" relatedness to ERCP using a causal attribution schema.[19] Disagreements were resolved by a third reviewer.

Statistical analysis

Sample size calculations were based on existing studies.[3,10,11,20] To estimate the event rates in the conscious sedation group, we primarily inferred from observational studies in which criteria for sedation-related AEs aligned with ours (0.7%-3.7%).[10,20,21] For anaesthesia, in one of these studies, only one event was observed,[10] and in another, the rate was 0.4%.[21] Therefore, to be conservative, we attenuated the difference between these 2 rates and, assuming a 2-sided alpha of 0.05, a power of 80.0%, and an anticipated absolute risk reduction in sedation-related AEs from 3.0% using conscious sedation to 0.5% using anaesthesia, we calculated that a minimum of 431 procedures would need to be included in each group to demonstrate this difference. Student's *t*-tests were used to compare continuous variables, and chi-squared tests were used to compare categorical variables. Confidence intervals (95% CIs) were calculated and reported. *P*-values of <.05 were considered significant for the primary outcome. For all secondary outcomes (those other than sedation-related AEs), Bonferroni's correction for multiple outcomes was applied, increasing the significance threshold to 0.003 and changing CIs from 95% to 97.7%.

Analyses to determine differences in outcomes used multivariable logistic regression and multiple linear regression,

reported using adjusted odds ratios (ORs) or adjusted mean differences. Covariates included any variables that could potentially impact procedural success, AEs, or tolerability. Because the primary outcome is rare, Firth logistic regression was used, applying a penalized likelihood estimation method to reduce bias.[22]

As a sensitivity analysis, propensity scores were created, comprising variables potentially indicative of higher procedural complexity. Calliper matching (0.25 times the SD of the propensity score) without replacement was performed to match conscious sedation and anaesthesia-supported procedures 1:1, after which conditional logistic regression was applied, with any covariates with standardized mean difference >10% adjusted for.

Results

Descriptive characteristics

Between September 2018 and May 2023, 3174 first-time biliary ERCPs were performed by 37 endoscopists across 8 centres, with 433 (13.6%) of these employing anaesthesia-administered sedation (Figure 1). Endoscopists had a mean of 15 years in independent practice (SD, 12) and performed an estimated mean of 312 ERCPs annually (SD 91). Female patients comprised 52.5% of the cohort and the mean age was 61.2 years. Mean Charlson Comorbidity Index scores were comparable (3.14, SD 2.81 in the conscious sedation group vs 2.96, SD 2.91 in the anaesthesia group, P = .24). A total of 9 sedation-related AEs occurred with conscious sedation (0.3%), while 2 (0.5%) occurred with anaesthesia (P >.99). These events included transient hemodynamic instability (n=5), use of reversal agents (n=3), transient hypoxaemia requiring bag mask ventilation (n=2), and cardiac arrest with subsequent intensification and recovery (n=1).

Overall procedural success was 91.5% in the conscious sedation group and 90.1% in the anaesthesia group (P =.62). Of the failed procedures, 25 ERCPs (0.9%) in the conscious sedation group were aborted due to the inability to appropriately sedate the patient. Major AEs occurred at a rate of 10.1% and 11.2% in the conscious sedation and anaesthesia groups, respectively (P =.33). Full patient and procedure characteristics of ERCPs compared between groups are provided in Table 1. Comparisons between conscious sedation, monitored anaesthesia care, and general anaesthesia are provided in the Supplementary Materials, as are additional anaesthesia-related data including Mallampati class, history of adverse anaesthesia reactions, body mass index, presence of diagnosed sleep apnoea and associated scoring,[23] American Society of Anesthesiologists score,[24] and total anaesthesia time. Propensity score matching achieved adequate balances of covariates, with no P-values of <.05 observed following 1:1 matching of patients.

Primary outcome and other AEs

The use of conscious sedation was not associated with an increase in sedation-related AEs (odds ratio [OR] 0.35, 95% CI, 0.04-2.55) compared with anaesthesia. There

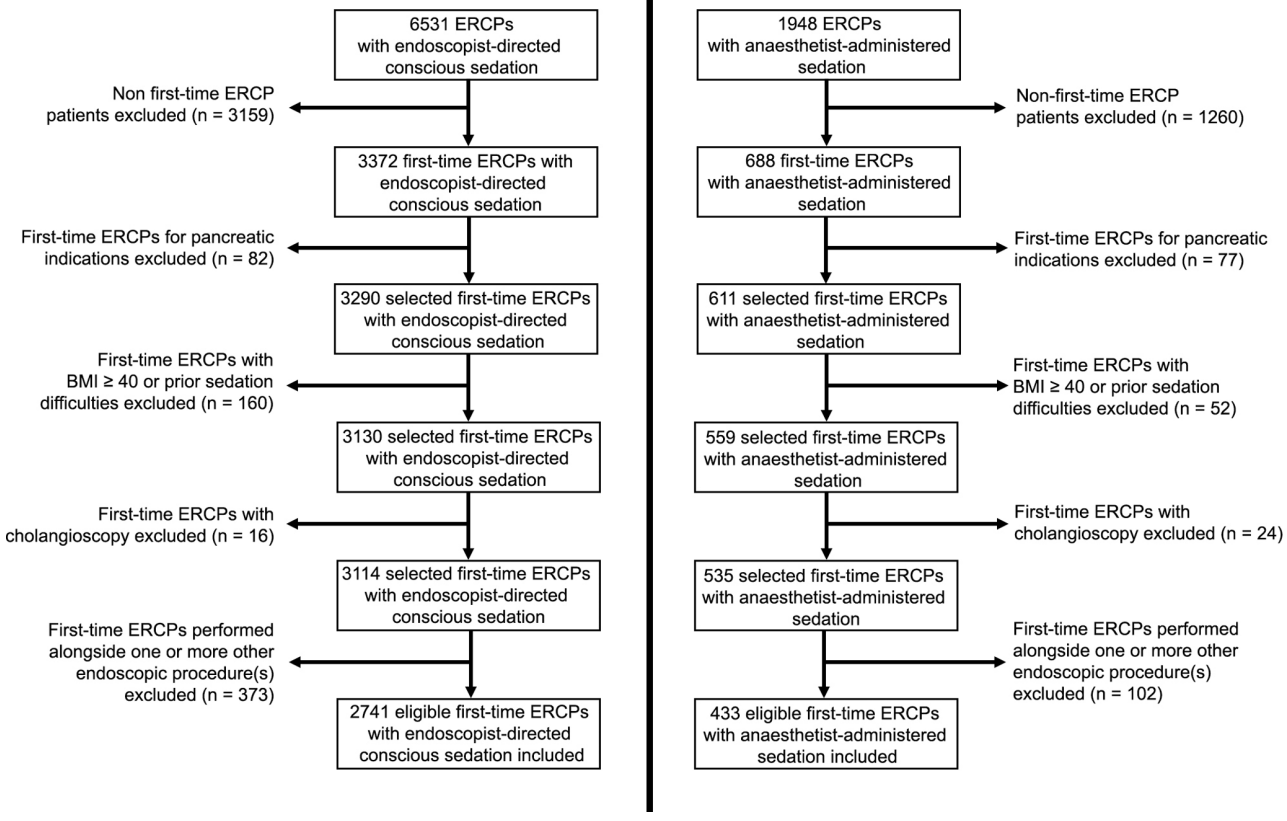

Figure 1. Study flow chart showing excluded cases with reasons for exclusion according to eligibility criteria.

Table 1. Patient- and procedure-related characteristics compared for patients undergoing ERCP with EDCS vs AAS.

	EDCS (n = 2741)	AAS (n = 433)	P-value
Female sex (%)	1451 (52.9)	216 (49.9)	.26
Mean age (SD)	64.0 (17.7)	58.9 (18.3)	.004
Patient disposition			.23
Inpatient (%)	1775 (64.8)	294 (67.9)	
Outpatient (%)	965 (35.2)	139 (32.1)	
Mean Charlson Comorbidity Index (SD)	3.1 (2.8)	3.0 (2.9)	.24
Mean body mass index (SD)	31.6 (12.8)	28.3 (6.7)	.78
Procedural indication			.005
CBD stones (%)	1581 (57.7)	224 (51.7)	
Biliary stricture (%)	238 (8.7)	35 (8.1)	
Bile leak (%)	140 (5.1)	16 (3.7)	
Cholangitis (%)	128 (4.7)	18 (4.2)	
Other (%)	654 (23.9)	140 (32.3)	
Cannabinoid use at baseline (%)	581 (21.2)	66 (15.2)	.005
Opioid use at baseline (%)	333 (12.1)	43 (9.9)	.21
Moderate or heavy EtOH use at baseline (%)	512 (18.7)	61 (14.1)	.02
Mean midazolam dose, mg (SD)	5.1 (7.8)	N/A	N/A
Mean fentanyl dose, mcg (SD)	97.6 (41.2)	N/A	N/A
Mean diphenhydramine dose, mg (SD)	47.0 (9.0)	N/A	N/A
Rectal NSAID for PEP prophylaxis (%)	1617 (59.0)	259 (59.8)	.86
Trainee involved (%)	1557 (56.8)	164 (37.9)	<.001
Cannulation attempts			.92
1 or 2 (%)	1063 (38.8)	176 (40.6)	
3 to 5 (%)	695 (25.4)	105 (24.2)	
6 to 10 (%)	364 (13.3)	57 (13.2)	
>10 (%)	417 (15.2)	66 (15.2)	
Mean cannulation time in minutes (SD)	6.6 (8.8)	7.2 (9.4)	.23
Pre-cut methods performed (%)	294 (10.7)	31 (7.2)	.03
Needle-knife access performed (%)	333 (12.1)	62 (14.3)	.23
Balloon sphincteroplasty performed (%)	412 (15.0)	59 (13.6)	.53
PD cannulation (%)	846 (30.9)	132 (30.5)	.93
CBD stent(s) placed (%)	814 (29.7)	158 (36.5)	.07
PD stent(s) placed (%)	353 (12.9)	71 (16.4)	.05
Overall procedure time, minutes (SD)	23.3 (14.8)	25.9 (19.0)	.007
Overall procedural success (%)	2508 (91.5)	390 (90.1)	.62
Aborted due to sedation failure (%)	25 (0.9)	0 (0.0)	.12

Abbreviations: AAS, anaesthesia-assisted sedation; CBD, common bile duct; EDCS, endoscopist-directed conscious sedation; ERCP, endoscopic retrograde cholangiopancreatography; EtOH, ethyl alcohol; NSAID, non-steroidal anti-inflammatory drug; PD, pancreatic duct; PEP, post-ERCP pancreatitis.

were no significant differences between conscious sedation and anaesthesia in terms of pancreatitis (OR 0.85, 95% CI, 0.47-1.53), cholangitis (OR 0.68, 95% CI, 0.33-1.41), cardiorespiratory events (OR 1.02, 95% CI, 0.45-2.33), clinically significant bleeding (OR 3.66, 95% CI, 0.83-16.05), or perforation (only 3 events across both groups). ORs from multivariable analyses for AEs are provided in Table 2. Propensity score-matched analyses yielded no differences with regards to the primary outcome (OR for sedation-related AEs 0.60, 95% CI, 0.05-4.52) or other AEs, technical success, peri-procedural parameters, or patient-reported experiences compared with primary analyses (Supplementary Materials).

Technical success and peri-procedural parameters

There were no differences in technical success between conscious sedation and anaesthesia groups (OR 1.21, 97.7% CI, 0.36-4.08). Cannulation time was similar (mean difference –0.59 minutes, 97.7% CI, –2.10 to +0.92 minutes), as was the total number of cannulation attempts (OR 1.10, 95% CI, 0.72-1.68 for >5 attempts vs ≤5). The use of pre-cut or needle-knife access was also similar (OR 1.31, 97.7% CI, 0.81-2.11). The odds of inadvertent pancreatic duct cannulation were similar (OR 0.98, 97.7% CI, 0.60-1.62), as were the odds of performing a pancreatogram, partial or full (OR 1.46, 97.7% CI, 0.60-3.52). Overall procedure time was lower for conscious sedation procedures

Table 2. Adjusted odds ratios of AEs for patients undergoing ERCP with EDCS vs AAS from multivariable Firth's logistic regression and with propensity score matching.

	SRAE	PEP	Bleeding	Cholangitis	Cardiorespiratory AE
Adjusted odds ratio for EDCS vs AAS (confidence intervals[a])	0.35 (0.07-2.37)	0.83 (0.36-2.16)	2.92 (0.56-46.41)	0.67 (0.24-2.13)	0.98 (0.32-3.83)
***P*-value**	.26	.53	.07	.28	.96
Number of events/total patients in EDCS group	9/2741	120/2741	41/2741	55/2741	51/2609
Number of events/ total patients in AAS group	2/433	18/433	3/433	15/431	10/430
Adjusted odds ratio for EDCS vs AAS after propensity score matching (confidence intervals[a])	0.60 (0.05-4.52)	1.07 (0.36-3.21)	4.30 (0.69-70.88)	0.84 (0.22-3.00)	1.26 (0.31-5.50)
***P*-value**	.61	.86	.02	.67	.62
Number of events/ total patients in EDCS group	1/363	16/363	10/363	10/363	10/363
Number of events/ total patients in AAS group	2/363	15/363	2/363	12/363	8/363

Multivariable models included sex, age, Charlson comorbidity index, disposition, indication, cannabinoid use, opioid use, EtOH use, and trainee involvement. Propensity scores included the above variables in addition to ASGE complexity grade, rectal NSAID use, pancreatic stent placement, biliary stent placement, use of double wire technique, and use of pre-cut or needle-knife access methods.
[a]95% confidence intervals for SRAE; 99.7% confidence intervals for all other outcomes following Bonferroni's correction.
Abbreviations: AE, adverse event; AAS, anaesthesia-assisted sedation; EDCS, endoscopist-directed conscious sedation; ERCP, endoscopic retrograde cholangiopancreatography; PEP, post-ERCP pancreatitis; SRAE, sedation-related AE.

Table 3. Adjusted odds ratios of technical success and peri-procedural parameters for patients undergoing ERCP with EDCS vs AAS from multivariable logistic or linear regression, and with propensity score matching.

	Failure of ERCP	Procedure time in min.	Cannulation time in min.	Cannulation attempts (greater than 5 vs 5 or fewer)	Use of pre-cut or needle-knife access methods	PD cannulation	Pancreatogram
Adjusted odds ratio for EDCS vs AAS (confidence intervals[a])	1.21 (0.36-4.08)	–2.74 (–5.14, –0.35)	–0.59 (–2.10, 0.92)	1.10 (0.72-1.68)	1.31 (0.81-2.11)	0.98 (0.60-1.62)	1.46 (0.60-3.53)
***P*-value**	.64	.001	.25	.52	.10	.92	.21
Adjusted odds ratio for EDCS vs AAS after propensity score matching (confidence intervals[a])	0.75 (0.27-2.06)	–3.31 (-7.03, 0.42)	–0.54 (–2.75, 1.67)	1.07 (0.66-1.73)	1.27 (0.75-2.15)	1.01 (0.63-1.62)	2.00 (0.73-5.46)
***P*-value**	.40	.009	.47	.68	.18	.94	.04

Multivariable models included sex, age, Charlson comorbidity index, disposition, indication, cannabinoid use, opioid use, EtOH use, and trainee involvement. Propensity scores included the above variables in addition to ASGE complexity grade, rectal NSAID use, pancreatic stent placement, biliary stent placement, use of double wire technique, and use of pre-cut or needle-knife access methods.
[a]95% confidence intervals for SRAE; 99.7% confidence intervals for all other outcomes following Bonferroni's correction.
Abbreviations: AAS, anaesthesia-assisted sedation; EDCS, endoscopist-directed conscious sedation; ERCP, endoscopic retrograde cholangiopancreatography; PD, pancreatic duct.

(mean difference -2.74 minutes, 97.7% CI, –5.14 to –0.35 minutes). ORs from multivariable analyses for intra-procedural parameters and technical success are provided in Table 3.

Patient-reported experiences

Significant intra-procedural awareness, defined as a score >6 on the Patient-reported Scale for Tolerability of Endoscopic Procedures, was higher with conscious sedation compared with anaesthesia (OR 16.19, 97.7% CI, 4.81-54.53), as was significant intra-procedural discomfort (OR 21.25, 97.7% CI, 4.44-101.61). Symptoms at discharge were similar between groups, including post-procedural abdominal pain, throat pain, nausea, and distention. ORs from multivariable analyses for patient-reported experiences are provided in Table 4.

Discussion

Our study found no significant differences in sedation-related or other AEs between endoscopist-directed conscious sedation and anaesthesia-administered sedation in a large multi-centre prospective cohort undergoing first-time biliary ERCP. Similarly, all technical parameters were equivalent. While intra-procedural tolerability of ERCPs from the patient perspective was expectedly poorer with conscious sedation, symptoms at discharge were similar between groups. Overall, our results demonstrate that conscious sedation is safe, effective, and well-tolerated for routine first-time biliary procedures.

The transition to widespread utilization of anaesthesia for ERCP in the United States has occurred despite a relative paucity of data directly comparing approaches for patients undergoing ERCP.[10,12] The perceived advantages are likely

Table 4. Adjusted odds ratios of patient-reported experience measures for patients undergoing ERCP with EDCS vs AAS from multivariable logistic regression and with propensity score matching.

	Intra-procedural awareness (PRO-STEP >6)	Intra-procedural discomfort (PRO-STEP >6)	Post-procedural abdominal pain (PRO-STEP >6)	Post-procedural throat pain (PRO-STEP >6)	Post-procedural nausea (PRO-STEP >6)	Post-procedural distention (PRO-STEP >6)
Adjusted odds ratio for EDCS vs AAS (confidence intervals[a])	16.19 (4.81-54.53)	21.25 (4.44-101.61)	0.64 (0.32-1.25)	0.51 (0.21-1.27)	0.47 (0.19-1.15)	0.92 (0.27-3.15)
***P*-value**	<.001	<.001	.05	.03	.01	.84
Adjusted odds ratio for EDCS vs AAS after propensity score matching (confidence intervals[a])	11.49 (3.33-39.61)	15.40 (3.16-75.09)	0.77 (0.34-1.73)	0.46 (0.13-1.67)	0.59 (0.19-1.78)	0.89 (0.19-4.08)
***P*-value**	<.001	<.001	.34	.07	.15	.82

Multivariable models included sex, age, Charlson comorbidity index, disposition, indication, cannabinoid use, opioid use, EtOH use, and trainee involvement. Propensity scores included the above variables in addition to ASGE complexity grade, rectal NSAID use, pancreatic stent placement, biliary stent placement, use of double wire technique, and use of pre-cut or needle-knife access methods.
[a]95% confidence intervals for SRAE; 99.7% confidence intervals for all other outcomes following Bonferroni's correction.
Abbreviations: AAS, anaesthesia-assisted sedation; EDCS, endoscopist-directed conscious sedation; ERCP, endoscopic retrograde cholangiopancreatography; PRO-STEP, patient-reported scale for tolerability of endoscopic procedures.

2-fold. First, a dedicated anaesthesia professional is able to identify impending AEs more quickly, and second, alternative medications used during anaesthesia, namely propofol, carry independent advantages when administered by appropriately trained personnel.[25–28] From randomized trials, these advantages can include shorter recovery times[25,26] and better procedural cooperation,[26,27] albeit with similar patient-reported satisfaction and tolerability.[26,28] However, mainly due to a lack of training and certification, endoscopist-administered propofol for conscious sedation is not widely utilized.

We analysed over 3000 first-time biliary ERCP patients, under 15% of which were performed with anaesthesia-administered sedation. Patients with BMI >40,[7] pancreatic indications, and cholangioscopy were all excluded to minimize selection bias. The few studies comparing conscious sedation with anaesthesia have varied widely in methodology and results. One study reported a higher rate of unplanned interventions for sedation-related AEs with conscious sedation,[8] and others reported higher rates of sedation failure with conscious sedation.[10,12] Conversely, in a 2018 non-randomized study, composite AEs were significantly lower in the conscious sedation group, with significantly shorter procedure and turnover times and no differences in cannulation or overall procedural success.[11]

Our study expands on existing knowledge in important areas. First, our study used a validated tool to assess intra- and post-procedural tolerability. A single-arm survey suggested that many patients undergoing ERCP with conscious sedation report pain, discomfort, and mental distress,[13] but it was limited by the use of a generic quality of life assessment tool not validated for use in gastrointestinal endoscopy. Moreover, this survey study did not have a group that received anaesthesia, and therefore, these outcomes are difficult to interpret comparatively. In our study, we identified lower reported intra-procedural tolerability of ERCP with conscious sedation compared with anaesthesia. However, at discharge, there were no differences in abdominal pain, throat pain, nausea, or distention between groups. This is particularly noteworthy given the known residual effects of ERCP in the day(s) following the procedure.[13] Second, the high level of data granularity achieved by our approach allowed for the assessment of the effect of sedation modality on various procedural parameters and outcomes. Prior studies have been limited by their design in their abilities to compare ERCP outcomes and AEs between our 2 groups of interest.[10–12] Using granular data, we did not identify any significant differences in sedation-related or other AEs. Intra-procedural performance parameters were also similar, further demonstrating the equivalence of both approaches. In addition, it is also noteworthy that ERCPs can be performed more efficiently with a conscious sedation approach, given that faster room turnover between cases is possible compared with anaesthesia-supported ERCP.

It is important to frame the results of this study in the context of its eligibility criteria. Specifically, patients with certain characteristics resulting in higher sedation risks (e.g., severe obesity, prior failed conscious sedation) were excluded, as were patients for whom a potentially long and/or complex procedure was planned (e.g., pancreatic indications or cholangioscopy). These are scenarios in which anaesthesia is clearly the preferred choice when available, both for safety considerations and potentially to avoid rebooking of procedures that could have otherwise been completed in a single session. Recent British Society of Gastroenterology guidance states that routine (Level I or II) ERCP can safely performed using conscious sedation, but that more complex ERCP likely benefits from anaesthesia support.[29] Our data strongly support the effectiveness and safety of a conscious sedation-based approach to routine biliary ERCP, given a reasonable and acceptable <1% sedation-related failure rate and comparable effectiveness and safety. This failure rate of <1% is consistent with a large observational study in which 27 of 7588 (0.4%) ERCPs with conscious sedation were aborted for sedation failure.[8] While centres that rely solely on anaesthesia for ERCP are unlikely to revert back to conscious sedation, our results provide useful knowledge to regions that continue to utilize conscious sedation for ERCP in large volumes—that in the vast majority of patients, this approach is safe and does not compromise technical success. The increased intra-procedural awareness and discomfort for patients undergoing ERCP with conscious sedation also need to be highlighted. While thankfully transient, the importance of such patient-reported measures should not be minimized

and should play a clear role in the selection of a sedation plan in addition to serving as an important area for future research.

Our study has limitations. First, variability existed within the anaesthesia group in our study, where either monitored anaesthesia care or general anaesthesia was used discretionarily. These techniques have been studied separately in the past,[3] but were grouped for our purposes. Nevertheless, supplementary analyses revealed no differences in outcomes between these groups. Second, though we adjusted for measured confounders through multivariable logistic regression modelling and propensity score matching and by including several highly granular covariates, we were unable to control for unmeasured confounders, a limitation only addressed by employing an randomized controlled trial design. For example, it could be argued that there could be a tendency for endoscopists to prematurely terminate and rebook cases performed under conscious sedation, but, in fact, our data demonstrate equivalent biliary stent placement rates between groups, arguing against this criticism. Furthermore, our definitions of procedural success were established a priori and incorporate reasonable expectations of success by indication. Additionally, it is important to note that our study was powered for the primary outcome of sedation-related AEs, and therefore, was underpowered for secondary outcomes; however, most point estimates favoured conscious sedation for all non-tolerability-related outcomes, making it unlikely that a larger sample would favour anaesthesia-based approaches. Finally, while we used a validated tool to assess intra- and post-procedural tolerability of ERCP, we did not collect data on nurse-led comfort scores, which could have been useful in terms of comparing a separate objective measurement of procedural tolerability to our data.

In conclusion, our large prospective multi-centre study demonstrates no differences in overall AEs or technical success between anaesthesia-administered sedation and endoscopist-directed conscious sedation for patients undergoing first-time biliary ERCP. Worse self-limited intra-procedural awareness and discomfort were associated with the use of conscious sedation, with no differences in patient-reported symptoms at the time of discharge. These findings are important as they confirm the validity of conscious sedation, which is especially relevant for practice settings with limited availability of anaesthetists. Within such settings, further work should be performed to develop clear criteria for procedures requiring anaesthesia vs conscious sedation.

Supplementary material

Supplementary material is available at *Journal of the Canadian Association of Gastroenterology* online.

Author contributions

Nauzer Forbes and Zachary L. Smith (conception and design). Zachary L. Smith, Ahmed Kayal, and Nauzer Forbes (drafting of the article). All authors (analysis and interpretation of the data, critical revision of the article for important intellectual content, final approval of the article).

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Conflicts of interest

None relevant to this work.

Conflict of interest disclosure forms (ICMJE) have been collected for all co-authors and can be accessed as supplementary material here.

Data availability

Data are potentially available upon reasonable request to the corresponding author.

Ethics statement

- Approval of the research protocol by an Institutional Reviewer Board: this study was approved by the Conjoint Health Research Ethics Board of the University of Calgary (REB21-1887).

- Informed Consent: informed consent was provided for all enrolled patients.

- Registry and the Registration No. of the study/trial. Though not a clinical trial, this prospective study was registered on *clinicaltrials.gov* (NCT05220774).

- Animal Studies: N/A.

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