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Safety and efficacy of physician-administered balanced-sedation for the endoscopic mucosal resection of large non-pedunculated colorectal polyps

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ABSTRACT

Background and study aims Because of concerns about peri-procedural adverse events (AEs), guidelines recommend anesthetist-managed sedation (AMS) for long and complex endoscopic procedures. The safety and efficacy of physician-administered balanced sedation (PA-BS) for endoscopic mucosal resection (EMR) of large non-pedunculated colorectal polyps (LNPCPs) ≥20 mm is unknown.

Patients and methods We compared PA-BS with AMS in a retrospective study of prospectively collected data from consecutive patients referred for management of LNPCPs (NCT01368289; NCT02000141). A per-patient propensity analysis was performed following a 1:2 nearest-neighbor (Greedy-type) match, based on age, gender, Charlson comorbidity index, and lesion size. The primary outcome was any peri-procedural AE, which included hypotension, hypertension, tachycardia, bradycardia, hypoxia, and new arrhythmia. Secondary outcomes were unplanned admissions, 28-day re-presentation, technical success, and recurrence.

Results Between January 2016 and June 2020, 700 patients underwent EMR for LNPCPs, of whom 638 received PA-BS. Among them, the median age was 70 years (interquartile range [IQR] 62–76 years), size 35 mm (IQR 25–45 mm), and duration 35 minutes (IQR 25–60 minutes). Peri-procedural AEs occurred in 149 (23.4%), most commonly bradycardia (116; 18.2%). Only five (0.8%) required an unplanned sedation-related admission due to AEs (2 hypotension, 1 arrhythmia, 1 bradycardia, 1 hypoxia), with a median inpatient stay of 1 day (IQR 1–3 days). After propensity-score matching, there were no differences between PA-BS and AMS in peri-procedural AEs, unplanned admissions, 28-day re-presentation rates, technical success or recurrence.

Conclusions Physician-administered balanced sedation for the EMR of LNPCPs is safe. Peri-procedural AEs are infrequent, transient, rarely require admission (<1%), and are experienced in similar frequencies to those receiving anesthetist-managed sedation.

Introduction

Sedation is increasingly being utilized to facilitate safe and effective upper and lower gastrointestinal endoscopy. Options include anesthetist-managed sedation (AMS) or physician-administered (PA) approaches. Specific to PA approaches, this may involve propofol monotherapy (PA-PM), standard sedation (PA-SS; benzodiazepine plus opioid) or balanced sedation (PA-BS; benzodiazepine plus opioid plus propofol) [1].

While PA approaches have been evaluated for complex upper endoscopic procedures, including endoscopic ultrasonography, endoscopic retrograde cholangiopancreatography, and antegrade balloon enteroscopy [2, 3], it has not been assessed in the setting of complex procedures within the colorectum, such as the endoscopic mucosal resection (EMR) of large non-pedunculated colorectal polyps (LNPCPs) ≥20 mm.

Because EMR has become firmly established as the cornerstone of LNPCP management, deemed as being safer and cheaper than surgery or endoscopic submucosal dissection (ESD) [4, 5, 6, 7, 8], the EMR technique is now performed in upwards of 2.48% of all colonoscopies in the United States [9]. Furthermore, complex lesions, such as those that have been previously attempted [10] or those located at the anorectal junction [11] or ileocecal valve [12], can be safely managed with EMR. In addition, technical advances have led to the adoption of adjunctive techniques, including recognition and management of deep mural injury (DMI) [13, 14], thermal ablation of the defect margin with snare-tip soft coagulation (STSC) to reduce the risk of recurrence [15], and cold avulsion with adjuvant snare-tip soft coagulation (CAST) for targeting non-lifting areas [16]. For these aforementioned reasons, it is unsurprising that LNPCP management requires expertise, dedicated time, cost and resources to perform.

We hypothesize that PA-BS may offer an intrinsic benefit in colorectal EMR procedures through the ability to administer incremental doses of propofol to maintain conscious sedation, after induction with a benzodiazepine and opioid. This may help to promote patient cooperation, maneuvers, and repositioning, and by extension, aid endoscopic visualization and resection [1]. Therefore, the aim of our study was to compare the safety and efficacy of PA-BS to AMS for the EMR of LNPCPs ≥20 mm.

Patients and methods

This manuscript was produced with guidance from the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) recommendations [17].

Endoscopic mucosal resection (EMR) technique

A standardized previously described inject and resect EMR technique was used [18, 19, 20, 21, 22]. All endoscopic procedures were performed by either a study investigator (accredited gastroenterologist with advanced training and an established tertiary referral practice in colorectal endoscopic resection) or a senior interventional endoscopy fellow under their supervision. Antiplatelet and anticoagulation medications were withheld pre-procedure, in accordance with consensus recommendations [23].

Currently, all colorectal EMRs are performed using high-definition Olympus 190 series variable-stiffness colonoscopes (Olympus, Tokyo, Japan). Carbon dioxide is used for insufflation. After lesion identification, optical evaluation under high-definition white-light and narrow-band imaging is performed to exclude features of submucosal invasive cancer (SMIC). In a systematic fashion, a submucosal cushion is created with injection of succinylated gelatin (Gelofusine; B. Braun, Bella Vista, Australia) with 0.4% indigo carmine and 1:100,000 epinephrine. Using a microprocessor-controlled generator (Erbe VIO Endo Cut Q, Effect 3; Erbe, Tubingen, Germany) snare excision is performed [18].

After complete resection, the defect is carefully examined to ensure no polypoid tissue remains and to assess for deep mural injury (DMI) [13]. Areas of significant injury (DMI III-V) are subsequently treated by mechanical clip closure. Thermal ablation of the resection margin to mitigate the risk of recurrence is performed using STSC (Erbe VIO Soft Coag: 80 W, Effect 4; Erbe, Tubingen, Germany) to create a 2-to 3-mm rim of ablated tissue. Clinically significant intra-procedural bleeding is treated with coagulation forceps or mechanical hemostasis. The resected defect of LNPCPs located in the proximal colon are closed with mechanical clips to reduce the risk of clinically significant post-EMR bleeding [24]. Resection specimens are collected and evaluated by specialist gastrointestinal pathologists. Where appropriate, histopathology is confirmed with surgical specimen evaluation.

After completion of the procedure, patients are observed for 4 hours. If well, they are subsequently discharged on a clear fluid diet overnight. At 2 weeks, patients are contacted by a study coordinator and undergo a structured telephone interview to identify peri-procedural adverse events (AEs).

Sedation

At our institution, two proceduralists are involved in each complex tissue resection, including colorectal EMR. This typically comprises one study investigator (consultant gastroenterologist) and one senior interventional endoscopy fellow. The sedation options at our institution include either AMS or PA-BS, with PA-PM and PA-SS not offered. Thus, when utilizing PA-BS, one proceduralist is responsible for the administration of sedation medications and monitors the patient from a sedation perspective. PA-BS involved administration of low-dose of fentanyl (50 µg) and midazolam (2 mg) for induction, followed by intermittent boluses of propofol (10 mg) to maintain sedation.

Comparatively, AMS was performed by a qualified anesthetist, and involved an initial low dose of fentanyl and midazolam. This was followed by either intermittent boluses of propofol or use of a target-controlled infusion of propofol (TCI), at the discretion of the anesthetist. In addition, a dedicated anesthetic nurse was present for patient monitoring. During AMS, both proceduralists (study investigator and fellow) remained present for the entirety of the case.

All proceduralists (consultants and fellows) are formally trained in advanced life support, including the provision of air-

way support. Nursing staff are trained in basic life support. All proceduralists and nursing staff attend a formal sedation safety course (theoretical and practical) facilitated by our institution's anesthetic department annually.

All patients were oxygenated during the procedure through nasal prongs. Patients were pre-assigned to either the PA-BS or AMS group based on numerous factors, including pre-procedure assessment by a gastroenterologist (standard in our institution), availability of anesthetic lists and personnel, and experience of the proceduralists.

Study design

We sought to evaluate the safety of PA-BS vs. AMS in a retrospective study of prospectively collected data in a single-center cohort of consecutive patients who underwent EMR for the management of LNPCPs ≥20 mm between January 2016 and June 2020, after the introduction of electronic records software, which documented all anesthetic and procedure related parameters (NCT01368289; NCT02000141). Written informed consent was gained from each patient. Lesions that underwent ESD or piecemeal cold-snare polypectomy (P-CSP) were excluded from analysis. Lesions were classified as complex if they had been previously attempted or if they were located at the anorectal junction (ARJ) or ileocecal valve (ICV).

Using SPSS Statistics V26 (IBM, Armonk, New York, United States) software, a per-patient propensity analysis was performed following a 1:2 nearest-neighbor (Greedy-type) match, based on age, gender, Charlson comorbidity index (CCI) and lesion size. A one AMS to two PA-BS ratio was chosen to include as many PA-BS cases as possible in the propensity analysis without compromising accuracy of the match. In keeping with numerous studies pertaining to advanced endoscopy, baseline patient demographics, including comorbidities were recorded to calculate the CCI. This is a weighted index that assigns a different risk score (from 1 to 6) to 22 conditions, with a higher score indicating a greater 1-year mortality risk. Data related to the procedure, including the sedation strategy were systematically recorded.

Data extraction

Prospectively collected data included: 1) Patient characteristics: age, sex, American Society of Anesthesiologists (ASA) classification, CCI; 2) Lesion characteristics: location, size, Paris classification, surface granularity; 3) Resection characteristics: attempted en-bloc resection, presence of submucosal fibrosis; 4) Peri-procedural AEs; 5) Histopathology evaluation; 6) Post-procedural AEs: delayed perforation, hospitalization; 7) Admission and re-presentation rates; 8) Surveillance: endoscopic and histologic recurrence.

Patient follow-up was performed at 14 days post-EMR by dedicated research staff using a structured telephone interview to collect data regarding post-procedural AEs in accordance with American Society for Gastrointestinal Endoscopy (ASGE) guidelines [25]. Additional follow-up data were obtained at first surveillance colonoscopy (SC1) at 6 months and thereafter.

Outcomes

The primary outcome was any peri-procedural AE occurring during the procedure and in recovery. This was composed of hypotension (SBP <90 mm Hg), hypertension (SBP >190 mm Hg), tachycardia (HR >150 bpm), bradycardia (HR <50 bpm), sustained hypoxia (SpO_2 <90% for 30 seconds that did not respond to chin lift or jaw thrust or the need for oropharyngeal/nasopharyngeal devices) and new arrhythmia. Peri-procedural AEs were monitored and documented by an anesthetist (AMS group) or second proceduralist (PA-BS group).

Secondary outcomes were successful EMR, overall unplanned admission rates, sedation-related unplanned admission rates, length of stay, 28-day re-presentation, recurrence at surveillance colonoscopy (SC1), and post-procedural events, composed of pain, rectal bleeding and nausea/vomiting.

Statistical analysis

SPSS Statistics V26 (IBM, Armonk, New York, United States) and R software (Vienna, Austria) [26] were used to conduct all statistical analyses. Continuous values were summarized as median and interquartile range (IQR) or mean and standard deviation (SD) as appropriate. Categorical values were summarized as relative frequencies and percentages (%). Baseline parameters and outcomes between the PA-BS and AMS groups were compared using Wilcoxon rank-sum tests for continuous variables and Fisher's exact tests for categorical variables. Logistic regression was used to estimate unadjusted odds ratios (ORs). We used a significance level 5% and present two-sided *P* values for all hypotheses.

A per-patient propensity analysis was performed following the calculation of propensity scores between the AMS and PA-BS groups based on the covariates age, gender, CCI, and LNPCP size. Following this, we conducted a 1:2 nearest-neighbor (Greedy-type) matching of the SD of the logit of the propensity scores with a caliper width of 0.2, to obtain two comparable groups. Matching was performed without replacement and unpaired patients were excluded.

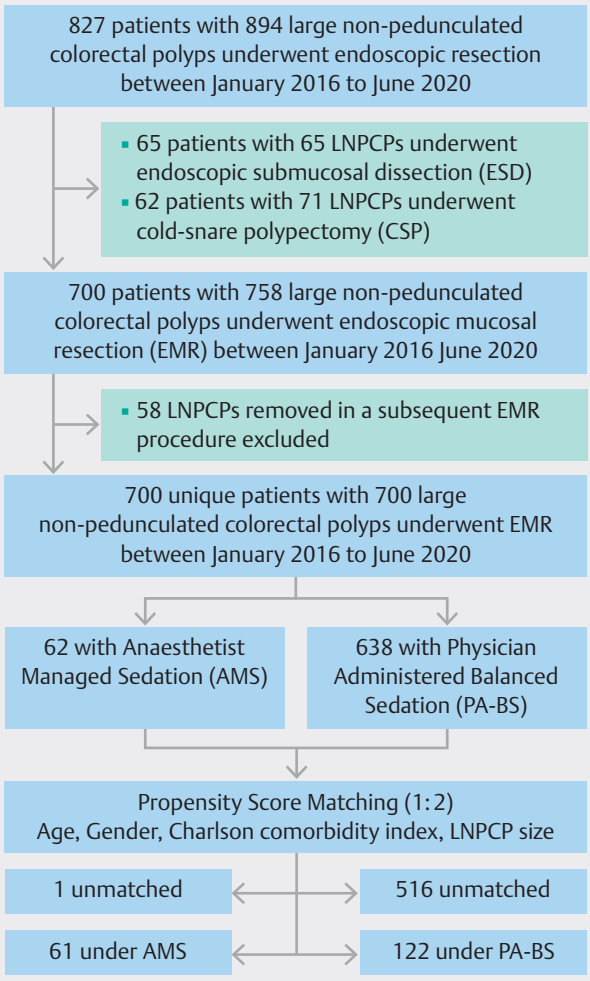
Results

Participants

Between January 2016 and June 2020, 700 patients underwent EMR for LNPCPs (▶ **Fig. 1**). A total of 638 (91.1%) received PA-BS (median age 70 years [IQR 62–76 years]; 339 [53.1%] male; ▶ **Table 1**). The use of PA-BS gradually increased from 87.1% in 2016 to 95.8% in 2020.

Patients undergoing PA-BS were likely to be younger (median 70 years [IQR 62–76 years] vs. 74 years [IQR 67–81 years], *P*= 0.002) and less comorbid (CCI 3 [IQR 2–4] vs. 4 [2]–[5], *P*= 0.001). Comorbidities such as atrial fibrillation, congestive cardiac failure, renal failure, and respiratory conditions were less likely in the PA-BS group when compared with AMS (▶ **Table 1**). Following matching, there was no difference in these comorbidities between the two groups.

In the PA-BS group, median propofol dose was 300 mg [IQR 200–500mg]. Low-dose fentanyl and midazolam were also ad-



▶ **Fig. 1** Flow of patients referred for the endoscopic management of large non-pedunculated colorectal polyps (LNPCPs). CSP, cold-snare polypectomy; EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection; PA-BS, physician-administered balanced sedation.

ministered in 628 (98.4%) and 624 patients (99.4%), respectively. Median lesion size was 35 mm (IQR 25–45 mm). Procedural duration was 35 minutes (IQR 25–60 minutes).

Procedural sedation outcomes prior to matching

In the PA-BS group, peri-procedural AEs occurred in 149 patients (23.4%), the most common being bradycardia (116; 18.2%; ▶ **Table 2**). Only five patients (0.8%) required an unplanned sedation-related admission due to AEs (2 hypotension, 1 arrhythmia, 1 bradycardia, 1 hypoxia), with a median inpatient stay of 1 day (IQR 1–3 days). There were no differences in peri-procedural AEs, overall unplanned admissions, unplanned admissions related to sedation, length of stay, 28-day readmission, technical success or recurrence.

Successful removal of all polypoid tissue was achieved in 615 patients (96.4%). By univariate analysis, male gender was associated with peri-procedural AEs (OR 1.6, 95%CI 1.1–2.3; P=0.010; ▶ **Table 3**). By multivariate analysis, when incorporating age and CCI, both of which appeared to possibly predict risk (P <0.1), only male gender remained a predictor (OR 1.6, 95%CI 1.1–2.4; P=0.008).

When stratified by ASA score, there was no difference in peri-procedural AEs between the PA-BS and AMS groups (▶ **Table 4**). The prevalence of peri-procedural AEs in those undergoing PA-BS was 31 (23.3%) in the first quartile versus 23 (18.4%) in the last quartile (P=0.333).

Propensity score-adjusted outcomes

Following propensity scoring (▶ **Fig. 2**), 61 AMS patients were matched to 122 PA-BS patients. In total, one AMS and 516 PA-BS patients remained unmatched and were excluded from propensity-matched analysis. Following matching, there were no difference in comorbidities between the two groups (▶ **Table 1**).

Patients receiving AMS were more likely to receive a larger dose of fentanyl. There was no difference in the doses of midazolam and propofol received between the two groups. There were no differences in peri-procedural AEs, overall unplanned admissions, unplanned admissions related to sedation, length of stay, 28-day readmission, technical success or recurrence (▶ **Table 2**).

Outcomes in complex LNPCPs

Of the 638 patients receiving PA-BS, 160 (25.1%) were complex lesions, either involving the ARJ, involving the ileocecal valve, or having been previously attempted. The number of complex LNPCPs increased from 21.6% in 2016 to 31.9% in 2020.

There was no difference in the proportion of patients undergoing PA-BS between complex and non-complex lesions (n= 160 [92%] vs. n=478 [90.9%], P=0.664).

Complex LNPCPs were likely to take longer to resect with EMR (45 vs. 30 minutes; P <0.001) and more likely to receive a higher cumulative dose of propofol (340 vs 300mg; P=0.002; ▶ **Table 5**). There was no difference in age, gender, CCI or LNPCP size. There was no difference in any peri-procedural or post-procedural AEs, admission rates, re-presentations or recurrence at surveillance colonoscopy.

Discussion

We show that PA-BS is safe and effective for the EMR of LNPCPs ≥20 mm. The majority of cases at our institution (n=638, 91.1%) underwent PA-BS, with peri-procedural AEs being infrequent, transient and rarely requiring unplanned admission (<1%). When compared to a propensity-matched group receiving AMS, there was no difference in peri-procedural AEs, unplanned hospital admission rates, technical failure or recurrence at surveillance colonoscopy. Moreover, PA-BS remained safe and efficacious regardless of LNPCP complexity. Thus, in the appropriate tertiary setting, PA-BS may be considered as a safe and efficacious first-line option for sedation in a patient undergoing EMR for LNPCP management.

In our institution, the use of PA-BS increased from 87.1% in 2016 to 95.8% in 2020. Furthermore, there were no differences

▶ **Table 1** Comparison of physician-administered balanced sedation versus anesthetist-managed sedation: Baseline characteristics before and after propensity score matching.

	Before matching (n = 700)			After matching (n = 183)		
	PA-BS (n = 638)	AMS (n = 62)	P value	PA-BS (n = 122)	AMS (n = 61)	P value
	Valid n (%) or median (IQR)			Valid n (%) or median (IQR)		
Patient and lesion characteristics						
Age (years)	70 (62–76)	74 (67–81)	0.002	74 (67–80)	74 (67–82)	0.729
Male gender	339 (53.1%)	33 (53.2%)	1.000	70 (57.4%)	32 (52.5%)	0.533
Tumor size (mm)	35 (25–45)	35 (30–50)	0.286	40 (30–50)	35 (30–50)	0.422
ASA score						
▪ ASA 1	107 (16.8)	4 (6.5)	< 0.001	19 (15.6)	4 (6.6)	0.010
▪ ASA 2	428 (67.1)	32 (51.6)		71 (58.2)	32 (52.5)	
▪ ASA 3	103 (16.1)	24 (38.7)		32 (26.2)	23 (37.7)	
▪ ASA 4	0 (0)	(3.2)		0 (0)	2 (3.3)	
Charlson comorbidity index	3 (2–4)	4 (2–5)	0.001	4 (2–5)	4 (2–5)	0.959
▪ Ischemic heart disease	64 (10.0)	8 (12.9)	0.477	18 (14.8)	7 (11.5)	0.543
▪ Atrial fibrillation	63 (9.9)	13 (21.0)	0.007	17 (14.0)	12 (19.7)	0.328
▪ Congestive cardiac failure	9 (1.4)	4 (6.5)	0.005	4 (3.3)	3 (4.9)	0.586
▪ Hypertension	326 (51.1)	30 (48.4)	0.684	67 (54.9)	29 (47.5)	0.346
▪ Asthma/COPD	110 (17.2)	18 (29.0)	0.022	29 (23.8)	17 (27.9)	0.547
▪ Renal impairment	12 (1.9)	6 (9.7)	< 0.001	4 (3.3)	6 (9.8)	0.066
▪ Liver impairment	12 (1.9)	1 (1.6)	0.881	4 (3.3)	1 (1.6)	0.521
▪ Diabetes mellitus	97 (15.2)	11 (17.7)	0.597	27 (22.1)	10 (16.4)	0.362
▪ Obesity	15 (2.4)	7 (11.3)	<0.001	1 (0.8)	7 (11.5)	0.001
Propensity Score (mean ± SD)	0.09 ± 0.05	0.11 ± 0.06	<0.001	0.11 ± 0.05	0.11 ± 0.05	0.941
Anesthetic and EMR parameters						
Fentanyl dose (µg)	50 (50–50)	100 (50–100)	<0.001	50 (50–50)	88 (50–100)	<0.001
Midazolam dose (mg)	2 (2.0–2.5)	2 (1.5–4.3)	0.266	2 (2.0–2.0)	2 (1.5–4.5)	0.218
Propofol dose (mg)	300 (200–500)	200 (140–375)	0.014	300 (220–493)	200 (140–375)	0.231
EMR time (minutes)	35 (25–60)	30 (29–53)	0.456	40 (30–60)	30 (28–48)	0.066

PA-BS, physician-administered balanced sedation; AMS, anesthetist-managed sedation; ASA, American Society of Anesthesiologists; COPD, chronic obstructive pulmonary disease; EMR, endoscopic mucosal resection; SD, standard deviation

in outcomes when comparing the first and last quartile of patients undergoing PA-BS. This suggests that with increasing experience, a greater proportion of patients can safely undergo PA-BS without an increase in AEs. In stark contrast, even for routine colonoscopy, the use of AMS has increased in the USA from 8.8% in 2003 to 25.0% in 2007 [27]. This, in part, may be driven by current product labeling, which in certain jurisdictions stipulate that propofol should be administered by anesthetists [28]. Furthermore, current guidelines recommend AMS in patients with an ASA ≥3 [29, 30]. This is despite the ASA classification system lacking inter-observer reliability or sensitivity for predicting peri-procedural AEs [31, 32, 33]. This drove our decision to utilize the CCI to perform propensity-score matching, which resulted in comorbidities being evenly represented between the PA-BS and AMS groups (▶ **Table 1**). The subsequent propensity-matched analysis revealed that when comparing comorbid PA-BS patients with those undergoing AMS, AEs and outcomes remained similar, thereby reflecting PA-BS as safe and efficacious. Further studies addressing the utility of PA-BS for colorectal EMR would be beneficial in providing evidence to assist with redefining guidelines in future.

▶ **Table 2** Comparison of physician-administered balanced sedation versus anesthetist-managed sedation: Outcomes before and after propensity score matching.

	Before matching (n = 700)			After matching (n = 183)		
	PA-BS (n = 638)	AMS (n = 62)	P value	PA-BS (n = 122)	AMS (n = 61)	P value
	Valid n (%) or median (IQR)			Valid n (%) or median (IQR)		
Primary Outcome						
Any peri-procedural AE	149 (23.4%)	12 (19.4%)	0.531	24 (19.7%)	12 (19.7%)	1.000
▪ Hypotension (SBP <90 mm Hg)	17 (2.7%)	0 (0%)	0.387	0 (0%)	0 (0%)	N/A
▪ Hypertension (SBP >190 mm Hg)	10 (1.6%)	0 (0%)	1.000	3 (2.5%)	0 (0%)	0.552
▪ Tachycardia (HR >150 bpm)	5 (0.8%)	1 (1.6%)	0.428	0 (0%)	1 (1.6%)	0.333
▪ Bradycardia (HR <50 bpm)	116 (18.2%)	10 (16.1%)	0.862	20 (16.4%)	10 (16.4%)	1.000
▪ New arrhythmia	1 (0.2%)	0 (0%)	1.000	0 (0%)	0 (0%)	N/A
▪ Hypoxia (SpO_2 <90% for 30 secs)	3 (0.5%)	1 (1.6%)	0.311	1 (0.8%)	1 (1.6%)	1.000
Secondary Outcomes						
Any post-procedural AE (In recovery)						
▪ Reduced level of consciousness	1 (0.2%)	0 (0%)	1.000	0 (0%)	0 (0%)	N/A
▪ Nausea or vomiting	31 (4.9%)	4 (6.5%)	0.540	3 (2.5%)	4 (6.6%)	0.224
▪ Abdominal pain	163 (25.5%)	18 (29.0%)	0.546	31 (25.4%)	17 (27.9%)	0.725
▪ Bleeding in recovery	20 (3.1%)	2 (3.2%)	1.000	2 (1.6%)	2 (3.3%)	0.602
Successful EMR	615 (96.4%)	59 (95.2%)	0.495	117 (95.9%)	59 (96.7%)	1.000
Overall unplanned admissions	51 (8.0%)	7 (11.3%)	0.338	14 (11.5%)	7 (11.5%)	1.000
Sedation-related unplanned admissions	5 (0.8%)	1 (1.6%)	0.555	1 (0.8%)	1 (1.6%)	1.000
▪ Length of stay (days)	1 (1–3)	1 (1–1)	0.655	1 (1–1)	1 (1–1)	1.000
28-day re-presentation	37 (5.8%)	7 (11.3%)	0.098	8 (6.6%)	7 (11.5%)	0.264
Recurrence at SC1	29 (4.5%)	3 (4.8%)	0.757	4 (3.3%)	3 (4.9%)	0.688

AMS, anesthetist-managed sedation; AE, adverse event; EMR, endoscopic mucosal resection; HR, heart rate; N/A, not applicable; PA-BS, physician-administered balanced sedation; SBP, systolic blood pressure; SC1, first surveillance colonoscopy; SD, standard deviation; SpO2, peripheral capillary oxygen saturation.

▶ **Table 3** Risk factors for peri-procedural adverse events.

Risk factor	OR (95% CI)	*P* value
Age	1.0 (1.0–1.0)	**0.094**
Proceduralist sedation	1.3 (0.7–2.5)	0.476
Male gender	1.6 (1.1–2.3)	**0.010**
ASA	0.9 (0.6–1.2)	0.456
CCI	0.9 (0.8–1.0)	**0.098**
EMR duration	1.0 (1.0–1.0)	0.248
Lesion size	1.0 (1.0–1.0)	0.512
Lesion complexity	0.9 (0.6–1.4)	0.675

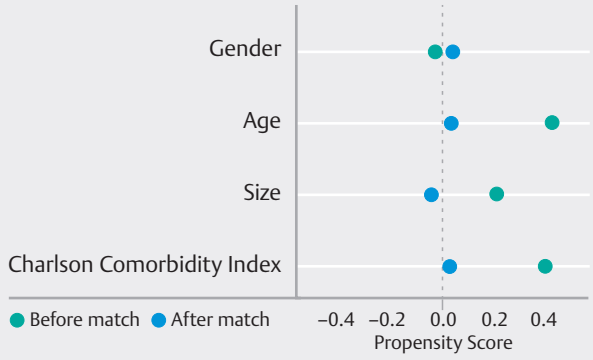
OR, odds ratio; ASA, American Society of Anesthesiologists; CCI, Charlson comorbidity index; EMR, endoscopic mucosal resection.

The safety of PA-BS is clearly demonstrated in our study, with a limited number of transient peri-procedural AEs, rarely requiring admission (<1%). Moreover, in the event of unplanned admission, the median length of stay was only 1 day (IQR 1–3 days), without long-term sequelae. The most frequently encountered peri-procedural AE was bradycardia (18.2% in the PA-BS group). This was likely related to propofol or a vasovagal response during colonoscopy. However, it was self-limiting with only one patient requiring admission for further monitoring. In addition, with advances in EMR and the adoption of adjunctive techniques such as STSC and CAST, an increasing number of complex cases are being managed endoscopically. In our study, over 25% of LNPCPs undergoing colorectal EMR were considered complex. Despite this, we found no differences in AEs or procedural outcomes, suggesting that PA-BS is a safe and effective strategy for the EMR of LNPCPs. Therefore, our findings further cement the idea that AMS is not required as a universal approach.

▶ **Table 4** Comparison of adverse events and short-term outcomes, stratified by sedation strategy and ASA score (n (%)).

		ASA 1	ASA 2	ASA 3	ASA 4
Any peri-procedural AE	PA-BS	26 (24.3)	103 (24.1)	20 (19.4)	0 (0)
	AMS	1 (25.0)	6 (18.8)	3 (12.5)	2 (100)
	P value	0.974	0.495	0.428	N/A
Overall unplanned admissions	PA-BS	7 (6.5)	32 (7.5)	12 (11.7)	0 (0)
	AMS	0 (0)	4 (12.5)	2 (8.3)	1 (50)
	P value	0.597	0.307	0.640	N/A
Sedation-related unplanned admissions	PA-BS	1 (0.9)	4 (12.5)	0 (0)	0 (0)
	AMS	0 (0)	0 (0)	0 (0)	1 (50)
	P value	N/A	0.453	N/A	N/A
28-day re-presentation	PA-BS	2 (1.9)	32 (7.5)	3 (2.9)	0 (0)
	AMS	0 (0)	2 (6.3)	5 (20.8)	0 (0)
	P value	0.783	0.798	0.001	N/A

ASA, American Society of Anesthesiologists; AE, adverse event; PA-BS, physician-administered balanced sedation; AMS, anesthetist-managed sedation.



▶ **Fig. 2** Propensity scores before and after matching between anesthetist-managed sedation and physician-administered balanced sedation.

Our utilization of PA-BS for colorectal EMR is not without precedence. Prior studies have evaluated various PA sedation strategies in complex upper endoscopic interventions including endoscopic retrograde cholangiopancreatography and endoscopic ultrasonography [2, 3], which may carry a higher risk of peri-procedural AEs such as aspiration. These studies demonstrated that regimens utilizing propofol (i. e. PA-BS or PA-PM) were advantageous when compared to PA-SS for patient cooperation, without any differences in AEs [2, 34]. Although intuitive, this is likely due to smaller doses of multiple medications resulting in a reduced risk of deep sedation. This is reflected in our study, with only a small dose of midazolam (2 mg) and fentanyl (50 µg) required for induction of sedation, following which small incremental doses of propofol (10 mg) were administered. Moreover, a significant advantage of propofol is that over-sedation can be managed without reversal agents due to its short half-life [34]. This is highlighted in our study, with there being no need for assisted ventilation or emergency calls. Although we did not compare different PA sedation strategies, we showed that PA-BS is safe in the colorectal EMR setting and only requires small doses of an opioid and benzodiazepine for induction of sedation.

While we clearly demonstrated the safety of PA-BS, certain patients may still benefit from AMS. We show that those receiving AMS were likely to be older (74 vs. 70 years; $P = 0.002$) and more likely to have comorbidities such as congestive cardiac failure, renal failure, and respiratory conditions. At our institution, the pre-procedure assessment is performed by a gastroenterologist. While in the ideal scenario, this would be conducted by an anesthetist, this is generally not feasible in a high-volume tertiary unit. As we show that outcomes with AMS and PA-BS are comparable, PA-BS could become the default sedation approach for colorectal EMR. However, each patient should be assessed clinically before EMR to determine the need for AMS.

In addition, there are several other benefits intrinsic to PA-BS, particularly in the setting of EMR for LNPCP management. While gastroscopy may benefit from deep sedation or general anesthesia at times, conscious sedation is seen as an advantage with colonoscopy as it can facilitate maneuvers and repositioning, to facilitate improved endoscopic visualization and resection [1]. By forgoing the anesthetic personnel required for AMS, there is the potential to reduce costs; however, economic modeling studies are required. In addition, PA-BS also enables limited resources such as anesthetic staff to be utilized in other areas of need. Future studies may also consider sedation administration by a registered nurse for colorectal EMR. However, this also carries an opportunity cost because nursing staff may be utilized elsewhere such as in the recovery bay. There is also

▶ **Table 5** Comparison of patients receiving physician administered balanced sedation for the endoscopic mucosal resection of complex and non-complex large non-pedunculated colorectal polyps.

	Complex lesions N = 160	Non-complex lesions N = 478	P value
	Valid n (%) or median (IQR)		
Patient and lesion characteristics			
Age (years)	69 (63–76)	70 (61–76)	0.842
Male gender	85 (53.1)	254 (53.1%)	0.998
Charlson comorbidity index	3 (2–4)	3 (2–4)	0.218
Tumor size (mm)	35 (25–50)	35 (25–45)	0.927
Anesthetic and EMR parameters			
Fentanyl dose (µg)	50 (50–50)	50 (50–50)	0.615
Midazolam dose (mg)	2 (2.0–3.0)	2 (2.0–2.0)	0.102
Propofol dose (mg)	340 (237.5–505.0)	300 (200–465)	0.002
EMR time (minutes)	45 (30–60)	30 (20–50)	<0.001
Primary outcome			
Any peri-procedural AE	36 (22.5%)	113 (23.6%)	0.768
▪ Hypotension (SBP <90 mm Hg)	4 (2.5%)	13 (2.7%)	1.000
▪ Hypertension (SBP >190 mm Hg)	2 (1.3%)	8 (1.7%)	1.000
▪ Tachycardia (HR >150 bpm)	1 (0.6%)	4 (0.8%)	1.000
▪ Bradycardia (HR <50 bpm)	30 (18.8%)	86 (18.0%)	0.830
▪ New arrhythmia	0 (0%)	1 (0.2%)	1.000
▪ Hypoxia (SpO_2 <90% for 30 secs)	0 (0%)	3 (0.6%)	0.577
Secondary outcomes			
Any post-procedural AE			
▪ Reduced Level of Consciousness	1 (0.6%)	0 (0%)	0.251
▪ Nausea or vomiting	7 (4.4%)	24 (5.0%)	0.742
▪ Abdominal pain	45 (28.1%)	118 (24.7%)	0.388
▪ Bleeding in recovery	2 (1.3%)	18 (3.8%)	0.186
Successful EMR	151 (94.4%)	464 (97.1%)	0.113
Overall unplanned admissions	12 (7.5%)	39 (8.2%)	0.790
Sedation-related unplanned admissions	1 (0.6%)	4 (0.8%)	1.000
28-day re-presentation	11 (6.9%)	26 (5.4%)	0.501
Recurrence at SC1	10 (6.3%)	19 (4.0%)	0.232

IQR, interquartile range; EMR, endoscopic mucosal resection; AE, adverse event; SBP, systolic blood pressure; HR, heart rate.

an inherent advantage in a dedicated physician administering sedation, as their understanding of the procedure, its steps, the required patient maneuvers, and projected duration may improve overall efficiency.

The main strength of our analysis was the size of the population analyzed and propensity matching. However, our study was not without limitations. This was a retrospective study of prospectively collected data, and therefore, may introduce selection bias because there may have been other variables that are unaccounted for in the propensity model. Furthermore, the statistical power of our study was limited by the small number of patients that underwent AMS. There may also be underreporting of re-presentation rates because patients may have visited other facilities post-EMR. We did not utilize capnography for respiratory monitoring, which may have resulted in delays in identifying patients at risk of developing hypoxia. Patient satisfaction scores comparing the two groups were not collected. We did not have a different PA comparator group such as

PA-PM or PA-SS; however, the purpose of our study was to compare PA-BS to AMS.

Conclusions

In conclusion, we show that PA balanced sedation is as safe and effective as AMS for the EMR of LNPCPs ≥20 mm when performed in a tertiary unit by proceduralists with adequate advanced life support training. Irrespective of lesion complexity, there is no difference in peri-procedural AEs, hospital admission rates, technical failure or recurrence at surveillance colonoscopy. In the appropriate setting, PA-BS may be considered as a default sedation strategy, with the need for AMS evaluated on case-by-case basis.

Conflict of Interest

Michael J. Bourke: research support from Olympus Medical, Cook Medical and Boston Scientific. The remaining authors have no conflicts of interest to disclose.

Clinical trial

Trial registry: Australian New Zealand Clinical Trials Registry (http://www.anzctr.org.au/)
Registration number (trial ID): NCT01368289; NCT02000141
Type of Study: Retrospective

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