Propofol sedation does not improve measures of colonoscopy quality but increase cost – findings from a large population-based cohort study

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Summary

Background Propofol is often used for sedation during colonoscopy. We assessed the impact of propofol sedation on colonoscopy related quality metrics and cost in a population-based cohort study.

Methods All colonoscopies performed at 21 hospitals in the province of Ontario, Canada, during an 18-month period, from April 1, 2017 to October 31, 2018, using either propofol or conscious sedation were evaluated. The primary outcome was adenoma detection rate (ADR) and secondary outcomes were sessile serrated polyp detection rate (ssPDR), polyp detection rate (PDR), cecal intubation rate (CIR), and perforation rate. Binary outcomes were assessed using a modified Poisson regression model adjusted for clustering and potential confounders based on patient, procedure, and physician characteristics.

Findings A total of 46,634 colonoscopies were performed, of which 16,408 (35.2%) received propofol and 30,226 (64.8%) received conscious sedation. Compared to conscious sedation, the use of propofol was associated with a lower ADR (24.6% vs. 27.0%, $p < 0.0001$) but not ssPDR (5.0% vs. 4.7%, $p = 0.26$), PDR (40.5% vs 40.4%, $p = 0.79$), CIR (97.1% vs. 96.8%, $p = 0.15$) or perforation rate (0.04% vs. 0.06%, $p = 0.45$). On multi-variable analysis, propofol sedation was not associated with any differences in ADR (RR = 0.90, 95% CI 0.74–1.10, $p = 0.30$), ssPDR (RR = 1.20, 95% CI 0.90–1.60, $p = 0.22$), PDR (RR = 1.00, 95% CI 0.90–1.11, $p = 0.99$), or CIR (RR = 1.00, 95% CI 0.80–1.26, $p = 0.99$). The additional cost associated with propofol sedation was $12,730,496 for every 100,000 cases.

Interpretation The use of propofol sedation was not associated with improved colonoscopy related quality metrics but increased costs. The routine use of propofol for colonoscopy should be reevaluated.

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Keywords: Propofol; Colonoscopy; Quality assurance; Adenoma detection rate

Introduction

Colonoscopy is a common procedure with more than 13 million cases performed annually in the United States for a variety of indications, such as gastrointestinal bleeding, inflammatory bowel disease, and colorectal cancer detection and screening.[1] Despite its importance, it can be a painful procedure and generally requires some form of sedation.[2,3] This is typically provided as

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Research in context

Evidence before this study

The use of propofol in place of conscious sedation for colonoscopy has increased substantially over the past two decades. Although it increases the overall cost of the procedure, its benefits are unclear. Prior studies have reported on the effect of propofol on anesthesia related outcomes, such as pain and recovery time, with marginal benefits compared to conscious sedation found in both domains. What is less known is whether propofol affects the quality of the colonoscopy procedure itself, such as in the domain of adenoma detection rate. This is relevant since the type of sedation used can directly impact how the procedure is performed. A PubMed search between 1985 and 2023 revealed only three studies that examined the impact of propofol on the adenoma detection rate, albeit all had significant methodological limitations, such as small sample size, single center design, or involving a small number of endoscopist. As such, the generalizability of these studies is limited. Thus, the objective of this study was to examine the impact of propofol sedation on colonoscopy related quality metrics and assess the added case cost attributed to the use of propofol in a large, generalizable, population-based cohort.

Added value of this study

Propofol sedation did not affect the adenoma detection rate compared to conscious sedation. Furthermore, it did not affect other colonoscopy related quality metrics, including the sessile serrated polyp detection rate, polyp detection rate, cecal intubation rate, or perforation rate but did significantly increase the cost of the procedure ($12,730,496 CAD for every 100,000 propofol cases).

Implications of all the available evidence

Prior studies have reported limited benefit when propofol is used instead of conscious sedation with respect to anesthesia related outcomes and our study found no significant benefit with respect to colonoscopy related outcomes. Given these findings and the increased cost associated with the use of propofol, its routine use for colonoscopy should be reevaluated.

conscious sedation in the form of a short acting benzodiazepine and narcotic, such as midazolam and fentanyl, or as deep sedation, usually as propofol administered by an anesthesiologist or anesthesia assistant.[4] Over time, the use of propofol for colonoscopy has been rising, partly due to the belief that deep sedation is needed to provide a comfortable procedure for the patient.[4–7] However, this is not supported by the available evidence, as demonstrated in a recent systematic review and meta-analysis of 1427 patients from nine randomized controlled trials that found a high level of patient satisfaction regardless of sedation type, although propofol was associated with a slightly higher level of patient satisfaction (standardized mean difference 0.54, 95% CI 0.30–0.79).[8] As an illustrative example, the largest study in the meta-analysis (n = 600) reported only a 2% difference in favor of propofol when patient satisfaction was rated on a 5-point Likert scale (mean score 4.8 vs. 4.7). In this study, as in other studies in the field, patient satisfaction rather than a pain score was used as it encompasses other facets of the patient experience, such as anxiety and unpleasant memories. On a pragmatic level, five studies in the meta-analysis examined the proportion of patients who had early termination of the procedure and reported no early termination in three studies and early termination in two studies (in one study, there was an early termination in the propofol and conscious sedation arms whereas in the other study, there was one early termination in the conscious sedation arm only). Another driving force for the use of propofol is the perceived increase in patient turnover in the endoscopy unit due to the more rapid onset and clearance of the medication.[9,10] This too was examined in the meta-analysis and although the median difference in recovery time was 3 min 6 s shorter in favor of propofol, the amount of time saved is too small to be of any real-world benefit. Furthermore, there were no significant differences in total procedure time.[8]

Beyond the marginal benefits in patient satisfaction and recovery time, it is unclear whether the use of propofol sedation is associated with improvements in the non-anesthesia aspects of the procedure, such as the adenoma detection rate (ADR), cecal intubation rate (CIR), or perforation rate, which we collectively refer to as colonoscopy related quality metrics.[11,12] All three are highly relevant as the first is directly correlated with the risk of post-colonoscopy colorectal cancer, the second is a technical requirement for a complete procedure, and the third is the most serious complication of colonoscopy.[13] Furthermore, all three-quality metrics are potentially impacted by sedation strategies. Firstly, deep sedation impedes the ability to "roll" or reposition patients, which may hinder adenoma detection.[14,15] Secondly, an uncomfortable patient may divert the attention of the endoscopist or even prevent completion of the procedure altogether.[16] Lastly, deep sedation may increase the perforation risk due to the ability of the endoscopist to use greater force when advancing the colonoscope without fear of inducing pain and may disincentivize loop reduction.[17] Beyond its impact on colonoscopy related quality metrics, the use of propofol undoubtedly increases the costs of the procedure.[7] Thus, the objective of this study was to examine the impact of propofol sedation on colonoscopy related quality metrics

in a large population-based cohort and to estimate the per-procedure incremental cost of using propofol sedation compared to conscious sedation.

Methods

Study design and patient population

A population-based cohort study consisting of consecutive patients over the age of 18 who underwent colonoscopy at 21 community and academic hospitals in Ontario, Canada was conducted. All included hospitals are part of the Southwest Local Health Integration Network, a public entity tasked with the coordination of healthcare in the region. This network provides all endoscopy services with the exception of one private ambulatory endoscopy clinic. Patients younger than 18 years of age and procedures performed by endoscopists who completed less than 50 colonoscopies a year were excluded from the cohort.

Ethics statement

Data from this study was obtained from a dataset collected from the Southwest Endoscopy Quality Improvement and Performance Committee (SWEQUIP) database. Therefore, written informed consent was not required or obtained. The study was approved by the Western University Health Sciences Research Ethics Board.

Data collection

A bespoke quality assurance form was completed after each procedure by the endoscopist and participation was mandatory. This form captured: 1) patient variables, including age, sex, American Society of Anesthesiologists (ASA) grade, colonoscopy indication, whether the procedure was performed as an outpatient, and if split dose bowel preparation was used; 2) procedure variables, including sedation type, bowel preparation quality, involvement of trainees, hospital name, cecal intubation, polyp detection, and intra-procedural perforation; 3) endoscopist variable, including the specialty of the physician and years in practice determined by cross referencing their medical license number with a publicly available physician database (https://www.cpso.on.ca). There is no universally accepted bowel preparation scale and for this reason, the province of Ontario uses an ordinal scale defined as follows: good (adequate), fair (adequate with cleaning), and poor (inadequate). Pathology reports were manually reviewed by the study team except for six hospitals for which the study team did not have access. These six hospitals still contributed data to the analyses except for the outcomes of ADR and ssPDR, given the lack of pathology data in these cases. Delayed perforations, defined as perforations associated with hospitalizations up to 7 days post-colonoscopy, were captured using data from the Ontario Health Insurance Plan, the provincially mandated insurer for all Ontarians, and the Canadian Institute for Health Information's National Ambulatory Care Reporting System and its Discharge Abstract. Any cases of perforation identified were manually adjudicated for accuracy.

The accuracy of the dataset was validated by manually reviewing the charts of 944 (2%) randomly selected patient in the cohort in the following domains: patient characteristics (age, sex) and endoscopy characteristics (cecal intubation, sedation type, polyp detection, and perforation). The patient characteristic variables were 100% accurate. The endoscopy variables were 98.5%, 92.7%, 96.9%, and 100% accurate for cecal intubation, sedation type, polyp detection, and perforation, respectively.

Exposure definition

The exposure of interest was use of propofol sedation administered by an anesthesiologist with or without an anesthesia assistant, who are specially trained respiratory therapists or registered nurses. In contrast, conscious sedation was administered by the endoscopist/nurse in the form of midazolam, a short-acting benzodiazepine, and fentanyl, a short-acting opioid, both intravenously. Patients who chose to forgo sedation (n = 300) and procedures in which the type of sedation was not documented (n = 261) were excluded from the analysis.

Outcome definition

The primary outcome examined was ADR, defined as the proportion of colonoscopies with at least one tubular adenoma, tubulovillous adenoma, or villous adenoma detected. Secondary outcomes included the sessile serrated polyp detection rate (ssPDR), polyp detection rate (PDR), CIR, and perforation rate. Sessile serrated polyps was based on the 2017 US Multi-Society Task Force definition which excludes hyperplastic polyps.[18] Polyp detection rate was defined by the proportion of colonoscopies during which at least one polyp was detected. The CIR was defined as the proportion of colonoscopies where the endoscopist reached the cecum during the procedure. Perforation rate was defined as the proportion of colonoscopies where an intra-procedural or delayed colon perforation, up to 7 days, occurred.

Statistical analysis

Descriptive summaries were presented for the overall cohort and stratified using propofol vs. conscious sedation. Characteristics were summarized using mean (standard deviation) for continuous quantities or by proportion and percentage for categorical quantities. Potential imbalances in baseline characteristics by sedation type were examined using two-group t-tests for continuous variables or for categorical variables, a Pearson χ^2-test or else a Monte Carlo approximation of the Fisher exact test with 10,000 replicates when any

expected cell counts were <5 was used. Unadjusted outcome rates among procedures using propofol or conscious sedation were described as observed. Unadjusted and adjusted risk ratios were estimated for binary outcomes using the well-known modified Poisson regression model with cluster-robust variance estimates using physician as the unit of clustering.[19] Associations were adjusted using patient characteristics (sex, age, ASA grade), procedure characteristics (hospital setting, split dosing, quality of bowel preparation, indication, outpatient status) and physician characteristics (years of experience, specialty) and presence of trainees in the procedure. The association of interest was propofol vs. conscious sedation. The primary hypothesis tested was whether the rate ratio of adenoma detection using propofol compared to conscious sedation was different than 1 (H1: RR≠1) compared to the null hypothesis of no difference (H0: RR = 1), tested at a two-sided 5% significance level. No adjustment was made for multiplicity. A two-sided equality test was chosen because: (i) we did not know the direction of association with certainty *a priori*; (ii) using a test of equivalence or non-inferiority requires a justifiable choice of the "delta" difference which are best informed by considering the relative risks of adverse events associated with each sedation type, their relative costs, and an assumed degree of difference which may be considered clinically non-inferior (or equivalent)[20–24]; and (iii) If propofol use was found to be associated with significantly worse quality metrics, with or without improved adenoma detection, that observation would itself be important to present and discuss.

No formal sample size calculations were performed as the study included all available procedure data, in keeping with the STROBE recommendations.[25] Missing data were assumed to be missing at random and were not imputed and hence, omitted.

A sensitivity analysis was conducted concerning the potential consequences of misclassification in sedation type. This was done using 1000 simulations per scenario using the cohort data, where procedures were randomly selected to change the sedation type, mimicking misclassification. Both balanced and imbalanced misclassification errors were considered. For balanced misclassification, a 2% error rate was considered, in which 1% of each sedation type were randomly selected and the sedation type reclassified to the other type. In a second set of simulations, reclassifications were chosen to be only in one direction or the other, using the validation error rate to select the number of procedures of a single type for reclassification. The "reversal" rate is reported which would have led to the opposite conclusions based on the adjusted risk ratio of propofol vs. conscious sedation on adenoma detection. These scenarios represent two extremes of potential misclassification that could have occurred and resulted in bias of the results.

Statistical analyses were performed using Stata (version 16; StataCorp LLC.).

Costing analysis

We estimated the per-procedure incremental cost of using propofol using the Ontario Schedule of Benefits for Physicians, which lists the fee schedule for physician services provided by the provincially mandated Ontario Health Insurance Plan.[26] For conscious sedation, there is no physician fee when given by the endoscopist. For propofol sedation, we assumed anesthesiologists would bill 4 basic units and one time unit, at $15.49 CAD/unit, to provide and support propofol sedation for colonoscopy in general. Anesthesiologists receive additional payment for patients between 70 and 79 years of age (add 1 unit), older than 79 (add 3 units), BMI >40 (add 2 units), patients with systemic disease using the American Society of Anesthesiologists (ASA) Physical Status Classification System (ASA III add 2 units, ASA IV add 10 units), and if polyps were removed (add 4 units). The age distribution, distribution of systemic disease severity, and proportion of patients with polyp removal was not different between sedation groups in our study and so for the estimation of average anesthesiologist fee, we relied on the features of the overall population. We estimated the incremental cost of capnography used in the propofol group compared to nasal prongs used for conscious sedation (add $7.55 CAD per propofol case) and drug cost of propofol (200 mg/20 ml vial) compared to midazolam (5 mg vial) and fentanyl (100 mcg vial) (–$1 CAD per propofol case), using local hospital pharmacy procurement costs.

Role of the funding source

There were no funders for this study. SR, CL, CM, LG and MS had access to the data. MS is finally responsible for the decision to submit the current work for publication.

Results

Cohort characteristics

A total of 47,624 colonoscopies were performed during the 18-month study observation period. Of this, 990 (2.1%) patients were ultimately excluded due to being performed in patients less than 18 years of age (n = 61), by endoscopists who performed <50 colonoscopies/year (n = 368), in patients not receiving any sedation (n = 300), or in instances where the sedation type was not charted (n = 261). As such, the final study cohort consisted of 46,634 colonoscopies performed by 75 endoscopists (37.5% by gastroenterologists, 60% by general surgeons, 2.5% by others). Among these patients, 16,408 (35.2%) received propofol sedation, whereas 30,226 (64.8%) received conscious sedation. The overall mean (SD) age was 60.4 (13.9) years, and the distribution of females was similar between the two

groups (52.8% in the propofol group vs. 53.0% in the conscious sedation group, p = 0.63) (Table 1). Propofol cases were more likely to be performed by general surgeons than gastroenterologists (73.1% vs. 23.9%, p < 0.0001). Overall, 19,685 (42.2%) colonoscopies were performed at academic hospitals, which accounted for 5041 (30.7%) of propofol cases.

Colonoscopy related quality metrics

On crude analysis, the ADR was lower in the propofol sedation group compared to the conscious sedation group (24.6% vs. 27.0%, p < 0.0001) (Table 2). However, there were no statistically significant differences in the ssPDR (5.0% vs. 4.7%, p = 0.26), PDR (40.5% vs. 40.4%, p = 0.79), CIR (97.1% vs. 96.8%, p = 0.15) or perforation rates (0.04% vs. 0.06%, p = 0.45) between the two groups, respectively. On multivariable analysis adjusted for age, sex, ASA grade, indication, use of split dose bowel preparation, bowel preparation quality, endoscopist specialty, endoscopist experience, academic hospital, and involvement of trainees, we found no statistically significant differences in the ADR (RR 0.90, 95% CI 0.74–1.10, p = 0.30), ssPDR (RR 1.20, 95% CI 0.90–1.60, p = 0.22), PDR (RR 1.00, 95% CI 0.90–1.11, p = 0.99), or CIR (RR 1.00, 95% CI 0.80–1.26, p = 0.99) between patients who underwent colonoscopy with conscious sedation vs. propofol sedation (Table 2). Due to insufficient perforation events, this outcome could not be incorporated into the multi-variable model. Six smaller community hospitals did not have pathology data available. The characteristics of patients from these sites were compared to six community hospitals of comparable size and geography for which pathology data was available and overall, there were no clinically meaningful differences found between the sites with and without pathology data (Supplement 1).

Costing analysis

Following the Schedule of Benefits for Ontario, we estimated the average anesthesia units per patient.

All propofol patients started with 4 basic units plus one time unit. Additional units were added for patients of advanced age: 1 unit for the 21.1% of patients aged 70–79 years, and 3 units for the 6.2% of patients aged 80+. Additional units were added for patients with severe systemic disease affecting their anesthesia risk: 2

Factor	Total (n = 46,634)	Propofol (n = 16,408)	Conscious sedation (n = 30,226)	p-value
Age-mean (SD)	60.4 (13.9)	60.4 (13.6)	60.4 (14.1)	0.62
Sex-no. (%)				
Female	24,669 (52.9%)	8655 (52.8%)	16,014 (53.0%)	0.63
Male	21,963 (47.1%)	7752 (47.2%)	14,211 (47.0%)	
ASA grade-no. (%)				
1	11,512 (24.7%)	3778 (23%)	7734 (25.6%)	<0.0001[a]
2	23,536 (50.5%)	8242 (50.2%)	15,924 (50.6%)	
3	10,838 (23.2%)	4162 (25.4%)	6676 (22.1%)	
4	734 (1.6%)	222 (1.4%)	512 (1.7%)	
5	8 (0.0%)	4 (0.02%)	4 (0.02%)	
Indication-no. (%)				
Screening/Surveillance	21,192 (45.5%)	7974 (48.6%)	13,218 (43.7%)	<0.0001
FOBT+	1947 (4.2%)	870 (5.3%)	1077 (3.6%)	
Symptomatic	23,488 (50.4%)	7564 (46.1%)	15,924 (52.7%)	
Split dose bowel prep-no (%)	42,394 (90.9%)	15,353 (93.6%)	27,041 (89.5%)	<0.0001
Bowel prep quality-no. (%)				
Very good	38,743 (83.1%)	13,950 (85.1%)	24,793 (82.1%)	<0.0001
Fair	6537 (14.0%)	2077 (12.7%)	4460 (14.8%)	
Poor	1319 (2.8%)	363 (2.2%)	956 (3.1%)	
Specialty				
Gastroenterology	17,493 (37.5%)	3924 (23.9%)	13,569 (44.9%)	<0.0001[a]
General surgery	27,965 (60.0%)	11,987 (73.1%)	15,978 (52.9%)	
Internal medicine	673 (1.4%)	497 (3.0%)	176 (0.6%)	
General practice	503 (1.1%)	0 (0%)	503 (1.7%)	
Academic center-no. (%)	19,685 (42.2%)	5041 (30.7%)	14,644 (48.4%)	<0.0001
Trainee involved no. (%)	6022 (12.9%)	1039 (6.3%)	4983 (16.5%)	<0.0001
Physician length of practice (years), mean (SD)	14.4 (10.5)	15.7 (10.5)	12.1 (10.2)	<0.0001

[a]Monte Carlo approximation of the Fisher exact test using 10,000 replicates.

Table 1: **Patient baseline characteristics.**

	Crude Analysis			Multi-variable Analysis	
	Propofol-no. (%)	Conscious Sedation -no. (%)	p-value	RR[a] (95% CI)	p-value
Adenoma Detection Rate[b]	2864/11,660 (24.6%)	5683/21,053 (27.0%)	<0.0001	0.90 (0.74, 1.10)	0.30
Sessile serrate polyp detection rate[b]	578/11,660 (5.0%)	985/21,053 (4.7%)	0.26	1.20 (0.90, 1.60)	0.22
Polyp Detection Rate	4725/11,660 (40.5%)	8499/21,053 (40.4%)	0.79	1.00 (0.90, 1.11)	0.99
Cecal Intubation Rate	15,718/16,193 (97.1%)	28,952/28,952 (96.8%)	0.15	1.00 (0.80, 1.26)	0.99
Perforation	7/16,408 (0.04%)	18/30,226 (0.06%)	0.45	–	–

[a]The RR for each outcome in the table represents that of the propofol sedation group as compared to conscious sedation. Models are additionally adjusted for age, sex, ASA grade, indication, use of split dose bowel preparation, bowel preparation quality, endoscopist specialty (gastroenterology, surgery or other), endoscopist experience, academic hospital, and involvement of trainees. [b]The Adenoma Detection Rate and Sessile serrate polyp detection rate do not include the six hospitals that did not have pathology results.

Table 2: **Crude and multi-variable analyses of the association between propofol sedation and study outcomes.**

units for the 23.2% of patients who were ASA grade III and 10 units for the 1.6% of patients who were greater than ASA grade III. Four additional units were added for the 42.8% of patients who received a polypectomy during their colonoscopy. Under the Schedule of Benefits in Ontario, two additional anesthesia units are available for care of patients with a BMI over 40. Since our study did not collect BMI, we estimated the proportion of patients expected to have BMI over 40 in each age group using the age-specific population rate for Canada estimated in the Canadian Community Health Survey as reported by Statistics Canada.[27]

Overall, the incremental cost was $120.76 for physician fees when propofol was used. After taking into account use of capnography for propofol cases ($7.55 CAD) and the differences in the cost of the medications (−$1.00 CAD), the total incremental cost associated with the use of propofol was $127.30 CAD per case or $12,730,496 CAD for every 100,000 propofol cases performed in the province.

Sensitivity analyses

To address potential concern with over-dispersion when using the modified Poisson regression model, we repeated analyses using negative binomial regression (Supplement 2). The negative binomial model includes an α parameter which may be interpreted as explaining additional variance when over-dispersion is present. A 1-df likelihood ratio test of α was considered since the Poisson model can be seen as nested within the negative binomial (specifically, when $\alpha = 0$), however since the model pseudo-likelihood from both models were numerically identical, this test yields a p-value if 1.0 in all analyses. This was a strong rejection of the negative binomial model and unexplained over-dispersion. The robust (or modified) Poisson regression model is robust to model misspecification and was expected to adjust for any over-dispersion, as has been demonstrated.[28,29]

The apparent effect of any misclassification is summarized as the "reversal" rate, which would indicate the opposite conclusions. In the case of balanced misclassification, there was very little effect on the adjusted risk ratio for sedation type on ADR as an outcome. As a result, the conclusions did not change. When misclassification was only in one direction, where conscious sedation is misclassified as propofol, the RR tended to move closer to one, with a median value of 1.06 (IQR 0.98–1.15). Only 6% of the 1000 simulations showed a statistically significantly RR that would have yielded the opposite conclusion (i.e., RR > 1). Lastly, we consider misclassification only in the other direction. The median adjusted RR was 1.04 (IQR 0.96–1.11). Again, 6% of the 1000 simulations showed a statistically significantly RR that would have yielded the opposite conclusion (RR > 1). Therefore, the effect of differential misclassification is similar in both directions.

Discussion

In this large population-based cohort study, we examined whether the use of propofol sedation rather than conscious sedation affected colonoscopy related quality metrics. Although prior studies have shown marginal benefits in anesthesia-related outcomes, such as in the domains of patient satisfaction and shorter recovery time, the impact of sedation type on the quality of the procedure itself from an endoscopy perspective, such as ADR, is largely unknown. Three prior studies have attempted to address this, although all were significantly hampered by methodological limitations, including small sample sizes, single center designs, or involvement of a limited number of endoscopists, all of which threaten the generalizability of their findings.[9,10,16] In the first study, Nakshabendi et al. reported a retrospective series of 699 consecutive patients at a single center and found no difference in ADR between conscious sedation and propofol.[10] In the second study, Thirumurthi et al. reported their experience at MD Anderson Cancer Center and found no significant difference in ADR between the two sedation strategies in 2604 colonoscopies.[9] Lastly, Metwally performed the only multicenter study, albeit it consisted of only two centers and a total of five endoscopists. Regardless, after analyzing 3252 procedures, they too found no difference

in ADR based on sedation type.[16] In our study, the ADR in the crude analysis was significantly lower in the propofol group despite there being fewer FOBT+ and more poor bowel preparation cases in the conscious sedation group. However, the absolute difference in ADR was modest and FOBT+ and poor bowel preparation cases represented less than 4% of the study cohort. Regardless, our multi-variable analysis controlling for these variables did not detect a difference in the ADR based on sedation strategy, which is congruent with the prior studies. Accordingly, based on the findings from our study, propofol sedation did not have a significant effect on colonoscopy related quality metrics compared to conscious sedation yet was associated with increased cost.

These observations are interesting for several reasons. First, our findings support the overall safety of propofol in terms of perforation risk. It has been postulated that the deep sedation achieved with propofol may increase the risk of perforation by allowing the endoscopists to push harder and pay less attention to loop reduction,[17] which may in theory increase the risk of complications. However, this concern was not observed in our study, and our findings are congruent with a large registry study using administrative databases that also failed to identify an association between propofol use and the risk of perforation.[30] Second, the use of propofol makes repositioning or "rolling" of patients more difficult, which may in theory impair optimal visualization of colonic segments and reduce polyp detection.[14,15] However, this too was not observed as the ADR, ssPDR, and PDR were similar between the two groups, groups, albeit we could not measure the proportion of patients who were repositioned in each group. Third, the use of propofol did not increase the CIR despite providing deeper sedation, which was very high regardless of sedation strategies. We did not have data on the number of patients who could not tolerate colonoscopy with conscious sedation and had to return for another procedure with propofol, although this would be very low given approximately 97% of patients had cecal intubation in the conscious sedation group. Furthermore, even the 3% who did achieve cecal intubation would consist of a mix of patients who had unmitigated looping, pelvic adhesions, or obstructing tumors/strictures that precluded cecal intubation, not just those who were intolerant to conscious sedation. This point is perhaps best supported by the fact that approximately 3% of patients in the propofol group also failed cecal intubation. Beyond patient tolerance, it could be argued that given the use of propofol was not randomized, it is possible that patients with more difficult colons disproportionately received propofol and perhaps the CIR would have been higher in the propofol group were it not for this potential selection bias. However, we do not believe this significantly influenced our results since difficult colons are generally recognized after, rather than before, the procedure. Perhaps more importantly, the availability of propofol in our region is highly variable depending on the physician, endoscopy unit, and hospital. Thus, it is local availability rather than procedure difficulty that is the main driver of sedation strategy. Even if patients with difficult colons were more likely to receive propofol, they would have made up a very small fraction of cases as more than 1 in 3 patients received propofol in the cohort.

While propofol led to no difference in colonoscopy related quality metrics, the use of propofol sedation increased the cost of the procedure significantly due to the need for an additional healthcare provider, typically an anesthesiologist with or without an anesthesia assistant, to attend the case.[7,31] We found the use of propofol was associated with an incremental cost of $127.30 CAD per case or $12,730,496 CAD for every 100,000 propofol cases compared to conscious sedation. The difference in cost was driven by the incremental physician fees, representing $120.76 CAD of the additional $127.30 CAD per case. Furthermore, this estimate is likely conservative as we did not include the incremental cost of anesthesia assistants, which would further increase the cost of propofol cases. Regardless, a similar observation was reported in a nationwide registry study involving 4.6 million outpatient colonoscopy claims in the United States where the use of propofol was associated with higher costs among all payers, with a median additional cost of $182.43/case for commercial insurance and $232.62/case for uninsured individuals.[7] However, components of the cost were not presented in the study and thus, we cannot identify what aspect of the cost (i.e., physician fees or drug costs) are the source of the difference although we speculate it may have been the result of differences in anesthesia modifiers and rates of pay for anesthesia units between countries.

Due to the marginal benefits with respect to anesthesia-related outcomes[8] and the lack of differences in colonoscopy related quality metrics, the routine offering of propofol sedation for colonoscopy should be reevaluated. To be clear, we are not advocating for the elimination of propofol sedation for colonoscopy as there are clearly circumstances where propofol sedation is preferred, such as in patients who are difficult to sedate with conscious sedation.[5] However, these cases are the minority and our results provide support for a more rational use of propofol in selected patients who will benefit the most from deep sedation.

The primary strength of our study is its generalizability. Our population-based cohort involved over 46,000 consecutive and unselected colonoscopies performed at 21 hospitals, both academic and community, involved both gastroenterologists and general surgeons, and used minimal exclusion criteria. Thus, our findings encompass a wide range of patients, endoscopists, and clinical practices and as a result, are highly

generalizable. Additionally, our findings are internally valid, using a robust dataset that captured a wide range of clinical variables and analyzed using appropriate statistical tests.

There are several limitations that should be considered. Firstly, all observational studies are subject to confounding.[32] We mitigated this risk by measuring a broad range of patient, endoscopist, and procedural variables and controlled for them when appropriate. Nonetheless, the risk for residual confounding in observational studies cannot ever be fully mitigated. Secondly, we did not collect data on withdrawal times, which is a colonoscopy related quality metric associated with ADR, although physicians in our region follow a targeted minimal withdrawal time of at least 6 min. Furthermore, the definition of a confounder requires it be associated with the exposure (i.e., sedation type), the outcome (i.e., ADR), and not be along the causal pathway between the two.[32] Although the association between withdrawal time and ADR has been well established,[11,33] we are not aware of any high quality evidence linking withdrawal time with sedation type. Reassuringly, a recent meta-analysis found no difference in procedure time between sedation types, albeit they did not measure withdrawal time specifically.[8] Regardless, even the use of withdrawal time as a quality metric may be fading after a recent meta-analysis failed to demonstrate any improvement in ADR associated with withdrawal time monitoring.[34] Lastly, we did not have data on how commonly anesthesia assistants were used. As such, we instead reported a more conservative estimate of the incremental cost of propofol cases, which would have been higher had the additional cost of having an anesthesia assistant involved been included.

In conclusion, the use of propofol sedation did not improve key colonoscopy related quality metrics but did increase cost. The routine use of propofol sedation should be reevaluated given its healthcare cost implications.

Contributors

Dr. Sheikh Rahman, Dr. Lauren Cipriano, Cassandra McDonald, Dr. Leonardo Guizzetti and Dr. Michael Sey made substantial contributions to the conception or design of the work; or the acquisition, analysis or interpretation of the data for the work. Dr. Sarah Cocco, Dr. Ziad Hind, Dr. Debarati Chakraborty, Dr. Karissa French, Dr. Omar Siddiqi, Dr. Brian Yan and Dr. Vipul Jairath made moderate contributions to the conception or design of the work; or the acquisition, analysis or interpretation of the data for the work. Dr. Aze Wilson and Dr. Mayur Brahmania made contributions to the conception or design of the work; or the acquisition, analysis or interpretation of the data for the work. Dr. Sheikh Rahman, Dr. Jairath and Dr. Sey made significant contributions to drafting the work or revising it critically for important intellectual content. Dr. Lauren Cipriano, Dr. Mayur Brahmania, Dr. Aze Wilson, and Dr. Brian Yan made moderate contributions to drafting the work or revising it critically for important intellectual content. Cassandra McDonald, Dr. Leonardo Guizzetti, Dr. Sarah Cocco, Dr. Ziad Hindi, Dr. Debarati Chakraborty, Dr. Karissa French, and Dr. Omar Siddiqi made contributions to drafting the work or revising it critically for important intellectual content. All authors equally contributed to the final approval of the version to be published and agreement to be accountable for all aspects of the work.

Data sharing statement

Request for deidentified data sharing will be considered on a case-by-case basis based on the scientific merit, feasibility, and regulatory approval and subject to a data sharing agreement.

Declaration of interests

AW receives consulting fees from Fresnius Kabi and speaker fees from Takeda and Pfizer. MS is the Regional Endoscopy Lead for Ontario Health, a government agency tasked with quality assurance and quality improvement in the region's endoscopy units and receives a stipend for this work.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.eclinm.2024.102503.

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