Randomized controlled trial of procedural sequence for same-day bidirectional endoscopy under monitored anesthesia care (RECoVER Trial)

Ali El Mokahal, MD,1 Halim Bou Daher, MD,1 Rana Yamout, MD,2 Nour Hoshaimi, MD,2 Chakib Ayoub, MD,2 Yasser Shaib, MD,1 Ala I. Sharara, MD1

Background and Aims: Evidence regarding the ideal endoscopy sequence is inconclusive in patients undergoing same-day bidirectional endoscopy (BDE).

Methods: Adults undergoing endoscopy with moderate sedation were randomized to either colonoscopy first (C-E) or EGD first (E-C) under monitored anesthesia care and bispectral index (BIS) monitoring. The primary endpoint was time to recovery from sedation. Secondary endpoints were total amount of sedative, time in deep sedation (defined as BIS <60), patient and endoscopist satisfaction, and adverse events. Patients were contacted the following day for assessment of postdischarge events including delayed recovery and effects on cognitive function and memory.

Results: One hundred twenty consecutive patients were enrolled (60 per arm). Baseline characteristics were similar. There was no difference between the C-E and E-C groups in time to recovery (20.2 ± 8.8 minutes vs 17.9 ± 8.8 minutes), dose of propofol (219.9 ± 79.6 mg vs 217.6 ± 79.1 mg), total time spent in deep sedation (7.2 ± 6.6 minutes vs 9.5 ± 7.9 minutes), patient and endoscopist satisfaction, adenoma detection rate (38.3% vs 31.7%, P = .444), intraprocedural adverse events, or immediate adverse events. Time to reach the cecum was shorter for E-C patients (5.9 ± 3.5 minutes vs 7.3 ± 3.78 minutes, P = .033), whereas C-E patients reported higher rates of postdischarge dizziness (17.5% vs 3.5%, P = .015).

Conclusions: There are no clinically significant differences between procedural sequences in same-day BDE. Decisions regarding the preferred sequence may be individualized, taking into consideration procedural yield, individual risk, and other factors such as the potential for aerosol generation and staff exposure. (Clinical trial registration number: NCT04096339.) (iGIE 2023;1-10.)

Same-day bidirectional endoscopy (BDE) is often done for patients with iron deficiency anemia, unexplained abdominal pain, and visible or occult GI bleeding.1,2 BDE can also be done for patients who undergo endoscopic procedures receive BDE.5 Performing both procedures on the same day has been shown to reduce the amount of anesthetic, recovery time, procedure time, and costs compared with completing procedures on separate occasions.4

Despite its convenience, there is no established sequence for BDE, and the sequence is determined by provider preference. Multiple BDE sequence trials have been done assessing different facets of endoscopy (Table 1), including the amount of sedation, time to recovery, adverse event rate, outcomes of endoscopy, and patient and provider satisfaction. With respect to endoscopy outcomes and adverse events, Choi et al10 found no differences in adenoma detection rates, colonoscopy completion, or difficult cecal intubation rates. However, Cho et al10 found that the quality of EGD was higher when EGD was done first. Sayin et al9 showed no difference in the time needed to reach the cecum but did find a higher rate of adverse events in the EGD first and then colonoscopy (E-C) sequence, but another study by Chen et al8 found similar rates of adverse events with both sequences.

In studies where quantity of sedation was assessed, 5 studies showed that the E-C sequence required less sedation.5,8-12 Two studies were done with light sedation, whereas other studies used propofol, showing more sedation in the colonoscopy and then EGD (C-E) sequence in 1 study7 and no difference in quantity of sedation in the other.13 Some studies have shown that the E-C sequence is associated with less patient discomfort,5,10 whereas 2 studies showed no difference in patient discomfort.8,12 Sayin et al9 reported that both patients and providers were less satisfied with the E-C sequence.10
<table>
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<tr>
<th>Study</th>
<th>Study design</th>
<th>No. of patients</th>
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<td>Cho et al (2010)</td>
<td>Randomized prospective study</td>
<td>80</td>
<td>Limited (no benzodiazepine or propofol)</td>
<td>Procedure quality, Patient comfort</td>
<td>Quality of EGD is better when EGD is performed first Decreased discomfort with EGD first</td>
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<td>Hsieh et al (2011)</td>
<td>Randomized prospective study</td>
<td>176</td>
<td>Lidocaine spray, meperidine, propofol</td>
<td>Quantity of propofol used, Patient comfort, Recovery time, Procedure time</td>
<td>Total propofol used was less when EGD was done first Colonoscopy was better tolerated when EGD was done first No effect on procedure time, recovery time, or postprocedure discomfort</td>
</tr>
<tr>
<td>Choi et al (2013)</td>
<td>Randomized prospective study</td>
<td>1103</td>
<td>568 patients underwent sedation with midazolam and propofol</td>
<td>Colonoscopy completion rate, Adenoma detection rate</td>
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<td>Carter et al (2014)</td>
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<td>Total propofol dose, Recovery time, Duration of endoscopy, Patient satisfaction, Adverse effects, Endoscopic findings, Cardiopulmonary responses of the patients</td>
<td>Less recovery time in E-C sequence E-C sequence had a lesser decrease in mean arterial pressure Less propofol during E-C sequence No difference in satisfaction of patients or physicians between the groups No difference in adverse effects in either group No difference in pathologic findings</td>
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<tr>
<td>Sayn et al (2020)</td>
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<td>80</td>
<td>Fentanyl and propofol</td>
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<td>More propofol required in E-C sequence Total procedure duration and EGD duration longer in E-C sequence Higher adverse event rate in E-C sequence Lower endoscopist and patient satisfaction in E-C sequence No difference in time to reach cecum</td>
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<tr>
<td>Chen et al (2018)</td>
<td>Randomized prospective study</td>
<td>120</td>
<td>Midazolam and fentanyl</td>
<td>Total sedation used, Recovery time, Discomfort, Adverse events</td>
<td>Mean dose of fentanyl and midazolam were higher in the C-E group Aldrete scores at 15 and 25 min were higher in the E-C group No difference in discomfort No difference in adverse events</td>
</tr>
<tr>
<td>Hammami et al (2019)</td>
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<td>Jowhari et al (2020)</td>
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<td>Comfort scores, Amount of sedative required</td>
<td>E-C group required less midazolam Discomfort did not differ according to sequence on days 0 and 7 postprocedure</td>
</tr>
</tbody>
</table>

E-C, EGD first followed by colonoscopy; C-E, colonoscopy first followed by EGD.
sequence, and 3 other studies showed no difference in post-
procedure satisfaction. Of the studies that assessed re-
cov ery time, 3 reported faster recovery with the E-C
sequence, of which only 1 study used deep sedation
with propofol. On the other hand, 2 other studies showed
no difference in patients undergoing deep sedation. The
bispectral index (BIS) is a noninvasive tool that uses
electroencephalogram monitoring to provide anesthesiolo-
gists with a numerical representation of the depth of seda-
tion and effects of anesthesia. The American Society of
Anesthesiologists defines 4 levels of sedation: minimal,
m moderate, deep sedation, and general anesthesia. The
 corresponding BIS values, ranging from 100 to 0, are as fol-
ows: 100 to 95, awake; 95 to 70, light to moderate
sedation; 70 to 60, deep sedation with low probability of
explicit recall; 60 to 40, general anesthesia with low proba-
bility of consciousness; and <40, deep hypnotic state.
When patients receive general anesthesia, their sedatives
are usually titrated to maintain a BIS value of 40 to 60.17
As such, this tool can be used to identify states in which pa-
 tients are oversedated. The harms of oversedation include a
higher risk of hemodynamic instability, delayed recovery,
and potential for delayed effect on cognitive function.

Given the heterogeneity among existing studies, we con-
ducted a randomized controlled trial to assess the ef-
fect of procedural sequence on endoscopy parameters
(RECoVER: Reduction in sEdation: Colonocopy Vs Esopha-
goduodenoscopy first). Additionally, our study is the first
to directly assess the effect of procedural sequence on
oversedation, as detected by BIS monitoring.

METHODS

Study population

This was a randomized controlled trial conducted at the
American University of Beirut Medical Center in Lebanon.
Patient enrollment is described in Figure 1. Outpatients un-
dergoing elective BDE were included if aged >18 years and
scheduled for EGD and colonoscopy in the same session
with anesthesiologist-administered sedation. Exclusion
criteria were age <18 or >75 years; known allergy or
adverse reaction to propofol, midazolam, or opioid medica-
tion; sleep apnea; American Society of Anesthesiologists
class III; pregnancy; known cirrhosis; chronic kidney dis-
 ease (stage 4 or 5); known psychological disorder or cogni-
tive dysfunction; significant gastroparesis; gastric outlet
obstruction; ileus; known or suspected bowel obstruction;
presence of a stoma; compromised swallowing reflex or
mental status; prior colon resection or gastric surgery;
and chronic use of >1 psychoactive drug (benzodiazep-
ines, antidepressants, antipsychotics).

Informed consent was obtained from all enrolled pa-
tients. The study was approved by the institutional review
board. The trial was registered at clinicaltrials.gov on
September 19, 2019.

Primary and secondary outcomes

The primary outcome of this study was time to recovery
from sedation. Secondary outcomes were propofol re-
quirements; depth of anesthesia using the BIS scale; cogni-
tive function impairment up to 24 hours after discharge;
duration of induction; biopsy sample kit use; hemody-
namic instability; episodes of desaturations, apnea, drows-
iness, and impaired cognitive function; and need for airway
support.

Sample size and data analysis

Our sample calculation was based on similar study re-
results concerning recovery time. We estimated the subjects
undergoing EGD first to have a shorter recovery period by
almost 25%. Using patient recovery time as a primary
endpoint, with an α of .05 and a power of .80, we calcu-
lated the sample required to show significance to be 51 pa-
 tients per arm, assuming noninferiority. Assuming a 10% dropou t, we aimed to enroll 120 subjects.

Study design

Patients enrolled were divided into 2 groups: E-C
sequence or C-E sequence. Patients were randomized us-
ing an online randomization tool that was not accessible
by the endoscopists. Two senior gastroenterologists per-
fomed the procedures for this study. The endoscopists
perform 1000 to 1200 endoscopic procedures per year
and have 20+ and 25+ years of experience within the field.

After enrollment, patients were evaluated by the anes-
thesia team and prepared for endoscopy. Seven attending
physician anesthesiologists provided the sedation for the
procedures, each with 5+ years of work experience. Before
induction, the BIS electroencephalogram probes were
placed on the patient’s forehead, and the machine was
 turned on. The providing endoscopists, anesthesiologists,
and patients could not be blinded to the procedural
sequence. Endoscopy began when the patient was sedated
on assessment and with BIS values between 70 and 80.

Time of initiation of induction and the initial doses of
propofol, midazolam, and fentanyl were recorded. Time
of scope insertion and scope removal were recorded for
both procedures. At the end of the procedures, the time
to transfer to the postanesthesia care unit was recorded,
and transfer was determined at the discretion of the anes-
thesiologist. During the procedure, BIS readings, heart
rate, blood pressure, and oxygen saturation level were re-
corded at the start of sedation and every 5 minutes during
the procedure. Adverse events of interest were desatura-
tion requiring jaw thrust, desaturation requiring airway
insertion, bradycardia requiring atropine, hypotension
requiring neosynephrine or ephedrine, or patient move-
ment or awakening requiring an anesthetic bolus.

After the completion of both procedures, the anesthesiolo-
gist determined the total amount of propofol, fentanyl, and
midazolam used. Duration of induction and time to reach
the cecum were recorded. After the procedure, endoscopist
(quality sedation and bowel preparation) and patient satis-
faction were assessed. The patient’s BIS recordings were ex-
ported from the machine onto a computer, and the mean
BIS reading every minute per procedure was recorded.

To assess recovery time, the modified postanesthesia
discharge scoring system was used. This scoring system
uses vital signs, activity, presence of nausea or vomiting,
pain, or surgical bleeding to provide patients with a value.
The modified postanesthesia discharge scoring system has
been shown to be adequate for use in patients undergoing
endoscopic procedures.18 Patients with a value \(<9\) were
deemed ready for discharge. This was assessed by the
research assistant every 5 minutes until 2 consecutive
values \(\geq 9\) were recorded. The time to recovery was then
documented by calculating the difference in the time from
transfer to the postanesthesia care unit to the time the pa-
tient was deemed stable for discharge. Approximately 24
hours after procedures, patients were called and asked
about their day after their procedure, their comfort and level
of function, and their overall satisfaction with the procedure
and sedation.

**Sedation regimen**

Propofol at a dose of 100 to 150 \(\mu g/kg/min\) was used ac-
cording to patient weight and was delivered using an auto-
mated pump (Alaris GH Syringe Pump; BD, Eysins,
Switzerland). In addition, patients received a standard
dose of 50 \(\mu g\) fentanyl and 2 mg midazolam intravenously.
A trained anesthesiologist provided sedation during the
procedure for all patients. Patients were given boluses of
propofol or fentanyl if they were awakening or moving dur-
ing the procedure, and these boluses were recorded if
given.

**Data analysis**

The primary endpoint of this study was time to recov-
ery. Secondary endpoints were the amount of propofol
used, time spent with BIS score \(<60\) and the number of
times the patient’s BIS score dipped below 60, cognitive
impairment 24 hours after discharge, duration of induc-
tion, hemodynamic instability, episodes of desaturations
or apnea, or need for airway support.

Continuous variables are expressed as mean \pm standard
development (95% confidence interval). Categorical variables
are represented as counts with percentages. Group com-
parisons of qualitative variables were performed using \(\chi^2\)
tests and analysis of variance tests/Fisher exact test where applicable. \(P\) values \(<.05\) were deemed significant. IBM
SPSS, version 24 (IBM SPSS Statistics for Windows, Ar-
monk, NY, USA) was used for data analysis.

**RESULTS**

Baseline demographics for the 2 groups were similar
(Table 2). Thirty-four patients used alcohol occasionally,
of which 16 (26.7%) were in the C-E group and 18 (30%) were in the E-C group. Thirteen patients (10.8%) used 1 psychoactive medication, of which 7 (11.6%) were in the C-E group and 6 (10%) were in the E-C group. Ninety percent of patients had a history of sedation with general anesthesia (75%), of which 44 (73.3%) were in the C-E group and 6 (10%) were in the E-C group. Thirteen patients (10.8%) used 1 opioid drug use and 0 were in the E-C group and 0 in the C-E group.

TABLE 2. Baseline demographics of enrolled patients

<table>
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<tr>
<th>No. of cases (%)</th>
<th>No. of cases (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex</td>
<td>29 (48.3)</td>
<td>29 (48.3)</td>
</tr>
<tr>
<td>Smoker</td>
<td>21 (35.0)</td>
<td>20 (33.0)</td>
</tr>
<tr>
<td>Alcohol occasionally</td>
<td>16 (26.7)</td>
<td>18 (30.0)</td>
</tr>
<tr>
<td>Alcohol frequently</td>
<td>5 (8.0)</td>
<td>3 (5.0)</td>
</tr>
<tr>
<td>Psychotropic drug use</td>
<td>7 (11.6)</td>
<td>6 (10.0)</td>
</tr>
<tr>
<td>Opioid drug use</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Diabetes</td>
<td>7 (11.6)</td>
<td>6 (10.0)</td>
</tr>
<tr>
<td>Prior abdominal surgery</td>
<td>24 (40.0)</td>
<td>25 (41.67)</td>
</tr>
<tr>
<td>Previous general anesthesia</td>
<td>44 (73.3)</td>
<td>46 (76.67)</td>
</tr>
</tbody>
</table>

TABLE 3. Baseline characteristics of enrolled patients

| Age, y | 60 | 54.5 | 11.6 | 50.6-56.6 | 60 | 53.5 | 11.63 | 50.6-56.6 | .719 |
| Weight, kg | 60 | 74.9 | 13.9 | 71.3-78.5 | 60 | 80.5 | 17.55 | 76.0-85.1 | .055 |
| Height, m | 60 | 1.7 | .09 | 1.6-1.7 | 60 | 1.7 | .11 | 1.68-1.74 | .196 |

Postprocedure recovery from sedation and time with BIS <60

These findings are presented in Table 3. The primary endpoint, time to recovery, was not significantly different. Mean time to recovery was shorter in the E-C group (17.9 ± 8.8 minutes) compared with the C-E group (20.3 ± 8.8 minutes, P = .144). Time to discharge was also not significantly different in the E-C group (44.4 ± 2.3 minutes) compared with the C-E group (44.7 ± 16.6 minutes). The total procedure time was not significantly different in the C-E group (23.5 ± 5.2 minutes) compared with the E-C group (23.9 ± 6.2 minutes, P = .662).

Forty-four patients (88.9%) in the E-C group experienced dips in BIS <60 compared with 40 patients (88.9%) in the C-E group (P = .825). The time spent with BIS <60 was 2 minutes longer on average in the E-C group (9.08±7.68 minutes) compared with the C-E group (7.06 ± 6.28 minutes), but this was not statistically significant (P = .142). There was a statistically significant difference in the time it took patients to be ready for transfer to the postanesthesia care unit after the end of the procedures. In the E-C sequence, the time was 3.1 ± 2.7 minutes compared with 1.4 ± 1.8 minutes for the E-C sequence (P = .015).

Anesthetic usage

These findings are presented in Table 4. Total propofol use was similar in C-E group (219.9 ± 79.6 mg) and the E-C group (217 ± 79.1 mg, Z = .679). The same induction doses of propofol were given to patients in the C-E group (37.1 ± 11.6 mg) and the E-C group (38 ± 14.2 mg, Z = .505). There was no difference in the number of patients who required propofol boluses in the C-E group (55 [55.0%]) and the E-C group (26 [43.3%]), P = .201).

Total fentanyl use was higher in the E-C group (64.8 ± 21.4 µg) compared with the C-E group (59.8 ± 18.7 µg), but this was not statistically significant (P = .080). The induction dose of fentanyl was similar when comparing between the C-E (57.9 ± 17.3 µg) and E-C (61.9 ± 20.9 µg, Z = .153) groups. A larger number of patients received fentanyl boluses in the C-E group (20 [33%]) compared with the E-C group (9 [15.0%], P = .019). This was mainly driven by fentanyl boluses given between procedures, which were given to 18 patients (30%) in the C-E group and 4 patients (6.7%) in the E-C group (P < .001).

Midazolam was only used for induction. Its use was similar in the C-E group (1.9 ± .6 mg) compared with the E-C group (2.8 ± .6 mg, Z = .203).

Endoscopic parameters

These findings are presented in Table 5. The adenoma detection rate was similar in the C-E (38%) and E-C (32%) groups (P = .444). The overall adenoma detection rate was 35%, showing a high quality of colonoscopy. Similar biopsy samples were taken in both EGD and colonoscopy in the C-E group (31 [51.7%] and 33 [55.0%], respectively) and in the E-C group (26 [43.3%] and 37 [61.7%], respectively). The time to reach the cecum was
lower in the E-C group (5.9 ± 3.4 minutes) compared with the C-E group (7.3 ± 3.7 minutes, \( P = .033 \)). Endoscopist satisfaction with sedation and bowel preparation were high and similar in both groups.

Endoscopy adverse events
These findings are presented in Table 6. Adverse event rates were low overall. No patients had bradycardia requiring atropine, and only 1 patient in the E-C group...
required airway support with a nasopharyngeal tube. Desaturations requiring jaw thrust were higher in the C-E group (20 [33.3%]) compared with the E-C group (17 [28.33%]), but this was not statistically significant ($P = 0.510$). The rate of hypotension requiring neosynephrine was the same in both groups (3 [5%]). Patient movement requiring a bolus was lower in the C-E group (26 [43.33%]) when compared with the E-C group (30 [50.00%]), but this was not statistically significant ($P = 0.464$).

**Assessment 24 hours postprocedure**

These findings are presented in Table 7. Patients noted high rates of overall satisfaction with the procedure, and this was similar in the C-E and E-C groups. Adverse events in the 24 hours after the procedure were rare overall. Two patients in the C-E group reported memory problems compared with 3 in the E-C group ($P = 1.000$). Seven patients (12.3%) in the C-E group reported nausea compared with 4 patients (7.0%) in the E-C group ($P = 0.341$). Dizziness was higher in the C-E group, occurring in 10 patients (17.5%) compared with 2 patients (3.5%) in the E-C group ($P = 0.015$). Difficulty focusing was the most common adverse event, reported by 12 patients (21.1%) in the C-E group and 9 patients (15.8%) in the E-C group ($P = 0.469$). Despite all patients counseled not to drive after the procedure, 30 patients drove (25%), including 15 patients from each group. None of the patients surveyed reported any accidents or issues with driving.

**DISCUSSION**

In this randomized controlled trial of sequence in BDE, we found no meaningful difference in our primary endpoint, namely time to recovery from sedation. Other studies have shown conflicting results. Hsieh et al$^9$ found no significant difference in recovery time between the 2 sequences. Others found that recovery was faster for the E-C sequence.$^8,10,11$ In the studies by Tang et al$^{10}$ and Chen et al,$^8$ sedation was given using only midazolam and fentanyl, without propofol. Compared with other agents used, propofol is known to have shorter recovery times.$^{19}$ It is plausible that the use of propofol for sedation may have

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<th>TABLE 5. Endoscopy outcomes</th>
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<tr>
<td>Colonoscopy first, then EGD sequence</td>
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<tr>
<td>Adenoma detection rate</td>
</tr>
<tr>
<td>60 (100)</td>
</tr>
<tr>
<td>EGD biopsy samples taken</td>
</tr>
<tr>
<td>Colonoscopy biopsy samples taken</td>
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<tr>
<td>Endoscopist 1</td>
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</table>

<table>
<thead>
<tr>
<th>Time to cecum, min</th>
<th>Mean</th>
<th>Standard deviation</th>
<th>95% Confidence interval</th>
<th>Mean</th>
<th>Standard deviation</th>
<th>95% Confidence interval</th>
<th>$P$ value</th>
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<tbody>
<tr>
<td>60</td>
<td>7.3</td>
<td>3.7</td>
<td>6.3-8.3</td>
<td>60</td>
<td>5.8</td>
<td>3.4</td>
<td>4.99-6.77</td>
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<tr>
<td>Withdrawal time, min</td>
<td>60</td>
<td>11.6</td>
<td>5.7</td>
<td>10.1-13.0</td>
<td>60</td>
<td>11.4</td>
<td>4.6</td>
</tr>
<tr>
<td>Endoscopist satisfaction with sedation (0-5 scale)</td>
<td>60</td>
<td>4.5</td>
<td>.8</td>
<td>4.2-4.7</td>
<td>60</td>
<td>4.6</td>
<td>.6</td>
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<tr>
<th>TABLE 6. Endoscopy adverse events</th>
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<tr>
<td>Colonoscopy first, then EGD sequence</td>
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<tr>
<td>Desaturation requiring jaw thrust</td>
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<tr>
<td>60 (100)</td>
</tr>
<tr>
<td>Desaturation requiring airway</td>
</tr>
<tr>
<td>Bradycardia requiring atropine</td>
</tr>
<tr>
<td>Hypotension requiring pressors</td>
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<tr>
<td>Patient movement requiring bolus</td>
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</table>
elminated any difference in time to recovery between the 2 sequences, as was seen in the studies using midazolam and fentanyl for sedation. Cao et al. found a mean difference of 2.2 minutes in recovery. Because we assessed recovery every 5 minutes, our intervals of assessment may not have been precise enough to detect such a small difference. Additionally, Cao et al. used intermittent boluses of propofol to maintain sedation, whereas we used a continuous propofol drip with boluses as needed. It is unclear if an anesthesiologist was present in their procedures, and the presence of trained anesthesiologists in our study may have contributed to the absence of a difference. In calculating the power required for our study, we also assumed a 25% difference in recovery times, and this study may not have been powered adequately to detect a smaller difference in time to recovery. We did find that recovery was 2.3 minutes longer with the C-E sequence, whereas 1 study found no difference and 1 study found a larger amount was required when using the C-E sequence. Additionally, a meta-analysis of 4 of the 5 studies showing lower amounts of sedation required confirms this. This difference seems to persist regardless of whether midazolam or propofol was used as the sedative. We and others also did not find a significant difference in the rates of adverse events between the 2 sequences. As such, the clinical significance of a difference in sedation doses may be unlikely. Additionally, the studies that reported a statistically significant difference in the amounts of sedation used did not report a markedly large difference. We did, however, find a lower rate of postprocedural dizziness in the 24 hours after the procedure when EGD is done first. However, there were no differences in the rates of nausea, memory loss, or difficulty focusing, and overall satisfaction with the procedures was high irrespective of sequence. We are unsure what the cause of this discrepancy was, particularly when the amount of sedation and time to recovery were not different and there were no identified differences between the 2 cohorts at baseline. However, it may be reasonable to identify patients who report a predisposition or history of dizziness and to begin with endoscopy in that subset of patients.

We also found no difference in the time spent in deep sedation or the number of dips into deep sedation. In our experience, the intubation phase of EGD is more uncomfortable than colonoscopy, and we speculated that performing the EGD initially may be optimal because the initial induction medications would remain in the body and that any additional anesthetic usage would also carry forward into the colonoscopy. This contrasts with beginning with colonoscopy where we expected the need for added sedation and more boluses to complete the EGD while maintaining patient comfort. This is reflected in our study with our higher use of fentanyl when transitioning from colonoscopy to endoscopy. However, this was not associated with a statistical or clinically significant difference in the time spent in deep sedation. The absence of a difference in deep sedation between the 2 procedures can also be explained by the fact that patients in both sequences required similar amounts of sedation.

The similar amount of anesthetic required in our study goes against the grain when compared with most other studies. Five studies found that the amount of sedation required was lower with the E-C sequence, whereas 1 study found no difference and 1 study found a larger amount was required when using the C-E sequence. Additionally, a meta-analysis of 4 of the 5 studies showing lower amounts of sedation required confirms this. This difference persists regardless of whether midazolam or propofol was used as the sedative. We and others also did not find a significant difference in the rates of adverse events between the 2 sequences. As such, the clinical significance of a difference in sedation doses may be unlikely. Additionally, the studies that reported a statistically significant difference in the amounts of sedation used did not report a markedly large difference. We did, however, find a lower rate of postprocedural dizziness in the 24 hours after the procedure when EGD is done first. However, there were no differences in the rates of nausea, memory loss, or difficulty focusing, and overall satisfaction with the procedures was high irrespective of sequence. We are unsure what the cause of this discrepancy was, particularly when the amount of sedation and time to recovery were not different and there were no identified differences between the 2 cohorts at baseline. However, it may be reasonable to identify patients who report a predisposition or history of dizziness and to begin with endoscopy in that subset of patients.

Overall, we did not find an appreciable difference to justify 1 sequence over the other. With the myriad factors assessed in the literature, it is difficult to identify 1 sequence that is optimal in all scenarios, and as such the decision of which procedure is done first needs to be determined by the setting and the patient population in which the

### Table 7. Assessment 24 hours postprocedure.

<table>
<thead>
<tr>
<th></th>
<th>Colonoscopy first, then EGD sequence</th>
<th>EGD first, then colonoscopy first</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Memory problems</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>57</td>
<td>2 (3.5)</td>
<td>55 (96.5)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>57</td>
<td>10 (17.5)</td>
<td>47 (82.5)</td>
</tr>
<tr>
<td>Difficulty focusing</td>
<td>57</td>
<td>12 (21.1)</td>
<td>45 (78.9)</td>
</tr>
<tr>
<td>Drove after procedure</td>
<td>57</td>
<td>15 (26.3)</td>
<td>42 (73.7)</td>
</tr>
<tr>
<td>&quot;How long did it take you to go back to normal after discharge,&quot; h</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>No. of cases</td>
<td>Mean</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Total</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>57</td>
<td>3.80</td>
</tr>
</tbody>
</table>
procedures are conducted. One major benefit of performing EGD first is that biopsy forceps used in EGD are reusable in colonoscopies, but the reverse is not possible. In our colonoscopy-first cohort, 26 of 60 patients required subsequent EGD biopsy sampling, and in all these cases new forceps had to be used. This can add significant costs to endoscopy, which may merit consideration in low-resource areas or areas in the world where biopsy forceps are harder to attain. Finally, since December 2019 the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus led to a global pandemic with which we continue to grapple to this day.21 This pandemic put healthcare workers and their families at increased risk of contracting the virus.22 Although this risk has since been decreased by the advent of vaccines,23,24 1 group at a higher risk of contracting the virus are those involved in aerosol-generating procedures. EGD is an aerosol-generating procedure,25 and aerosols containing SARS-CoV-2 have been shown to remain stable for 3 hours.26 Masking and universal precautions are of paramount importance in these circumstances, and given the absence of clinically significant differences between the 2 sequences, we recommend that in times where SARS-CoV-2 cases rise or in any future concern of an airborne epidemic that colonoscopy be done first to minimize the exposure time of healthcare providers to aerosolized infectious agents in the examination room.

This study had several limitations. First, neither the endoscopists nor anesthesiologists performing the procedures could be blinded to the sequence of endoscopic performance. Furthermore, the study was performed by 2 senior endoscopists, and it is unclear how generalizable our results may be to other providers. Additionally, this study only assessed patients undergoing sedation with propofol, and our findings may not be generalizable to other methods of procedural sedation.

In conclusion, we did not find clinically significant differences between the 2 sequences of BDE when we assessed time to recovery, quantity of sedative used, patient satisfaction, adverse events, or endoscopist satisfaction with the procedure. Additionally, we did not find any differences in oversedation as detected by BIS monitoring. One strength of this study is the novel use of BIS monitoring to detect differences in sedation. BIS monitoring provides an objective method to assess oversedation that is not subject to bias, particularly because the endoscopist and anesthesiologist could not be blinded to procedural sequence. It also allows us to detect subclinical oversedation. Although we did not find a difference in procedural sequence, this study also shows that oversedation does often take place in endoscopy, and further assessment of subclinical oversedation in future studies is warranted to decrease the risks of oversedation in endoscopy. Based on the above, the decision regarding preferred sequence may be individualized, taking into consideration procedural yield, individual risk, additional cost of accessories, and other factors such as the potential for aerosol generation and staff exposure.

DISCLOSURE

All authors disclosed no financial relationships.

REFERENCES
