Original Article

Safety of chronic obstructive pulmonary disease patients undergoing carbon dioxide insufflation in extended endoscopic procedures

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ABSTRACT

Introduction: Carbon dioxide (CO_2) insufflation for endoscopies has been shown to be more comfortable and safe, but only in patients without underlying chronic obstructive pulmonary disease (COPD). The aim of this study was to show that using CO_2 is safe in COPD patients. **Methods:** Patients were retrospectively identified who underwent extended endoscopic procedures during the time period of January 2012 to December 2017. Patients were included if they also had COPD. A matched control group without COPD was created during the same timeframe. All the patients were sedated with continuous monitoring of their CO_2 levels by end-tidal CO_2 ($EtCO_2$). **Results:** One hundred and ten patients had COPD and underwent an extended endoscopic procedure. These patients had a higher severity of their comorbidities (American Society of Anesthesiologists class 3 or 4) (93.6% [95% confidence interval [CI], 87.4%–96.9%] vs. 60.3% [95% CI, 51.1%–69.0%]; $P < 0.01$) and an increase of co-existing obstructive sleep apnea (33.6% vs. 6.3%, $P < 0.01$). There was no difference in baseline $EtCO_2$, but the peak $EtCO_2$ and postprocedure $EtCO_2$ were both significantly higher in the COPD group. The only postprocedural complication found was an inability to be extubated immediately following the procedure with subsequent need to hospitalize the patient, which occurred in three patients (2.8%; 95% CI, 0.9%–7.9%) in the COPD group and one (0.9%; 95% CI, 0.2%–4.9%) in the non-COPD group ($P = 0.37$). **Conclusion:** The present study, which was the only study looking at CO_2 insufflation specifically in COPD patients, provides evidence that CO_2 insufflation is safe in COPD despite a slight increase in $EtCO_2$.

KEY WORDS: Anesthesia, carbon dioxide, chronic obstructive pulmonary disease, endoscopy, humans

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INTRODUCTION

Carbon dioxide (CO_2) insufflation is used laparoscopic surgery and only recently has been adopted in endoscopic procedures performed by gastroenterologists. There have been many studies showing that using CO_2 in these procedures significantly reduces peri-procedural pain, but with concerns for CO_2 retention.[1-9] Many studies have shown CO_2 insufflation is safe in healthy sedated patients, associated with only minimal rises in either transcutaneous CO_2 or end-tidal CO_2 ($EtCO_2$) measurements.[1-3,10-14] All these studies excluded patients with underlying pulmonary disease. We sought to show the

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safety of CO_2 insufflation in chronic obstructive pulmonary disease (COPD) patients.

METHODS

We conducted a retrospective cohort study at a single tertiary referral center, comparing the $EtCO_2$ and postprocedural outcomes for COPD versus non-COPD patients for all extended endoscopic procedures performed between January 2012 and December 2017. The term "extended endoscopic procedure" was defined as an upper or lower enteroscopy using either a single or double balloon technique. COPD was defined as nonreversible airflow obstruction on a pulmonary function test. The institutional review board approved the study protocol 18-002171.

In the time period listed, we identified all patients (≥18 years of age) diagnosed with COPD who underwent an extended endoscopic procedure with CO_2 insufflation. Patients were excluded from this group if they did not have a pulmonary function test within 1 year of the procedure. A control group was defined by a matched group of non-COPD patients who underwent an extended endoscopic procedure during the same timeframe.

All patients were monitored by either an anesthesiologist or certified registered nurse anesthetist. Patients received sedation by propofol, midazolam, fentanyl, or any combination. In order to obtain the duration of procedure, the insertion and withdrawal times were recorded. $EtCO_2$ measurements were used to estimate the CO_2 levels. Continuous monitoring was possible as most patients were intubated and when not intubated a capnograph was attached to a nasal cannula. The $EtCO_2$ readings were recorded every 5 min throughout the procedures. For this study, only $EtCO_2$ readings from the start, peak $EtCO_2$ achieved, and end of the procedure were used.

The primary endpoint for the present study was that the procedure was safe with no more complications, including hospitalizations, inability to be extubated, and mortality. Secondary endpoints were $EtCO_2$ levels were going to be higher throughout the study.

Statistical analyses were performed using JMP version 14.0.0 (SAS Institute Inc., Cary, North Carolina, United States). Continuous data were analyzed using a nonparametric Wilcoxon rank sum test. Pearson's Chi-square or Fisher's exact test, depending on the size of analyzed variables, was used for categorical data. Complication rates were analyzed by exact binomial 95% confidence intervals. $P < 0.05$ was considered statistically significant.

RESULTS

A total of 220 patients who underwent an extended endoscopic procedure were selected for this study with 110 of those patients having COPD. The baseline characteristics of both groups are displayed in Table 1. Both groups had similar age, sex, and race breakdowns. The COPD group had significantly more comorbidities (American Society of Anesthesiologists [ASA] Class 3 and 4) (93.6% [95% confidence interval [CI], 87.4%–96.9%] vs. 60.3% [95% CI, 51.1%–69.0%]; $P < 0.01$), along with more current smokers, more patients with co-existing obstructive sleep apnea, and supplemental oxygen use. In the COPD group, the mean FEV1 was 59.45% ±15.93%. In the COPD group, 108 patients (98.18%) were on a short-acting beta-agonist, 34 patients (30.91%) were on a long-acting muscarinic agent, 37 patients (33.62%) were on a long-acting beta-agonist, and 43 patients (39.09%) were on inhaled corticosteroid.

The specifics of the procedure including type of procedure, length of procedure, endotracheal intubation rate, type of sedating medications, and amount of sedating medications were all similar in both groups [Table 2]. From the continuously monitored $EtCO_2$, there was no significant difference between the groups at the start of the procedure. In the COPD group, both the peak $EtCO_2$ (50 ± 12.9 vs. 46.6 ± 7.4; $P = 0.01$) and postprocedural $EtCO_2$ (43.2 ± 13.2 vs. 37.1 ± 12.4; $P < 0.01$) were higher [Table 2]. In both groups, there was a slight increase in $EtCO_2$ from baseline, but for the non-COPD group, it was in the normal range [Figure 1].

In this cohort in which the majority were intubated, there was no difference in total complications ($P = 0.37$) between the COPD (2.8%; 95% CI; 0.9%–7.85%) and non-COPD (0.9%; 95% CI; 0.1%–4.97%) groups [Table 3]. The only complication that occurred in both groups was an inability to extubate the patient immediately following the procedure, resulting in a short hospital stay (maximum length of stay was 3 days). This complication occurred in three patients (2.8%; 95% CI, 0.9%–7.9%) in the COPD group and one (0.9%; 95% CI, 0.2%–4.9%) in the non-COPD group ($P = 0.37$). The anesthesiologist was

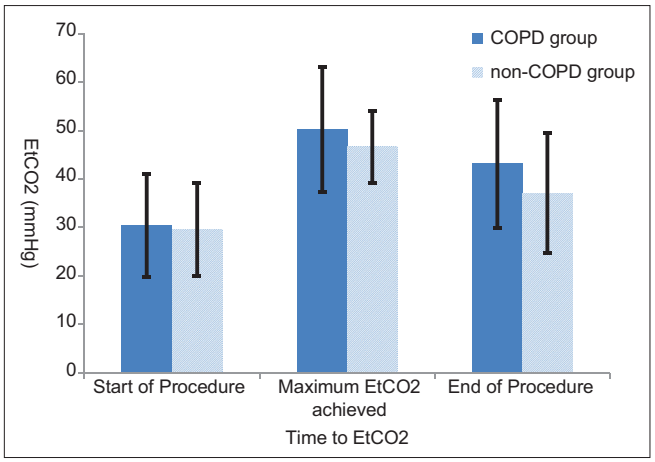

Figure 1: End-tidal CO_2 measured values with 95% confidence interval for COPD and non-COPD groups. CO_2: Carbon dioxide, COPD: Chronic obstructive pulmonary disease, $EtCO_2$: End-tidal CO_2

concerned for an inability to protect the airway with potentially increased secretions for all patients who were not extubated immediately following the procedure in both groups. There was no difference in complication rate by severity of COPD (two patients had severe and one had moderate; $P = 0.47$), length of procedure (1 of 100 min, 1 of 110 min, 1 of 135 min, and 1 of 185 min; $P = 0.65$), ASA class (1 in Class 2 and 3 in Class 3; $P = 0.93$), OSA (0 in OSA patients; $P = 0.32$), oxygen use (0 in patients who used oxygen; $P = 0.48$), and smoking status (one former smoker and three never smokers; $P = 0.17$).

Table 1: Baseline patient characteristics

	COPD group (*n*=110), *n* (%)	Non-COPD group (*n*=110), *n* (%)	*P*
Gender, female	68 (61.8)	71 (64.6)	0.28
Age (year)	69.1±9.9	57.8±10.1	0.44
BMI	30.07±9.27	28.17±6.8	0.0218
Race			
Black	11 (10)	11 (10)	0.3011
Native Hawaiian	1 (0.9)	0	
White	98 (89.1)	97 (88.2)	
Not disclosed	0	2 (1.8)	
ASA class			
Class 1	0	3 (2.7)	<0.0001
Class 2	7 (6.4)	42 (38.2)	
Class 3	87 (79.1)	60 (54.5)	
Class 4	16 (14.5)	5 (4.5)	
Smoking status			
Current	30 (27.3)	12 (10.9)	<0.0001
Former	67 (60.9)	36 (32.7)	
Never	13 (11.8)	62 (56.4)	
OSA	37 (33.6)	7 (6.3)	<0.0001
Treated	21 (80.8)	5 (83.3)	0.8847
Supplemental oxygen	22 (20)	2 (1.8)	<0.0001

COPD: Chronic obstructive pulmonary disease, BMI: Body mass index, ASA: American Society of Anesthesiologists physical status classification, OSA: Obstructive sleep apnea

Table 2: Parameters of enteroscopy in chronic obstructive pulmonary disease and nonchronic obstructive pulmonary disease groups

	COPD group (*n*=110)	Non-COPD group (*n*=110)	*P*
Intubated for procedure	106 (96.4)	109 (99.1)	0.1747
Medications			
Propofol used	106 (96.4)	108 (98.2)	0.4077
Amount of propofol (mg)	221±223	232±198	0.1891
Fentanyl used	65 (59.1)	69 (62.7)	0.5805
Amount of fentanyl (mcg)	121±53	117±60	0.2585
Midazolam used	0	3 (2.7)	0.0812
Amount of midazolam (mg)	0	1.3±0.6	1
Length of procedure (min)	143.5±58.6	140.2±55.4	0.2340
Initial $EtCO_2$ (mmHg)	30.4±10.6	29.6±9.6	0.5941
Peak $EtCO_2$ (mmHg)	50.2±12.9	46.6±7.4	0.0120
Peak time into procedure (min)	84.9±52.4	78.6±45.1	0.0224
Post $EtCO_2$ (mmHg)	43.2±13.2	37.1±12.4	0.0004

COPD: Chronic obstructive pulmonary disease, $EtCO_2$: End-tidal carbon dioxide

DISCUSSION

This study is the first to demonstrate the safety of CO_2 insufflation in COPD patients for extended endoscopies. Our results show that it is safe for COPD patients, despite severity, to undergo these procedures while intubated. This study does show that the patient's $EtCO_2$ will rise, but without an increase rate of complications.

Concerns over the safety of CO_2 insufflation in the COPD population have been expressed. Several studies looked at the COPD population in specifically gastric endoscopic submucosal dissection.[15,16] In both of these studies, the total procedure time was about 60 min, which is approximately half of the total procedure time of the current study. Second, moderate sedation was used without any patients being intubated. Third, the severity of COPD in these studies was very mild with a FEV_1 above 70%. The patients in those studies had a minimal risk to develop complications from the procedure based on their severity level. Our study included all severity levels of COPD along with having these patients undergo procedures at least twice as long.

The maximum $EtCO_2$ reached was 79 mmHg in the COPD group and 73 mmHg in the non-COPD group. The elevated $EtCO_2$ is likely due to the CO_2 insufflation with some respiratory depression, which other studies have shown.[17-20] These maximum levels were not maintained long because the patient was mechanically ventilated. In addition, the postprocedure $EtCO_2$ was in the normal range for both groups. With COPD patients, this study shows their $EtCO_2$ level can increase to a dangerous level, but with close $EtCO_2$ monitoring and anesthesia support there are minimal complications.

This study has some limitations. First, this was a single-center retrospective analysis. Second, this study did not look at one type of procedure but any extended endoscopic procedure, so we can only generalize about extended procedures. The procedures included in the study were all significantly longer than

Table 3: Outcome data for both chronic obstructive pulmonary disease and nonchronic obstructive pulmonary disease groups

	COPD group (*n*=110), *n* (%)	95% CI	Non-COPD group (*n*=110), *n* (%)	95% CI	*P*
Total complications	3 (2.8)	0.9%-7.85%	1 (0.9)	0.1%- 4.97%	0.3669
Hospitalization	3 (2.8)		1 (0.9)		0.3669
Prolonged PACU stay	0		0		
Not extubated	3 (2.8)		1 (0.9)		0.3669
Death	0		0		

COPD: Chronic obstructive pulmonary disease, 95% CI: 95% confidence interval, PACU: Postanesthesia care unit, CI: Confidence interval

esophagogastroduodenoscopies and colonoscopies, which the length of time under sedation increases the risk for COPD patients to retain CO_2. Third, the sedation medication or intubation was not standardized and at the discretion of the anesthesiologist. Furthermore, there was no accounting of actual minute ventilation at the time of measurements which would have varied by anesthesiologist. This variation could have occurred because of experience with COPD patients and recognizing that this group of patients needs to be ventilated more aggressively.

CONCLUSION

This study suggests that CO_2 insufflation is safe for patients with COPD undergoing extended endoscopies. In these COPD patients, the majority were intubated for the procedure for easier ventilation, but there remains a risk for a dangerous increase in CO_2, so $EtCO_2$ should be monitored closely.

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Conflicts of interest
There are no conflict of interest.

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