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Obstructive Sleep Apnea Increases the Risk of Cardiopulmonary Adverse Events Associated with Ambulatory Colonoscopy Independent of Body Mass Index

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Abstract

Background—The relationship between body mass index (BMI) and cardiopulmonary adverse events (CAEs) for ambulatory colonoscopy is unclear.

Aim—To assess the association of BMI and CAEs associated with ambulatory colonoscopy.

Methods—This is a retrospective cohort analysis of 418 patients who underwent outpatient colonoscopy at the Durham Veterans Affairs Medical Center categorized as normal/overweight (BMI < 30), obese (BMI 30–34), or morbidly obese (BMI ≥ 35). Adjusted logistic regression analyses were performed.

Results—At least one CAE occurred in 46.4% of patients (220 events, 72.7% were hypoxia). The rate of CAEs (BMI < 30: 43.8%, BMI 30–34: 48.0%, BMI ≥ 35: 50.6%, $p = 0.53$) and rate of hypoxia (BMI < 30: 34.8%, BMI 30–34: 40.9%, BMI ≥ 35: 43.2%, $p = 0.32$) were numerically higher for obese and morbidly obese patients, but not statistically significant. Obese (OR 1.10,

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95% CI 0.70–1.73) and morbidly obese (OR 1.07, 95% CI 0.61–1.85) patients did not have an increased risk of CAEs after adjusting for age, ASA class, obstructive sleep apnea (OSA), and type of sedation. OSA was independently associated with an increased risk of CAEs (OR 1.71, 95% CI 1.09–2.74, $p = 0.02$) after adjusting for BMI, age, ASA class, and type of sedation.

Conclusion—OSA confers a higher risk of CAEs independent of BMI and sedation type. Consideration of undiagnosed OSA is recommended for appropriate pre-procedure risk stratification. While not statistically significant in this study, there may be clinically significant increased risks of CAEs and hypoxia for patient with BMI > 30 that require further evaluation with larger studies.

Keywords

Colonoscopy; Body mass index; Adverse events; Patient safety

Introduction

Large studies provide estimates of the risk of cardiopulmonary adverse events (CAEs) for colonoscopy ranging from 0.14 to 1.1% [1–5]. Advanced age, cardiopulmonary comorbidities, and American Society of Anesthesiologists (ASA) class III or higher are associated with risk of CAEs for endoscopic procedures [6–8]. No study has evaluated whether BMI increases the risk of CAEs for low-risk ambulatory colonoscopy independent of ASA class or comorbidities, especially for obese and morbidly obese patients with BMI between 30 and 40. Existing studies have mixed results [9–17] and combine inpatient and outpatient procedures, and different endoscopic procedures. Colonoscopy may confer lower risks compared to upper endoscopy (micro-aspiration, airway impingement, and laryngeal irritation) and advanced procedures (longer, more complex, deeper sedation). Furthermore, these studies variably define CAEs ranging from minor fluctuations in oxygen saturation or other vital signs, to life-threatening events such as respiratory or cardiac arrest.

The primary aim of this study was to assess the independent effect of BMI on CAEs for outpatient colonoscopy, adjusting for clinically important covariates. The secondary aim was to evaluate the need for an intervention for a CAE, as a measure of the CAE's clinical significance.

Methods

This is a retrospective cohort study conducted at the Durham Veterans Affairs (VA) Medical Center (DVAMC), a large tertiary care center. The VA clinical data warehouse was employed to identify 442 consecutive patients who underwent ambulatory colonoscopy at DVAMC between July 1, 2013, and July 1, 2014, with accessible pre-procedure, endoscopy, and nursing documentation. After excluding patients with unsedated procedures ($n = 5$), BMI < 20 or missing BMI data ($n = 14$), and age over 75 years ($n = 5$), 418 patients were eligible for the study. Each patient underwent only one colonoscopy during the study period.

Patient demographic and comorbidity (ICD-9 codes) data were extracted from the VA Computerized Patient Record System (CPRS). Charlson comorbidity index (CCI), a measure

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of comorbidity burden, was calculated using the Quan method [18]. Through manual chart review of pre-procedure assessment notes, endoscopy reports, and nurse/nurse anesthetist procedure flowsheets, several other clinical variables were gathered, including (1) procedure times, (2) CAEs and interventions required during the procedure or in the 30-min recovery period, and (3) type of sedation. Type of sedation was defined as monitored anesthesia care (MAC) with propofol and a deeper degree of sedation, or moderate sedation (MS) with fentanyl and midazolam with or without diphenhydramine administered by the gastroenterologist and a lighter degree of sedation. There were no cases using general anesthesia.

Patients were categorized as: BMI < 30 (normal/pre-obese), BMI 30–34.99 (obese class I), and BMI ≥ 35 (obese classes II and III) for the primary analysis. These definitions were based on the widely recognized World Health Organization classification system [19] because we deemed these as clinically significant cutoffs. Additional analyses were performed to compare categories of (1) BMI < 30 versus ≥30 and (2) BMI < 30 versus BMI 30–40. The primary outcome was the occurrence of CAEs, defined as hemodynamic events (systolic blood pressure, SBP < 90 or > 200, heart rate, HR < 55 or > 120 for any duration), cardiac arrhythmia, hypoxia (oxygen saturation < 90% for any duration), acute myocardial infarction, stroke, or cardiopulmonary arrest during the procedure or recovery period. We included minor cardiopulmonary events that resolved without intervention (such as transient hypoxia), and defined hypoxia as oxygen saturation < 90%. The secondary outcome was the need for intervention for a CAE, including increasing nasal cannula (NC) oxygen above 2 L/min, placement of a facemask, or placement of a nasopharyngeal airway or oropharyngeal airway, use of the chin lift, or endotracheal intubation, use of reversal agents, increasing intravenous fluids, use of hemodynamic medications, or cardiopulmonary resuscitation.

Baseline characteristics of the groups, and rates of CAEs and interventions were each compared across levels of BMI using ANOVA or Chi-square tests for continuous and categorical variables, respectively. A logistic regression model was built for two binary outcomes: (1) the occurrence of CAEs and (2) the need for intervention for CAEs. Model covariates were selected based on the results of univariate analyses and existing literature [6, 7, 12, 13]. Logistic regression model covariates included: (1) BMI, (2) type of sedation, (3) age, (4) ASA class [20], (5) and OSA. Odds ratios (OR) for covariates were considered statistically significant with a p value < 0.05. Statistical analysis was performed using R [21]. The rate of adverse events has varied between 13.9 and 44.4% in prior studies. BMI has been shown to be a risk factor for adverse events, with OR ranging between 1.02 and 2.0 [13, 22]. A minimum sample size for a multiple logistic regression model for this study was calculated to be 396 patients using an estimate of 12% for event proportion and odds ratio 1.5, with a type I error rate of 0.05 and 80% power [23].

Results

The range of BMI in the sample was 20.1–54.1 kg/m^2. Among all obese patients (BMI > 30), the mean BMI was 35.0 kg/m^2 (± 4.6). The majority of the sample was classified as ASA class II (94.7%), with 4 patients (0.9%) classified as ASA class I and 18 patients (4.3%) as ASA class III.

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A total of 220 CAEs occurred in 194 patients (Table 1). The most common type of CAE was hypoxia (160/220 events, 72.7%). The rate of serious CAEs, including cardiac arrhythmias, acute MI, stroke, or cardiac arrest, was 0.0%. A total of 180 interventions were performed. The most common intervention was increasing nasal cannula above 2L NC (158/180 interventions, 87.8%). Other airway maneuvers including use of facemask or nasopharyngeal airway occurred among 2.4% of patients. More serious interventions such as endotracheal intubation or use of reversal agents did not occur.

Significant differences across BMI categories included (1) ASA class ($p = 0.01$), (2) use of MAC for procedural sedation ($p \leq 0.01$), (3) presence of OSA ($p < 0.01$), and (4) use of CPAP ($p \leq 0.01$). Obese patients had a higher frequency of hypoxia compared to normal/pre-obese patients, as well as a higher frequency of requiring increase in NC oxygen (Table 2). BMI > 30 patients (OR 1.10, 95% CI 0.70–1.73) and BMI ≥ 35 patients (OR 1.07, 95% CI 0.61–1.85) did not have an increased risk of CAEs compared to normal/overweight patients (Table 3) after adjusting for age, ASA class, and OSA. Presence of OSA, however, was associated with an increased risk of CAEs (OR 1.71, 95% CI 1.09–2.74, $p = 0.02$) in adjusted analyses. In unadjusted and adjusted analyses, neither BMI 30–34.99 nor BMI ≥ 35 patients had an increased risk of interventions for CAEs (OR 1.17, 95% CI 0.73–1.86 and OR 1.21, 95% CI 0.69–2.11, respectively) compared to normal/overweight patients. Presence of OSA had an increased risk of need for intervention in unadjusted analysis (OR 1.11, 95% CI 1.00–1.23, $p = 0.05$). In adjusted analyses, OSA demonstrated a trend toward increased risk of need for intervention for CAEs (OR 1.49, 95% CI 0.93–2.36, $p = 0.09$). Additional analyses using BMI categories of (1) BMI < 30 versus ≥30 and (2) BMI < 30 versus BMI 30–40 showed no differences for risk of CAEs ($p = 0.28$ and $p = 0.25$, respectively), risk of interventions ($p = 0.20$ and $p = 0.21$, respectively), or risk of hypoxia ($p = 0.14$ and $p = 0.15$, respectively).

Discussion

Guidelines from the American Gastroenterology Association, the ASA, and the American Society for Gastrointestinal Endoscopy recommend consideration of MAC for patients with OSA [24, 25]. However, existing data specifically pertaining to endoscopy safety in obese patients are sparse [10], and there are no evidence-based guidelines addressing whether BMI should be considered an independent risk factor for CAEs for ASA class I and II patients with BMI 30–40 for outpatient colonoscopy when comorbidities such as OSA are absent. This is the first study aimed to evaluate the independent effect of BMI on CAEs in obese and morbidly obese patients for outpatient colonoscopy, as well as to characterize the type of CAEs that occurred and whether interventions were required as a measure of clinical significance. Higher BMI was not independently associated with an increased risk of CAEs or need for interventions in our study. This remained true when examining patients with BMI < 30 versus ≥30 and patients with BMI < 30 versus BMI 30–40. One possible reason why other studies [13, 17] have found an association between BMI and adverse events is because these studies included upper endoscopies and advanced procedures such as ERCPs that possibly confer different risks to colonoscopy given proximity to the airway and patient positioning. However, we did note that obese and morbidly obese patients had numerically higher frequencies of overall CAEs, hypoxia, and requiring increase of oxygen above 2L NC

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compared to normal/overweight patients. While these differences were not statistically significant in our study, we believe they may be clinically significant. While this study is a larger study than prior studies investigating this issue, its results point out that even larger cohorts are needed to detect smaller statistically significant effect sizes and re-examine this relationship in greater detail. OSA did confer a higher risk of CAEs, with a trend toward a risk of requiring an intervention performed as well. This supports previous studies of endoscopic procedures that found increased risks associated with OSA rather than with BMI [9, 12]. Previous studies have mixed results regarding type of sedation (administered by anesthesia or not) and risk of CAEs [11, 12]. While our study was not powered to examine this issue directly, univariate analyses did not demonstrate a statistically significant difference in CAE risk between MAC versus MS.

ASA class was not associated with higher risk of CAE in this study, as has been shown in previous studies for patients who are ASA class III or higher [4, 7, 13]. However, 24 of the 29 (82.8%) patients with BMI > 40 were classified as ASA class II instead of ASA class III (as is recommended by the ASA) by physicians during the preprocedure assessment. This suggests that physicians may downgrade ASA class for morbidly obese patients or may not prioritize BMI in comparison with other comorbidities when assigning ASA class. This may be why no association between ASA class and risk of CAE was found in this study. This suggests that physicians may need to place a greater importance on a patient's BMI when assigning ASA score during pre-procedure triage.

Our overall CAE rate (46.4%) was high, but comparable to other studies [13, 22] based on varying definitions of the outcome. Of note, studies have found that the most common unplanned cardiopulmonary event during endoscopic procedures is hypoxemia, and it occurs in up to 10–70% of patients depending on the definition of hypoxemia, level and type of sedation, type of endoscopy, and patient population [4, 17]. Our event rate was consistent with these estimates. The rates of serious events (0.0%) and clinically significant interventions (2.4%) were also consistent with other studies [12, 13].

These results should be interpreted in the context of study limitations. First, there is the possibility of inaccuracies during manual abstraction. To address this, we used a detailed data dictionary and the amount of data manually abstracted was minimized. Second, there is likely some variability in recording some CAEs. However, clinically significant complications are generally better documented and unlikely to have been missed. Third, we cannot control for unobserved confounders, such as actual dosage of sedative received, given that sedation was defined by type and degree as MAC (deep) versus MS (lighter), and also Mallampati score (which has either not been included in previous studies or has not demonstrated an independent effect on adverse events [7, 13, 17]). Lastly, this study was conducted at a single, large, tertiary VA center with experienced anesthesia specialists, and rates of complications may differ from other centers.

This study found that OSA confers an increased risk of complications independent of BMI and type or degree of sedation. Our results also suggest that the majority of CAEs in BMI > 30 patients are transient and resolve with minor interventions. It is important for physicians

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to consider the possibility of undiagnosed OSA to allow appropriate triaging of these patients to prevent adverse events and improve the quality of colonoscopy performance.

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Table 1

Sample baseline characteristics and rates of CAEs

Total sample	**(*n* = 418)**
Mean age in years (±SD)	61.4 (±7.9)
Male gender (%)	91.1%
Mean BMI in kg/m^2 (±SD)	30.5 (±7.8)
BMI < 30 (%, *n* = 210)	50.2%
BMI 30–34.99 (%, *n* = 127)	30.4%
BMI ≥ 35 (%, *n* = 81)	19.4%
Mean procedure time in minutes (±SD)	34.6 (±18.3)
Mean ASA class (±SD)	2.0 (±0.2)
Use of MAC (%)	8.6%
Presence of OSA (%)	37.0%
Mean CCI (±SD)	2.6 (±1.5)
Trainee involvement (%)	69.9%
Total number of CAEs	220
Number of O2 <90 events (% of events)	160 (72.7)
Number of HR <55 events (% of events)	42 (36.0)
Number of SBP <90 events (% of events)	16 (3.8)
Other[*] (% of events)	2 (0.9)
Number of serious[a] CAEs (% of events)	0 (0.0)
Number of patients with at least 1 CAE (%)	194 (46.4)
Number of patients with 2 + CAEs (%)	23 (5.5)
Number of patients with 3 + CAEs (%)	1 (0.2)
Total number of interventions performed	180
Increasing NC above 2L (% of interventions)	158 (87.8)
Other airway maneuvers[b] (% of interventions)	10 (5.6)
Increasing IV fluid (% of interventions)	11 (6.1)
Other[**] (% of interventions)	1 (0.5)
Other serious interventions[c] (% of interventions)	0 (0.0)
Number of patients with at least 1 intervention (%)	164 (39.2)
Number of patients with 2 + interventions (%)	12 (2.9)
Number of patients with 3 + interventions (%)	2 (0.5%)

[a] Serious CAE defined as cardiac arrhythmia, acute MI, stroke, cardiac arrest

[b] Other airway maneuvers that occurred included use of facemask or nasopharyngeal airway

[c] Chin lift, oropharyngeal airway, endotracheal intubation, use of reversal agents, hemodynamic medications, cardiopulmonary resuscitation

[*] These two events consisted of patient agitation

[**] This intervention consisted of Trendelenburg positioning of the patient

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Table 2

Patient demographics, clinical data, and event frequency by BMI category

BMI category	<30 (n = 210)	30–34.99 (n = 127)	≥35 (n = 81)	p value*
Mean age in years (SD)	61.4 (8.6)	61.4 (6.8)	61.6 (7.6)	0.98
(95% CI)	(44.5–78.3)	(48.0–74.8)	(46.7–76.5)	
Male (%)	91.4	92.4	88.9	0.60
(95% CI)	(87.2–94.6)	(84.9–96.9)	(80.0–94.8)	
Mean ASA class (SD)	2.0 (0.2)	2.0 (0.1)	2.1 (0.4)	0.01
(95% CI)	(1.6–2.4)	(1.8–2.2)	(1.4–2.8)	
CHF[a](%)	4.8	1.6	6.2	0.20
(95% CI)	(2.3–8.6)	(0.2–5.6)	(2.0–13.8)	0.55
CAD[b](%)	13.8	17.3	12.3	0.54
(95% CI)	(9.4–19.2)	(11.1–25.0)	(6.1–21.5)	
COPD or asthma[c](%)	12.4	8.7	12.3	
(95% CI)	(8.2–17.6)	(4.4–15.0)	(6.1–21.5)	
Presence of OSA (%)	15.2	30.7	51.9	<0.01
(95% CI)	(10.7–20.8)	(22.8–39.5)	(40.5–63.1)	<0.01
Use of CPAP/BiPAP (%)	7.6	20.5	34.6	
(95% CI)	(4.4–12.1)	(13.8–28.5)	(24.3–46.0)	
Mean Charlson Comorbidity Index (SD)	2.7 (1.6)	2.5 (1.5)	2.6 (1.4)	0.45
(95% CI)	(0.0–5.8)	(0.0–5.4)	(0.0–5.5)	
Use of MAC for sedation (%)	7.1	5.5	17.3	<0.01
(95% CI)	(4.1–11.5)	(2.2–11.0)	(9.8–27.3)	
Mean procedure time, minutes (SD)[d]	34.4 (17.2)	33.5 (16.5)	37.0 (23.2)	0.40
(Range)	(5.0–85.0)	(6.0–94.0)	(13.0–122.0)	
CAEs by BMI category				
Overall frequency of CAEs (%)	43.8	48.0	50.6	0.53
(95% CI)	(37.0–50.8)	(39.1–57.1)	(39.3–61.9)	
Systolic BP < 90	3.7	4.7	1.2	
Systolic BP >200	0.0	0.0	1.2	
Heart rate <55	8.6	11.0	8.6	

BMI category	<30 (*n* = 210)	30–34.99 (*n* = 127)	≥35 (*n* = 81)	*p* value*
Heart rate >120	0.0	0.0	0.0	
Hypoxia <90%	34.8	40.9	43.2	
(95% CI)	(28.3–41.6)	(32.3–50.0)	(32.2–54.7)	0.32
Overall frequency of intervention[e]				
At least one intervention	36.1	40.9	44.4	0.39
(95% CI)	(29.7–43.1)	(32.3–50.0)	(33.4–55.9)	
At least 2 interventions	2.4	3.9	3.7	
At least 3 interventions	0.4	1.6	1.2	
Intervention type				
Increase IV fluids	2.9	2.4	1.2	
>2L NC oxygen	34.3	40.2	43.2	
(95% CI)	(27.9–41.1)	(31.6–49.2)	(32.2–54.7)	
Facemask	0.4	0.0	0.0	
Nasopharyngeal airway	1.0	3.1	3.7	
(95% CI)	(0.1–3.4)	(0.9–7.9)	(3.7–10.4)	

[a] CHF = congestive heart failure

[b] CAD = coronary artery disease

[c] COPD or Asthma = COPD or asthma

[d] Total procedure time = time from scope insertion to removal of scope from patient at end of procedure

[e] Number of interventions required in one procedure

* *p* value from unadjusted ANOVA testing

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Table 3

Odds ratios (OR) with 95% confidence intervals for risk of CAEs and intervention for CAEs (adjusted ordinal logistic regression models) for obese patients compared to normal/pre-obese patients

	Risk of CAEs		**Risk of intervention for CAE**	
	OR (95% CI)	***p* value**	**OR (95% CI)**	***p* value**
BMI < 30 (reference)				
BMI 30–34.99	1.10 (0.70–1.73)	0.68	1.17 (0.73–1.86)	0.51
BMI ≥ 35	1.07 (0.61–1.85)	0.82	1.21 (0.69–2.11)	0.51
Age	1.00 (0.98–1.03)	0.87	0.99 (0.97–1.02)	0.64
ASA class	0.83 (0.34–2.02)	0.68	0.86 (0.34–2.10)	0.74
Use of MAC	1.32 (0.65–2.68)	0.43	1.24 (0.61–2.50)	0.55
Presence of OSA	1.72 (1.09–2.74)	0.02	1.49 (0.93–2.36)	0.09