



The association of vaping and electronic cigarette use with postoperative hypoxemia and respiratory complications: a retrospective cohort analysis

Association du vapotage et de l'utilisation de cigarette électronique avec l'hypoxémie postopératoire et les complications respiratoires : une analyse de cohorte rétrospective

Remie Saab, MD · Eva Rivas, MD, PhD · Esra Kutlu Yalcin, MD · Lloyd Chen, MD · Mateo Montalvo, MD · Federico Almonacid-Cardenas, MD · Karan Shah, MS · Kurt Ruetzler, MD · Alparslan Turan, MD

Received: 1 June 2023 / Revised: 25 April 2024 / Accepted: 25 April 2024
© The Author(s) 2024

Abstract

Purpose Initially introduced as a safer alternative to smoking, electronic cigarettes (e-cigarettes) and vaping have since been associated with lung injury. Nevertheless, there is limited perioperative data on their potential contribution to the harmful effects of mechanical ventilation on the lungs. We hypothesized that, in adults undergoing noncardiothoracic surgeries, preoperative

vaping/e-cigarette use is associated with hypoxemia during the first postoperative hour, and with an increased incidence of intraoperative and postoperative pulmonary complications.

Methods We conducted a retrospective cohort study in which we included patients reporting as vapers/e-cigarette users within one year before surgery as the exposure group, and nonvapers as the control group. The primary outcome was the time-weighted average (TWA) SpO_2/FiO_2

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s12630-024-02801-6>.

R. Saab, MD · M. Montalvo, MD · F. Almonacid-Cardenas, MD
Department of Outcomes Research, Anesthesiology & Pain Management Institute, Cleveland Clinic, Cleveland, OH, USA

E. Rivas, MD, PhD
Department of Outcomes Research, Anesthesiology & Pain Management Institute, Cleveland Clinic, Cleveland, OH, USA

Department of Anaesthesia, Hospital Clinic de Barcelona, Institute D'Investigacions Biomediques August Pi I Sunyer (IDIBAPS), University of Barcelona, Barcelona, Catalonia, Spain

CIBER of Respiratory Diseases (CibeRes), Madrid, Spain

E. K. Yalcin, MD
Department of Outcomes Research, Anesthesiology & Pain Management Institute, Cleveland Clinic, Cleveland, OH, USA

Department of General Anesthesiology, Anesthesiology & Pain Management Institute, Cleveland Clinic, Cleveland, OH, USA

L. Chen, MD · K. Ruetzler, MD
Department of Outcomes Research, Anesthesiology & Pain Management Institute, Cleveland Clinic, Cleveland, OH, USA

School of Medicine, Case Western Reserve University, Cleveland, OH, USA

K. Shah, MS
Department of Outcomes Research, Anesthesiology & Pain Management Institute, Cleveland Clinic, Cleveland, OH, USA

Department of Quantitative Health Sciences, Lerner Research Institute, Cleveland Clinic, Cleveland, OH, USA

A. Turan, MD (✉)
Department of General Anesthesiology, Anesthesiology & Pain Management Institute, Cleveland Clinic, Cleveland, OH, USA

Department of Outcomes Research, Anesthesiology & Pain Management Institute, Cleveland Clinic, 9500 Euclid Ave, Cleveland, OH 44195, USA

e-mail: turana@ccf.org

ratio in the postanesthesia care unit during the first postoperative hour. The secondary outcome was a composite of intraoperative and postoperative pulmonary complications until discharge. We used entropy balancing to adjust for confounding, and fit weighted linear regression and logistic regression models to estimate treatment effects.

Results A total of 110,940 patients met the inclusion criteria, and 1,941 of these were vapers/e-cigarette users. The average treatment effect on the treated for TWA SpO₂/F_IO₂ ratio (N = 109,217) was estimated to be a mean difference of 4 (95% confidence interval [CI], 1 to 8; P = 0.007). This is equivalent to a 4% change in SpO₂ at a 30% F_IO₂ (or at a fixed F_IO₂). The difference was statistically significant. The average treatment effect on the treated for experiencing intraoperative and postoperative pulmonary complications (N = 110,940) was an odds ratio of 1.04 (95% CI, 0.71 to 1.54; P = 0.84).

Conclusion Vaping/e-cigarette use was neither associated with clinically significant hypoxemia during the first hour in the postanesthesia care unit nor with an increase in pulmonary complications. Nevertheless, our findings cannot definitively exclude the deleterious effects of vaping and e-cigarette use on the lungs, and anesthesiologists should consider potential perioperative complications.

Résumé

Objectif Initialement introduites comme une alternative plus sécuritaire au tabagisme, les cigarettes électroniques et le vapotage ont depuis été associés à des lésions pulmonaires. Néanmoins, il existe peu de données périopératoires concernant leur contribution potentielle aux effets nocifs de la ventilation mécanique sur les poumons. Nous avons émis l'hypothèse que, chez les adultes bénéficiant de chirurgies non cardiothoraciques, l'utilisation préopératoire de vapotage/de cigarette électronique était associée à une hypoxémie au cours de la première heure postopératoire et à une incidence accrue de complications pulmonaires peropératoires et postopératoires.

Méthode Nous avons mené une étude de cohorte rétrospective dans laquelle nous avons inclus les patient-es déclarant avoir vapoté ou utilisé des cigarettes électroniques dans l'année précédant la chirurgie comme groupe d'exposition, et les personnes ne vapotant pas comme groupe témoin. Le critère d'évaluation principal était le rapport de SpO₂/FIO₂ moyen pondéré dans le temps en salle de réveil pendant la première heure postopératoire. Le critère d'évaluation secondaire était un mélange de complications pulmonaires peropératoires et postopératoires jusqu'au congé de l'hôpital. Nous avons utilisé l'équilibrage d'entropie pour ajuster les facteurs de

confusion et ajusté les modèles de régression linéaire pondérée et de régression logistique pour estimer les effets du traitement.

Résultats Au total, 110 940 patient-es répondaient aux critères d'inclusion, dont 1941 étaient des vapoteurs ou vapoteuses/utilisaient des cigarettes électroniques. L'effet moyen du traitement sur le rapport de SpO₂/FIO₂ moyen pondéré dans le temps des personnes traitées (N = 109 217) a été estimé à une différence moyenne de 4 (intervalle de confiance [IC] à 95 %, 1 à 8; P = 0,007). Cela équivalait à une variation de 4 % de la SpO₂ à 30% FIO₂ (ou à une FIO₂ fixe). La différence était statistiquement significative. L'effet moyen du traitement sur les personnes traitées pour des complications pulmonaires peropératoires et postopératoires (N = 110 940) était un rapport de cotes de 1,04 (IC 95 %, 0,71 à 1,54; P = 0,84).

Conclusion L'utilisation du vapotage et de la cigarette électronique n'était associée ni à une hypoxémie cliniquement significative au cours de la première heure en salle de réveil, ni à une augmentation des complications pulmonaires. Néanmoins, nos résultats ne peuvent exclure de manière définitive les effets délétères du vapotage et de l'utilisation de la cigarette électronique sur les poumons, et les anesthésiologistes devraient tenir compte des complications périopératoires potentielles.

Keywords electronic cigarettes · hypoxemia · postoperative pulmonary complications · vaping

Electronic cigarettes (e-cigarettes) and vaping were developed to be a new substitute for smoking and were advertised as a safer option than conventional cigarettes despite the paucity of safety data. Electronic cigarettes entered the USA market around 2007 and have become the most common tobacco product used by American youths since 2014.¹ According to a 2018 Centers for Disease Control report, 3.2% of USA adults (around 8.1 million) were current e-cigarette users.²

Fewer toxic chemicals have been detected in the aerosol from e-cigarettes compared with conventional cigarette smoking.³ Nevertheless, these new devices are not entirely harmless, and emerging pulmonary complications increase concerns about their safety. The most known harmful substance is vitamin E acetate, which is present in tetrahydrocannabinol (THC)-containing products, and has been associated with the development of e-cigarette or vaping product use associated lung injury (EVALI).⁴ Many other chemicals, flavours, and metals are also used in these devices and can lead to pulmonary toxicities.⁵⁻⁷

Hypoxemia and pulmonary complications are among the most common preventable postoperative complications independent of smoking and vaping.^{8,9} Postoperative hypoxemia is common and prolonged in patients recovering from major noncardiac surgery, with around 20% having at least 10 min·hr⁻¹ of SpO₂ < 90%.¹⁰ Postoperative hypoxemia can be caused by atelectasis, ventilator-induced lung injury, ventilation/perfusion mismatch, hypoventilation, and pulmonary edema.^{9,11,12} Hypoxemia is associated with prolonged hospitalization, intensive care unit admissions, mortality, and increased cost of care.

Available evidence suggests that vaping/e-cigarette use should be of concern to anesthesiologists, with a possible higher risk of postoperative hypoxemia and pulmonary complications. There are apparently no data on perioperative outcomes for patients who vape or use e-cigarettes. Therefore, we sought to undertake an evaluation of perioperative outcomes for vapers. Our primary hypothesis was that preoperative vaping/e-cigarette use, in adults undergoing noncardiothoracic surgery, is associated with increased hypoxemia (defined by the peripheral oxygen saturation divided by the fraction of inspired oxygen [SpO₂/F_IO₂ ratio], a surrogate measure of oxygenation) during the first postoperative hour. Our secondary hypothesis was that vaping is associated with a higher risk of intraoperative and postoperative pulmonary complications compared with nonvaping.

Methods

The current analysis was a retrospective, single-centre, cohort study using data from the Cleveland Clinic Perioperative Health Documentation System (Cleveland, OH, USA) and was conducted after approval by the Institutional Review Board of the Cleveland Clinic Foundation on 7 April 2021, with waived individual consent.

We included data from all adults undergoing noncardiothoracic surgeries lasting more than 1 hr under general anesthesia with mechanical ventilation at the Cleveland Clinic Main Campus between January 2015 and April 2021. We excluded data from patients who had missing postanesthesia care unit (PACU) SpO₂ and F_IO₂ data, as well as patients who had another surgery during the same hospitalization or received mechanical ventilation during the 48 hr before surgery. Patients who were intubated within 24 hr after surgery were excluded from the primary analysis.

The exposure of interest was vaping/e-cigarette use within one year before surgery. It was identified from providers' notes on social history in the electronic health

record and by searching for the International Classification of Diseases (ICD)-10 code (F17.29) for vaping nicotine. We also planned to record the specific type of vaping and e-cigarettes, what substance was used (e.g., nicotine, THC, etc.), the frequency of use, and dual smoking/vaping status when these data were available. Control group patients were identified as patients who did not use e-cigarettes in the year before surgery. No restrictions were placed on the absence of vaping screening as it was unavailable for most patients. Conventional cigarette smokers were part of both the treatment and control groups, but we adjusted for smoking status as a confounder in our analysis.

Our primary outcome was time-weighted average (TWA) SpO₂/F_IO₂ ratio in the PACU during the first postoperative hour. Peripheral oxygen saturation data were collected from the electronic record. Fraction of inspired oxygen was estimated from the type of device and the oxygen flow based on the conversion table (Electronic Supplementary Material [ESM] eTable 1), assuming that F_IO₂ was unchanged between recordings. The SpO₂/F_IO₂ ratio has been used as a reliable continuous and noninvasive surrogate for the partial pressure of arterial oxygen to F_IO₂ (PaO₂/F_IO₂) ratio in adults with acute lung injury and acute respiratory distress syndrome (ARDS),^{13,14} and accepted as a replacement for the PaO₂/F_IO₂ ratio in the respiratory part of the Sequential Organ Failure Assessment score.¹⁵ A 10% difference in the SpO₂/F_IO₂ ratio between the two groups, corresponding to a 10% change in SpO₂ at a fixed F_IO₂, was considered significant, a threshold based on previous studies that showed a 10% decrease in PaO₂/F_IO₂ from baseline was clinically meaningful for lung injury.^{16,17}

Our secondary outcome was a collapsed composite of intraoperative and postoperative pulmonary complications that occurred at any time between the beginning of the surgery and 72 hr postoperatively or discharge, whichever came first. This outcome was defined as the presence of at least one of the following complications as identified by their ICD-9/ICD-10 codes, including but not limited to: pulmonary infection and pneumonia, respiratory failure, bronchospasm, atelectasis, pulmonary oedema, pneumothorax, ARDS, pulmonary embolism, and all vaping-related disorders (ESM eTable 2).

Statistical analysis

For our primary hypothesis, we estimated the average treatment effect on the treated (ATT) for the TWA SpO₂/F_IO₂ ratio. The ATT represents the effect of being exposed to vaping in our current vaping population and thus, correspondingly, how much harm could be prevented if patients were prevented from vaping. We used entropy balancing to adjust for confounding. This is similar to

inverse probability of treatment weighting using logistic regression models, but offers certain advantages.¹⁸ Inverse probability of treatment weighting using logistic regression models is often an iterative process in which the propensity score model is tweaked and modified until satisfactory balance is achieved on confounders. Entropy balancing, on the other hand, uses optimization techniques to directly find weights that balance covariates between the two groups, thus obviating the need to perform an *ad hoc* search for the correct model specification.¹⁹

To calculate the ATT, we first estimated the weights using entropy balancing. All patients in the vaping group received a weight of 1, while patients in the nonvaping group received the estimated weight w_i . Intuitively, the idea is to give more weight to nonvapers who are similar to vapers on confounder distribution, and less weight to those who are dissimilar. The distribution of weights was examined, and extreme weights were removed by trimming to the first and 99th percentile. Then, we evaluated the balance on the specified covariates using the absolute standardized difference (ASD), with an $ASD > 0.10$ indicating imbalance. Weighted outcome regression models were then fit to estimate ATT.

In the primary analysis, ATT mean difference was estimated using a weighted linear regression model with the TWA SpO_2/F_iO_2 ratio as the outcome and vaping/e-cigarette use as the primary covariate of interest. Robust standard errors were calculated using the sandwich estimator. We adjusted for smoking status, comorbidities, and demographic factors (Table 1).

For the secondary analysis, we used a similar procedure. We fitted a weighted logistic regression model to estimate the ATT odds ratio with a composite of intraoperative and postoperative pulmonary complications as the outcome and vaping/e-cigarette use status as the primary covariate of interest. Robust standard errors were calculated using the sandwich estimator.

We conducted two sensitivity analyses: the first one was conducted using the minimum SpO_2/F_iO_2 as the outcome instead of TWA SpO_2/F_iO_2 . In the second one, we defined certain confounders to be treated as mediators. This is because a limitation of our analysis is that the patients were measured at only one time point. Thus, it is possible that some of the listed confounders are in fact mediators (e.g., a patient could have developed chronic obstructive pulmonary disease [COPD] after they started vaping). Lung cancer, COPD, and asthma were identified as potential mediators (Figure). These mediators were not used when calculating the new weights, allowing us to estimate the *total* effect of vaping.

All analyses were conducted at a significance level of 0.05. R version 4.0.2 (R Foundation for Statistical

Computing, Vienna, Austria) was used for all statistical analyses.

Sample size justification

PLANNED

Based on a preliminary query, about 300 out of 10,000 surgery patients at the Cleveland Clinic used vaping/e-cigarettes per year. Assuming a TWA PACU SpO_2/F_iO_2 ratio mean of 300 and a residual standard deviation of 80 after adjusting for other confounders and without considering any interaction, we planned to have more than 80% power to detect a difference of 10 or larger, assuming a minimal final sample size of 600 vapers and 19,400 nonvapers.

ACTUAL

The final primary analysis population had 1,907 vapers out of a total of 109,217 patients. Weighting procedures, such as entropy balancing or inverse probability of treatment weighting, generally increase the variance of statistical estimates, which should be taken into account when estimating the power. The effective sample size (ESS) is a metric that quantifies this loss of precision and represents the number of unweighted observations that the weighted observations would be equivalent to. After weighting, the ESS was 1,907 vapers and 40,608 nonvapers. Keeping other parameters the same as before, we had more than 80% power to detect a mean difference of 10 or larger for TWA SpO_2/F_iO_2 ratio as planned.

Results

We identified a total of 110,940 patients (1,941 vapers) who met the specified inclusion and exclusion criteria for the study. Of these, 109,217 (1,907 vapers) patients were included in the primary analysis after excluding patients with missing outcomes data, and those who were intubated in the 24 hr following surgery. There were no meaningful differences in the rates at which vapers were excluded for postoperative intubation (0.9%) compared with nonvapers (0.8%). All patients were included in the secondary analysis. For the primary analysis, we achieved satisfactory balance ($ASD < 0.1$) on all variables using entropy balancing (Table 1, Figure).

In the PACU, oxygen was delivered with a nasal cannula in 85% of the patients, with simple face masks in 14% of the patients, and with other devices in less than 1% of the patients (ESM eTable 3). This distribution was similar between both groups.

Table 1 Baseline characteristics of primary analysis patients

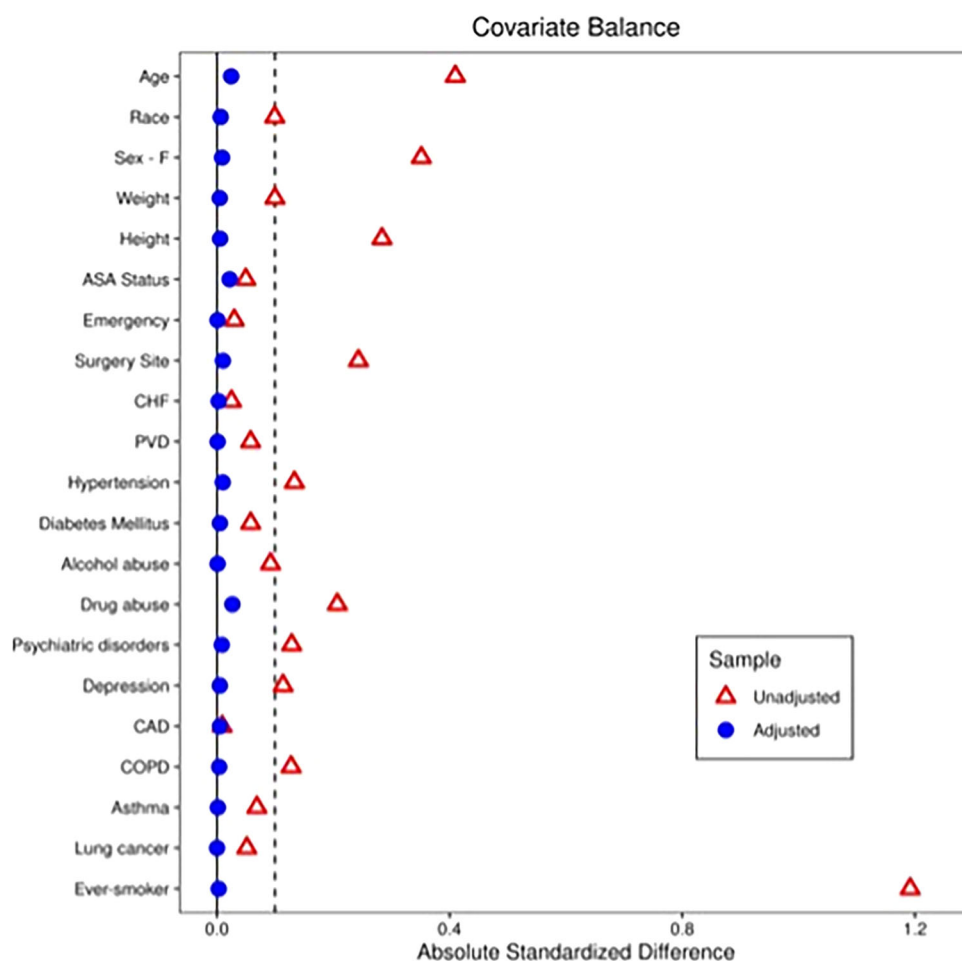
Characteristic	Unweighted			Weighted		
	Vapers N = 1,907	Nonvapers N = 107,310	ASD	Vapers	Nonvapers	ASD
Age (yr), mean (SD)	51 (16)	57 (16)	0.410	51 (16)	51 (16)	0.024
Race, n/total N (%)			0.100			0.006
Black	304/1,907 (16%)	13,592/107,310 (13%)		16	16	
White	1,551/1,907 (81%)	90,044/107,310 (84%)		81	82	
Other	52/1,907 (3%)	3,674/107,310 (3%)		3	3	
Sex (female), n/total N (%)	722/1,907 (38%)	59,151/107,310 (55%)	0.351	38	38	0.009
Weight (kg), mean (SD)	88 (23)	85 (23)	0.100	88 (23)	88 (23)	0.005
Height (cm), mean (SD)	173 (10)	170 (11)	0.284	173 (10)	173 (10)	0.005
ASA Physical Status, n/total N (%)			0.050			0.022
I	47/1,907 (3%)	2,887/107,310 (3%)		3	3	
II	512/1,907 (27%)	27,502/107,310 (26%)		27	27	
III	1,222/1,907 (64%)	69,271/107,310 (65%)		64	64	
IV	124/1,907 (7%)	7,623/107,310 (7%)		7	7	
V	1/1,907 (0.1%)	24/107,310 (< 0.1%)		0.1	0.1	
VI	1/1,907 (0.1%)	3/107,310 (< 0.1%)		0.1	< 0.1	
Emergency surgery, n/total N (%)	44/1,907 (2%)	2,017/107,310 (2%)	0.030	2	2	0.001
Surgery site, n/total N (%)			0.243			0.010
Digestive system	528/1,907 (28%)	26,594/107,310 (25%)		28	28	
Musculoskeletal system	356/1,907 (19%)	17,656/107,310 (17%)		19	19	
Integumentary system	155/1,907 (8%)	12,175/107,310 (11%)		8	8	
Urinary system	177/1,907 (9%)	11,437/107,310 (11%)		9	9	
Nervous system	238/1,907 (13%)	10,654/107,310 (10%)		13	12	
Female genital organs	103/1,907 (5%)	9,278/107,310 (9%)		5	6	
Male genital organs	99/1,907 (5%)	5,785/107,310 (5%)		5	5	
Endocrine system	30/1,907 (2%)	3,187/107,310 (3%)		2	2	
Nose, mouth, and pharynx	57/1,907 (3%)	3,070/107,310 (3%)		3	3	
Cardiovascular system	53/1,907 (3%)	2,131/107,310 (2%)		3	3	
Hemic/lymphatic system	36/1,907 (2%)	1,981/107,310 (2%)		2	2	
Respiratory system	39/1,907 (2%)	1,474/107,310 (1%)		2	2	
Ear	12/1,907 (0.6%)	838/107,310 (0.8%)		0.6	0.6	
Eye	18/1,907 (0.9%)	750/107,310 (0.7%)		0.9	0.9	
Obstetrical procedures	5/1,907 (0.3%)	79/107,310 (0.1%)		0.3	0.2	
Miscellaneous procedures	1/1,907 (0.1%)	221/107,310 (0.2%)		0.1	0.1	
Congestive heart failure, n/total N (%)	72/1,907 (4%)	4,578/107,310 (4%)	0.025	4	4	0.003
Pulmonary circulation disease, n/total N (%)	4/1,907 (0.2%)	613/107,310 (0.6%)	0.058	0.2	0.2	0.001
Hypertension, n/total N (%)	788/1,907 (41%)	51,443/107,310 (48%)	0.133	41	42	0.010
Diabetes mellitus, n/total N (%)	290/1,907 (15%)	18,622/107,310 (17%)	0.058	15	15	0.005
Alcohol abuse, n/total N (%)	38/1,907 (2%)	959/107,310 (0.9%)	0.092	2	2	0.001
Drug abuse, n/total N (%)	87/1,907 (5%)	1,218/107,310 (1%)	0.207	5	4	0.027
Psychiatric disorders, n/total N (%)	94/1,907 (5%)	2,683/107,310 (3%)	0.129	5	5	0.008
Depression, n/total N (%)	354/1,907 (19%)	15,398/107,310 (14%)	0.114	19	18	0.005
Coronary artery disease, n/total N (%)	173/1,907 (9%)	10,014/107,310 (9%)	0.009	9	9	0.005
COPD, n/total N (%)	163/1,907 (9%)	5,698/107,310 (5%)	0.128	9	9	0.004
Asthma, n/total N (%)	16/1,907 (0.8%)	1,709/107,310 (2%)	0.069	0.8	0.9	0.002
Lung cancer, n/total N (%)	19/1,907 (1%)	586/107,310 (0.5%)	0.051	1	1	< 0.001
Ever-smoker, n/total N (%)	1,844/1,907 (97%)	55,777/107,310 (52%)	1.192	97	97	0.003

Data presented as mean (SD) for continuous variables or n/total N (%) for categorical variables, using the group sample sizes as the denominator for calculating the percentages. For categorical variables, after weighting, only percentages are reported since the weights were not normalized. There was no missing data on the baseline characteristics. The ASD was defined as the difference in means/proportions divided by the pooled standard deviation, was used to evaluate balance on characteristics. An ASD greater than 0.10 indicates imbalance.

ASA = American Society of Anesthesiologists; ASD = absolute standardized difference; COPD = chronic obstructive pulmonary disease; SD = standard deviation

Figure Balance on confounders between vapers and nonvapers, before and after weighting using entropy balancing

ASA = American Society of Anesthesiologists;
CAD = coronary artery disease;
CHF = cardiac heart failure;
COPD = chronic obstructive pulmonary disease;
PVD = pulmonary vascular disease



The unadjusted median [interquartile range] TWA $\text{SpO}_2/\text{F}_1\text{O}_2$ ratio ($N = 109,217$) was 350 [302–396] in the vaping group and 348 [297–379] in the nonvaping group. The ATT mean difference [vapers – nonvapers] for the TWA $\text{SpO}_2/\text{F}_1\text{O}_2$ ratio was estimated to be 4 (95% confidence interval [CI], 1 to 8; $P = 0.007$). This is equivalent to a 4% change in SpO_2 at a 30% F_1O_2 (or at a fixed F_1O_2). The estimated treatment effect was statistically significant (Table 2). The interaction between vaping and smoking status was not statistically significant ($P = 0.22$). Similar results were observed when repeating the analysis with a more fine-grained categorization of smoking status, i.e., current smoker, former smoker, and never smoker (ESM eTable 4).

The intraoperative and postoperative pulmonary complications ($N = 110,940$) incidence was 1.4% ($n = 27$) in the vaping group and 1.3% ($n = 1,447$) in the nonvaping group. The ATT odds ratio (vapers/nonvapers) for experiencing pulmonary complications was estimated to be 1.04 (95% CI, 0.71 to 1.54; $P = 0.84$). The estimated treatment effect was not statistically significant (Table 2).

Our first sensitivity analysis showed that, when we used the minimum $\text{SpO}_2/\text{F}_1\text{O}_2$ ratio as the outcome, the ATT

mean difference was estimated to be 2 (95% CI, –2 to 5; $P = 0.35$). The average minimum $\text{SpO}_2/\text{F}_1\text{O}_2$ ratio was estimated to be 309 (95% CI, 303 to 315) in the vaping group and 307 (95% CI, 301 to 303) in the nonvaping group.

In the second analysis, we excluded predefined mediators, i.e., asthma, COPD, and lung cancer. The ATT mean difference for the TWA $\text{SpO}_2/\text{F}_1\text{O}_2$ ratio was estimated to be 4 (95% CI, 1 to 7; $P = 0.01$). The mean TWA $\text{SpO}_2/\text{F}_1\text{O}_2$ ratio was estimated to be 348 (95% CI, 344 to 352) in the vaping group and 344 (95% CI, 342 to 346) in the nonvaping group.

Discussion

Our primary outcome was hypoxemia ($\text{SpO}_2/\text{F}_1\text{O}_2$ ratio), a reliable surrogate for the $\text{PaO}_2/\text{F}_1\text{O}_2$ ratio.^{13,14} We used this outcome to power the detection of vaping/e-cigarette use effect on the lungs even without having a definite documented diagnosis of a pulmonary complication. Although there is no other available perioperative data regarding vaping/e-cigarette use and hypoxemia that we

Table 2 Summary of primary and secondary analysis

Outcome	Vapers N = 1,941	Nonvapers N = 108,999	Unadjusted treatment effect (95% CI) N = 110,940	Average treatment effect on the treated (95% CI) N = 110,940
<i>Primary outcome</i>	<i>Median [IQR]</i>		<i>Mean difference</i>	<i>ATT mean difference</i>
Time-weighted average SpO ₂ /F ₁ O ₂ ratio	350 [302–396] N = 1,907	348 [297–379] N = 107,310	4 (1 to 7) N = 109,217	4 (1 to 8) N = 109,217
<i>Secondary outcome</i>	<i>Incidence, n/total N (%)</i>		<i>Odds ratio</i>	<i>ATT odds ratio</i>
Intraoperative and postoperative pulmonary complications	27/1,941 (1.4%)	1,447/108,999 (1.3%)	1.00 (1.00 to 1.01)	1.04 (0.71 to 1.54)

The ATT estimates were obtained by first calculating entropy balancing weights, and then fitting weighted linear (mean difference) or logistic (odds ratio) regression models. This procedure is similar to inverse probability of treatment weighting, but differs in the method used to estimate the weights. The ATT estimates represent the average effect of vaping in a sample with baseline characteristics similar to our study's sample of vapers. We adjusted for age, sex, race, height, weight, ASA Physical Status, emergency surgery, surgery site, smoking status, and patient medical history (congestive heart failure, pulmonary circulation disease, hypertension, diabetes mellitus, alcohol abuse, drug abuse, psychiatric disorders, depression, coronary artery disease, chronic obstructive pulmonary disease, asthma, and lung cancer).

ASA = American Society of Anesthesiologists; ATT = average treatment effect on the treated; CI = confidence interval; IQR = interquartile range; SpO₂/F₁O₂ ratio = peripheral oxygen saturation divided by the fraction of inspired oxygen

can refer to or establish a comparison with, it is worth reporting that, in the nonoperative setting, hypoxia was the main presenting vital abnormality in vapers/e-cigarette users that were subsequently diagnosed with EVALI.²⁰ Based on these data, we expected to observe more severe hypoxemia in vapers/e-cigarette users than in nonusers. The results of our analysis ultimately did not support this hypothesis.

Vaping/e-cigarette use was also not associated with a statistically significant increase in intraoperative and postoperative pulmonary complications. As with hypoxemia, there are no perioperative data on the effects of vaping on postoperative pulmonary complications. Nevertheless, a previous study in the nonoperative setting compared the lung function of 30 healthy individuals who had vaped in the last six months to 30 control individuals who had not. In the vaping group, they observed a significant reduction in lung function secondary to peripheral obstructive airway disease.²¹

Multiple factors could explain the lack of evidence for an association between vaping and pulmonary complications observed in our study. One important reason might be that our population was at lower risk of developing pulmonary complications. Only 28% had intra-abdominal surgeries, where complications are common. Another reason might be that we did not account for duration or intensity of vaping. It is reasonable to hypothesize that higher levels of exposure to vaping would result in greater lung damage. It has been shown that prolonged exposure to toxic substances and more severe lung damage is needed to detect postoperative

pulmonary complications in middle age.^{22–24} Nevertheless, these details were not available for our analysis.

Our results should be interpreted cautiously considering the many limitations of our study. One limitation is that we used SpO₂ as a continuous and noninvasive surrogate, instead of arterial blood samples, to assess postoperative lung function in the PACU. Nevertheless, the SpO₂/F₁O₂ ratio is a validated measure of oxygenation that allows continuous and early detection of impaired oxygenation and lung injury, and it is a predictor of early development of ARDS and hospital mortality.^{13,25,26} Another limitation is that we assessed oxygenation only within the first hour of admission to the PACU. Therefore, delayed effects of vaping on oxygenation would be overlooked. A third important limitation is the risk of exposure underdocumentation since it is a new entity in preoperative screening. This would explain the low prevalence of vaping in our patient population compared with estimates from other studies. In general, providers are not used to completing and documenting vaping and e-cigarette use, or they may erroneously document it as smoking, which could be confused with cigarette smoking. Nevertheless, the Cleveland Clinic has already added a specific screening tool for vaping to its electronic medical record system, and we also used a free-text search to enhance the detection of exposure. A related limitation is that the specific type of substance used does not need to be documented in the screening tool. It is important to differentiate between nicotine, cannabidiol, THC, butane hash oils (dabs), and many other illicit products that can cause a different range of complications.²⁷ Unfortunately,

we did not have sufficient data to disaggregate the effects of different substances. Moreover, the extent to which patients abstained from vaping before surgery, which would impact the harmful effect on lungs, was also not documented. Finally, it is worth mentioning that most of the patients in the exposure group were either current or former smokers, and although the interaction between vaping and smoking status was not significant, we had only limited power to assess differential effects of vaping in nonsmokers compared with smokers.

In summary, our analysis of patients undergoing noncardiothoracic surgery did not show evidence of a clinically meaningful association between vaping/e-cigarette use, and either hypoxemia during the first hour in PACU or an increased risk of postoperative pulmonary complications. Nevertheless, our findings cannot definitively exclude the deleterious effects of vaping and e-cigarette use on the lungs, and anesthesiologists should consider potential perioperative complications.

Author contributions Remie Saab, Eva Rivas, Esra Kutlu Yalcin, Lloyd Chen, Mateo Montalvo, Federico Almonacid-Cardenas, Kurt Ruetzler, and Alparslan Turan contributed to the conception and design of the study. Remie Saab, Eva Rivas, Esra Kutlu Yalcin, Lloyd Chen, Mateo Montalvo, Federico Almonacid-Cardenas, Karan Shah, and Alparslan Turan contributed to the acquisition of data. Karan Shah, Remie Saab, Eva Rivas, and Alparslan Turan contributed to the analysis of data. Karan Shah, Remie Saab, Eva Rivas, and Alparslan Turan contributed to the interpretation of data.

Disclosures None of the authors has a conflict of interest.

Funding statement No external funding and no competing interests declared. This study was supported by internal funding from the Department of Outcomes Research, Cleveland Clinic, Cleveland, OH, USA.

Prior conference presentations Poster presentation at the 2022 American Society of Anesthesiologists Annual Meeting (18–22 October, Philadelphia, PA, USA).

Editorial responsibility This submission was handled by Dr. Stephan K. W. Schwarz, Editor-in-Chief, *Canadian Journal of Anesthesia/Journal canadien d'anesthésie*.

Open Access This article is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License, which permits any non-commercial use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by-nc/4.0/>.

References

1. *Centers for Disease Control and Prevention*. Surgeon General's advisory on e-cigarette use among youth; 2018. Available from URL: https://www.cdc.gov/tobacco/basic_information/e-cigarettes/surgeon-general-advisory/index.html (accessed April 2024).
2. Creamer MR, Wang TW, Babb S, *et al*. Tobacco product use and cessation indicators among adults—United States, 2018. *MMWR Morb Mortal Wkly Rep* 2019; 68: 1013–9. <https://doi.org/10.15585/mmwr.mm6845a2>
3. National Academies of Sciences E, Medicine, Health, *et al*. *In: Eaton DL, Kwan LY, Stratton K, eds. Public Health Consequences of E-Cigarettes*. National Academies Press; 2018.
4. Blount BC, Karwowski MP, Morel-Espinosa M, *et al*. Evaluation of bronchoalveolar lavage fluid from patients in an outbreak of e-cigarette, or vaping, product use-associated lung injury—10 states, August–October 2019. *MMWR Morb Mortal Wkly Rep* 2019; 68: 1040–1. <https://doi.org/10.15585/mmwr.mm6845e2>
5. Iskandar AR, Zanetti F, Marescotti D, *et al*. Application of a multi-layer systems toxicology framework for in vitro assessment of the biological effects of Classic Tobacco e-liquid and its corresponding aerosol using an e-cigarette device with MESH™ technology. *Arch Toxicol* 2019; 93: 3229–47. <https://doi.org/10.1007/s00204-019-02565-9>
6. Williams M, Li J, Talbot P. Effects of model, method of collection, and topography on chemical elements and metals in the aerosol of tank-style electronic cigarettes. *Sci Rep* 2019; 9: 13969. <https://doi.org/10.1038/s41598-019-50441-4>
7. Antonini JM, Taylor MD, Zimmer AT, Roberts JR. Pulmonary responses to welding fumes: role of metal constituents. *J Toxicol Environ Health A* 2004; 67: 233–49. <https://doi.org/10.1080/15287390490266909>
8. *The LAS VEGAS Investigators*. Epidemiology, practice of ventilation and outcome for patients at increased risk of postoperative pulmonary complications: LAS VEGAS—an observational study in 29 countries. *Eur J Anaesthesiol* 2017; 34: 492–507. <https://doi.org/10.1097/eja.0000000000000646>
9. Canet J, Sabaté S, Mazo V, *et al*. Development and validation of a score to predict postoperative respiratory failure in a multicentre European cohort: a prospective, observational study. *Eur J Anaesthesiol* 2015; 32: 458–70. <https://doi.org/10.1097/eja.0000000000000223>
10. Sun Z, Sessler DI, Dalton JE, *et al*. Postoperative hypoxemia is common and persistent: a prospective blinded observational study. *Anesth Analg* 2015; 121: 709–15. <https://doi.org/10.1213/ane.0000000000000836>
11. Rothen HU, Sporre B, Engberg G, Wegenius G, Hedenstierna G. Re-expansion of atelectasis during general anaesthesia: a computed tomography study. *Br J Anaesth* 1993; 71: 788–95. <https://doi.org/10.1093/bja/71.6.788>
12. Suzuki S. Oxygen administration for postoperative surgical patients: a narrative review. *J Intensive Care* 2020; 8: 79. <https://doi.org/10.1186/s40560-020-00498-5>
13. Rice TW, Wheeler AP, Bernard GR, *et al*. Comparison of the SpO₂/F_iO₂ ratio and the PaO₂/F_iO₂ ratio in patients with acute lung injury or ARDS. *Chest* 2007; 132: 410–7. <https://doi.org/10.1378/chest.07-0617>
14. Festic E, Bansal V, Kor DJ, Gajic O. SpO₂/F_iO₂ ratio on hospital admission is an indicator of early acute respiratory distress syndrome development among patients at risk. *J Intensive Care Med* 2015; 30: 209–16. <https://doi.org/10.1177/0885066613516411>

15. Pandharipande PP, Shintani AK, Hagerman HE, et al. Derivation and validation of SpO₂/F_iO₂ ratio to impute for PaO₂/F_iO₂ ratio in the respiratory component of the sequential organ failure assessment score. *Crit Care Med* 2009; 37: 1317–21. <https://doi.org/10.1097/ccm.0b013e31819cefa9>
16. Douville NJ, Jewell ES, Duggal N, et al. Association of intraoperative ventilator management with postoperative oxygenation, pulmonary complications, and mortality. *Anesth Analg* 2020; 130: 165–75. <https://doi.org/10.1213/ane.0000000000004191>
17. Hovaguimian F, Lysakowski C, Elia N, Tramèr MR. Effect of intraoperative high inspired oxygen fraction on surgical site infection, postoperative nausea and vomiting, and pulmonary function: systematic review and meta-analysis of randomized controlled trials. *Anesthesiology* 2013; 119: 303–16. <https://doi.org/10.1097/aln.0b013e31829aaff4>
18. Hainmueller J, Xu Y. Ebalance: a Stata package for entropy balancing. *J Stat Softw* 2013; 54. <https://doi.org/10.2139/ssrn.1943090>
19. Harvey RA, Hayden JD, Kamble PS, Bouchard JR, Huang JC. A comparison of entropy balance and probability weighting methods to generalize observational cohorts to a population: a simulation and empirical example. *Pharmacoepidemiol Drug Saf* 2017; 26: 368–77. <https://doi.org/10.1002/pds.4121>
20. Pajak A, Bascoy S, Li JC, Benninghoff M, Deitchman A. E-cigarette or vaping product use associated lung injury among three young adults: a retrospective case series from Delaware. *Cureus* 2020; 12: e11031. <https://doi.org/10.7759/cureus.11031>
21. Meo SA, Ansary MA, Barayan FR, et al. Electronic cigarettes: impact on lung function and fractional exhaled nitric oxide among healthy adults. *Am J Mens Health* 2019; 13: 1557988318806073. <https://doi.org/10.1177/1557988318806073>
22. Marini S, Buonanno G, Stabile L, Ficco G. Short-term effects of electronic and tobacco cigarettes on exhaled nitric oxide. *Toxicol Appl Pharmacol* 2014; 278: 9–15. <https://doi.org/10.1016/j.taap.2014.04.004>
23. Flouris AD, Chorti MS, Poulianiti KP, et al. Acute impact of active and passive electronic cigarette smoking on serum cotinine and lung function. *Inhal Toxicol* 2013; 25: 91–101. <https://doi.org/10.3109/08958378.2012.758197>
24. Blagev DP, Harris D, Dunn AC, Guidry DW, Grissom CK, Lanspa MJ. Clinical presentation, treatment, and short-term outcomes of lung injury associated with e-cigarettes or vaping: a prospective observational cohort study. *Lancet* 2019; 394: 2073–83. [https://doi.org/10.1016/s0140-6736\(19\)32679-0](https://doi.org/10.1016/s0140-6736(19)32679-0)
25. Sleiman M, Logue JM, Montesinos VN, et al. Emissions from electronic cigarettes: key parameters affecting the release of harmful chemicals. *Environ Sci Technol* 2016; 50: 9644–51. <https://doi.org/10.1021/acs.est.6b01741>
26. Centers for Disease Control and Prevention. Outbreak of severe pulmonary disease associated with using e-cigarette, or vaping, products; 2020. Available from URL: https://archive.cdc.gov/www_cdc_gov/tobacco/basic_information/e-cigarettes/severe-lung-disease.html (accessed May 2024).
27. Breitbarth AK, Morgan J, Jones AL. E-cigarettes—an unintended illicit drug delivery system. *Drug Alcohol Depend* 2018; 192: 98–111. <https://doi.org/10.1016/j.drugalcdep.2018.07.031>

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.