Supplementary Digital Content

Determinants and practice variability of oxygen administration during surgery in the U.S., a retrospective cohort study

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Contents

1. Protocol (as posted on Open Source Framework 8/23/2020, osf.io/eq246)

Title:	Intraoperative oxygen administration
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Type of Study:	Multicenter observational cohort
IRB Status:	IRB Approved
Aims:	The aims of this study are to: 1. Assess intraoperative patient oxygenation practices across a large heterogenous cohort of medical centers and anesthesiologists. 2. Report associations between intraoperative patient oxygenation and patient, procedure, provider, and center factors.
Patients/Participants:	Adult patients receiving surgery at Multicenter Perioperative Outcomes Group (MPOG) participating medical centers with general anesthesia, tracheal intubation, and mechanical ventilation during surgery who are at increased risk of poor outcomes, defined as patients admitted to the hospital following surgery of at least two hours duration.
Proposed statistical analysis:	We will examine the distribution of intraoperative oxygen administration in the cohort, including variability across centers and anesthesiologists in the cohort. We will model intraoperative supplemental oxygen administrations using linear mixed-effect regression methods to determine what patient, procedure, center, or provider factors are associated with intraoperative supplemental oxygen administration.

INTRODUCTION

Supplemental oxygen is administered to almost all patients during surgery, but the amount of supplemental oxygen administered to patients during surgery is unknown. The optimal fraction of inspired oxygen (FIO_2) to administer patients during surgery is also unknown. Administering high FIO_2 has been thought to offer several advantages, including an improved safety margin for airway manipulation, increasing perioperative arterial and wound tissue oxygen tension to enhance oxidative killing by neutrophils (1,2), improved healing of anastomotic sites (3,4), and decreased postoperative nausea and vomiting (5,6). However hyperoxia may have a host of adverse effects, including promotion of absorption atelectasis (7), direct lung toxicity (8), increased airway inflammation (9), impaired regulation of blood glucose (10), and changes in cardiac index and peripheral vascular resistance (11-13). These different biologic effects may affect surgical patient outcomes and influence anesthesiologist FIO_2 administration practice.

Anesthesiologists consider potential risks and benefits of providing supplemental oxygen to patients during surgery, and anesthesiologists control the FIO_2 to patients throughout surgery. The FIO_2 administered to patients during surgery may be influenced by patient factors, procedure factors, provider preferences, and medical center customs. Because administration of supplemental oxygen during surgery may affect patient outcomes, we sought to describe current intraoperative oxygenation patterns across a large heterogenous cohort of patients having surgery and to determine what factors were associated with the FIO_2 administered to patients during surgery.

The aims of this study are to:

1. Assess intraoperative oxygenation practices across a large heterogenous cohort of medical centers and anesthesiologists in patients having surgery who are at increased risk of poor outcomes.
2. Report associations between intraoperative patient oxygenation and patient, procedure, provider, and center factors.

METHODS

Study design:

Multicenter observational cohort study

Study sites:

Multicenter Perioperative Outcomes Group (MPOG) participating medical centers

Study population:

Adult patients receiving general anesthesia with mechanical ventilation during surgery. The inclusion/exclusion criteria for the study are broad to capture a wide set of intraoperative oxygenation practices, a diverse patient population, and a patient population receiving a diverse set of surgical procedures. We included adult patients at increased risk of poor outcomes, defined as inpatient surgery of 120 minutes or longer requiring general anesthesia with endotracheal intubation, and we excluded patients who received surgery or anesthesia procedures that dictate higher concentrations of supplemental oxygen, such as jet ventilation or one lung ventilation.

Inclusion criteria:

- 18 years of age or older
- Duration of surgery of at least 120 minutes
- General anesthesia with tracheal intubation and mechanical ventilation
- Surgery from January 1, 2016 through January 1, 2019

Exclusion criteria:

- Pregnancy
- Outpatient surgery, defined according to surgical scheduling (i.e., patients who are scheduled outpatient but then are admitted to the hospital remain excluded)
- Airway surgery or bronchoscopy, documented using procedural codes
- One-lung or jet ventilation, documented by anesthesiologist
- Preoperative tracheal intubation
- Infrequent documentation of oxygenation during a case defined as any intraoperative periods of 5 minutes or more in which there are no FIO_2 or SpO_2 measurements or less than 60 intraoperative FIO_2 or SpO_2 measurements during the case.
- Previous participation in the study within 90 days (i.e., repeat surgery)

Characterizing of the study cohort:

We will characterize the study cohort by describing patient demographics, baseline medical data, procedural data, and intraoperative mechanical ventilation data. These patient characteristics will include age, sex, BMI, ASA physical status classification, past medical history including diagnosis of heart failure, diabetes, pulmonary disease, and other medical conditions using the Elixhauser comorbidity list, and baseline labs including hemoglobin, creatinine, lactate, and troponin, measured prior to surgery. We will record the specific surgery for each patient, the surgery type, the surgical service, and whether the surgery was considered emergent.

Intraoperative data collected will include minute-to-minute FIO_2, minute-to-minute SpO_2, minute-to-minute fraction of inspired nitrous oxide, duration of anesthesia, total fluid administration, total packed red blood cell transfusion, intraoperative hypotension, intraoperative PEEP and TV per kg IBW, and laboratory data including pO_2 and hemoglobin/hematocrit. Definitions for some of these variables are outlined in **Protocol Table 1**.

Measurement of intraoperative FIO_2:

We will measure intraoperative oxygen exposure using minute-to-minute FIO_2 data collected for each surgical case and submitted to MPOG. FIO_2 data are collected from intubation to extubation, or from intubation until out of room time for patients who are not extubated in the operating room. For minutes when the FIO_2 is not available, we will assign the FIO_2 as the mean between the previous value and the subsequent value if the missing period is $\leq$ five minutes. If there is no FIO_2 measurement for more than five minutes, the case will be excluded.

We will assess intraoperative oxygenation practice patterns overall and at the center and provider level to determine current practice patterns.

For multivariable modeling we will measure the independent associations between the median FIO_2 for each case and patient factors, procedure factors, center, and provider (attending provider, see below). We have chosen median FIO_2 to quantify oxygen exposure during maintenance anesthesia as opposed to mean, because the FIO_2 is typically increased to 100% during preoxygenation, induction, and intubation and also again during emergence and extubation, and these data will increase the mean value of FIO_2 independent of other patient, center, and provider factors of interest. The median FIO_2 better represents oxygen administration during maintenance anesthesia and provides better opportunity to assess associations between variability of FIO_2 administration and other factors since FIO_2 administration is much less variable at induction and emergence from anesthesia.

Missing Data:

Missing FIO_2 data will be imputed or cases excluded as described in the "Measurement of intraoperative FIO_2" section above.

Missingness in patient characteristics variables, including preoperative medical history, intraoperative surgical characteristics, and perioperative laboratory measurements, will be addressed using multiple imputation. The chained equations method with predictive mean matching (PMM) will be used to generate five complete datasets. Statistical analyses will be implemented separately for each completed dataset and the results pooled using Rubin's rules.
When preoperative hemoglobin, creatinine, lactate, and troponin are treated as covariates, we will additionally condition on the indicator variable that takes value one when the lab is measured, and zero otherwise.

Anesthesiologist Practice Variation in FIO_2 Administration:

We anticipate that the observed variation in delivered FIO_2 may be explained in part by patient-level factors and also in part by physician-level factors. Some anesthesiologists may typically administer a higher or lower FIO_2 than other anesthesiologists, independent of patient factors. To summarize anesthesiologist provider FIO_2 practice, we will calculate the mean and median FIO_2 of each case and then the mean and median FIO_2 of all cases managed by each provider. Anesthesiologist providers are given a number upon submission to MPOG center and will remain anonymous throughout the study. For cases in which an attending physician and a non-attending physician, nurse anesthetist, or other in-room provider are present, we will cluster cases according to the attending physician because the attending physician is responsible for and in charge of patient care. For cases in which multiple attending physicians care for the patient, we will assign the case to the first attending.

Medical Center Practice Variation in FIO_2 Administration:

We anticipate that due to historic, regional, educational, and cultural influences, some medical centers will typically provide a higher or lower FIO_2 independent of patient factors. To summarize center FIO_2 practice, we will calculate the mean and median FIO_2 of each case and then the mean and median FIO_2 of all cases at each center, similar to how we summarize anesthesiologist provider FIO_2 practice.

Statistical Analyses:

We will calculate FIO_2 metrics for each case. We will examine the distribution of these data across the entire cohort, within each center, and within each anonymous provider.

We will use multivariable linear mixed-effects regression to measure the independent associations between the median intraoperative FIO_2 and various patient factors, procedure factors, center, and provider. We have chosen factors that may be associated with FIO_2 administration. These factors include age, sex, BMI, ASA status, Elixhauser comorbidities (14), emergency surgery, preoperative hemoglobin concentration and its "ordered" indicator (an indicator variable that takes a value of one if preoperative hemoglobin was measured, and zero otherwise), preoperative creatinine concentration and its "ordered" indicator, preoperative troponin concentration and its "ordered" indicator, preoperative lactate concentration and its "ordered" indicator, and surgery type. We have included these indicator variables that take a value of one when the corresponding lab was ordered and measured, and zero otherwise, because the decision to order these labs (indication for ordering) may be associated with intraoperative oxygen administration. We will also include several intraoperative factors that may be associated with intraoperative FIO_2 including intraoperative hemoglobin desaturation (defined as the incidence of SpO_2 below several thresholds that are commonly used in clinical practice to guide FIO_2 administration, see below), duration of surgery, arterial pO_2 and its "ordered" indicator, nitrous oxide exposure (quantified as the median fraction of inhaled nitrous oxide, using minute to minute inhaled nitrous oxide data), median intraoperative tidal volume, median intraop PEEP, intraoperative fluid and blood administration, and intraoperative hypotension. We will model hemoglobin desaturation using minute-to-minute SpO_2 data and an ordinal variable of 4 categories: all

SpO_2 values >=96% (i.e., no desaturation), all SpO_2 >= 93%, all SpO_2 >= 90%, and some SpO_2 < 90%. We selected these values because these values are commonly used in clinical practice to guide FIO_2 administration. We do not include the periods of induction and emergence of anesthesia in the calculation of desaturation (defined as the first 15 minutes and before the last 15 minutes of the case), because patients may have brief desaturations during these periods of initiation and termination of controlled ventilation that are less likely to influence the provision of FIO_2 during maintenance anesthesia.

Because intraoperative oxygenation practices may influence or be influenced by other preceding, simultaneous, or subsequent intraoperative practices and procedures, and because there may be uncertainty regarding the causal associations among these concurrent intraoperative practices (i.e., oxygenation could impact other intraoperative factors and/or other intraoperative factors could impact oxygenation), we will, in addition, conduct a sensitivity analysis in which the regression model does not adjust for any intraoperative factors, specifically duration of surgery, nitrous oxide exposure, median intraoperative tidal volume, median intraop PEEP, any episode of desaturation not occurring at the time of anesthesia induction or emergence, arterial pO_2 and its ordered indicator, intraoperative fluid and blood administration, and intraoperative hypotension. This sensitivity analysis will help us to examine whether any effects of preoperative factors may be mediated by one or more of these intraoperative factors, and the degree to which the effect of oxygenation practices are independent of other intraoperative practices.

The effects of quantitative covariates will be modeled using a flexible splines method. Variability in intraoperative FIO_2 due to provider and center will be modeled using random intercepts indexed by provider and center, respectively, and summarized using the intraclass correlation (ratio of cluster-specific variance to total variance). In addition, we will also estimate the fraction of the total variability in median intraoperative FIO_2 that is explained by the fixed effects (preoperative and/or intraoperative factors) and each random effect (provider, center, and residual), using the method of Nakagawa *et al* (15).

As an exploratory analysis, we will also examine whether the variability among providers differs across centers. This will be implemented using an altered version of the regression model described above, where the provider random effect is nested within center, such that the variability among providers will be estimated separately for each center. Quantitative and graphical regression diagnostics will be examined. In the event that the fully adjusted regression model is not estimable, or when there is other evidence of overfitting, the model complexity will be reduced by omitting nonlinear terms, and additional terms, if necessary. Regression summaries will be presented as estimates, with 95% confidence intervals.

Limitations:

A limitation of this study is the inability to accurately measure the need for increased FIO_2. For example, we are unable to demonstrate that a high FIO_2 is secondary to patient oxygenation issues that mandate a high FIO_2 to maintain SpO_2 or if a high FIO_2 is due to other factors. This is due to the near universal practice of administering a FIO_2 greater than that which is required to maintain hemoglobin oxygenation during surgery. We have attempted to address this limitation by measuring and adjusting for the incidence of any SpO_2 data is < 90%, <93% and <96% during surgery, because those are SpO_2 values are thresholds that may cause the anesthesiologist to increase the FIO_2. Comparing the associations between hemoglobin desaturation below these thresholds and FIO_2 will provide some means, although incomplete, to understand if a high FIO_2 is secondary to a low SpO_2 or not.

Protocol Table 1. Intraoperative characteristic definitions

Variable	Definition	Description
Duration of procedure	Total procedure time	Total minutes from inroom to out of room
Fluid administration	ml of crystalloid	Total ml of crystalloid fluids
Blood transfusion	ml of packed red blood cells transfused	Total ml of packed red blood cells transfused
Intraoperative hypotension	AUC of MAP <60 mmHg	AUC of MAP<60 mm Hg
Measured Tidal Volume	TV in mL/kg/IBW	Median intraoperative TV in mL/kg/IBW
PEEP- measured	Median intraoperative PEEP	Median intraoperative PEEP in cm of H_2O
FIO_2	Intraoperative fraction of inspired oxygen	Minute to minute FIO_2 from intubation to extubation, or out of operative room for patients who remain intubated
Oxygen Saturation (SpO_2)	Intraoperative oxygen saturation	Minute to minute arterial hemoglobin oxygen saturation from intubation to extubation, or out of operative room for patients who remain intubated
Nitrous Oxide administration	Amount of nitrous oxide used for duration of case	Median of minute-to-minute fraction of inspired nitrous oxide data

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2. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	4-5
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6
Objectives	3	State specific objectives, including any prespecified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	8
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	8
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (*b*) For matched studies, give matching criteria and number of exposed and unexposed	9
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	9-12
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	9-12
Bias	9	Describe any efforts to address potential sources of bias	9-13
Study size	10	Explain how the study size was arrived at	8-9
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9-12
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding (*b*) Describe any methods used to examine subgroups and interactions (*c*) Explain how missing data were addressed (*d*) If applicable, explain how loss to follow-up was addressed (*e*) Describe any sensitivity analyses	10-13
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	14, Fig 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	14, Fig 2
Outcome data	15*	Report numbers of outcome events or summary measures over time	14, Fig 3

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	14-16, Figs 2-5
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	14-16, supp Figs 3-5
Discussion			
Key results	18	Summarise key results with reference to study objectives	17
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	19-20
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	17-20
Generalisability	21	Discuss the generalisability (external validity) of the study results	19
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	3

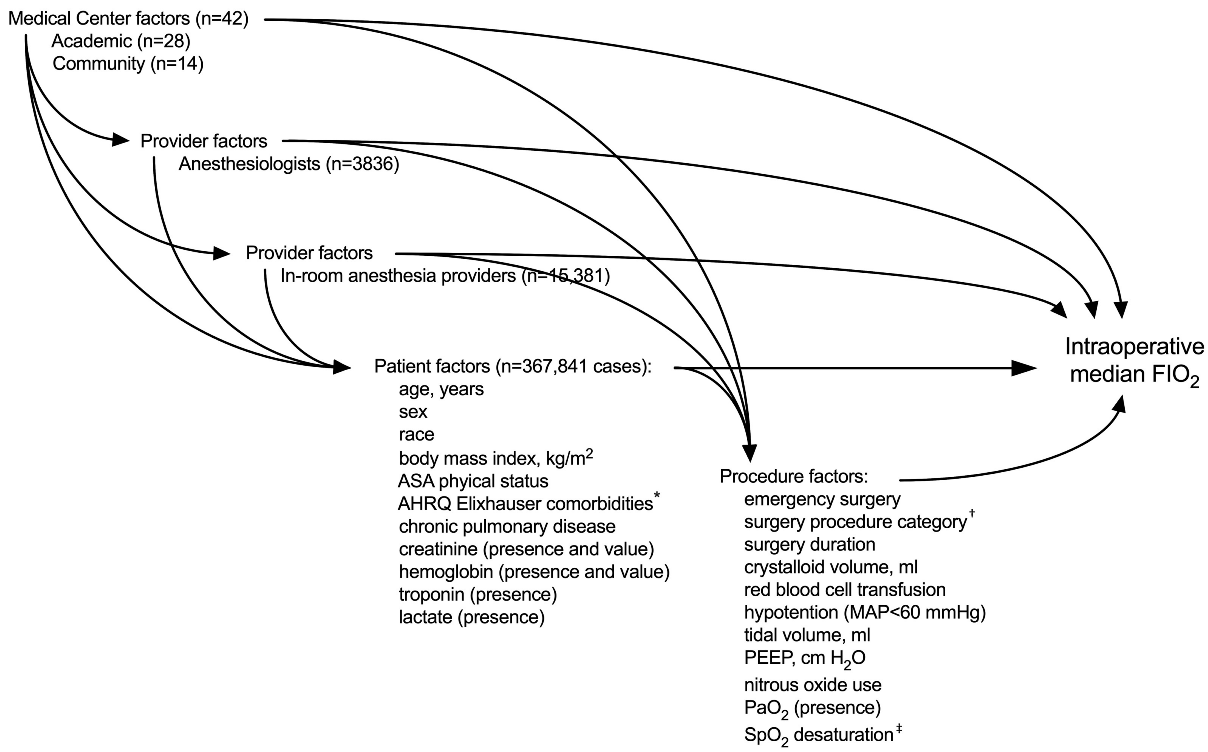
*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

3. **Supplementary Table 1**. Procedural categorization coding using primary anesthesia current procedural terminology (CPT) codes.

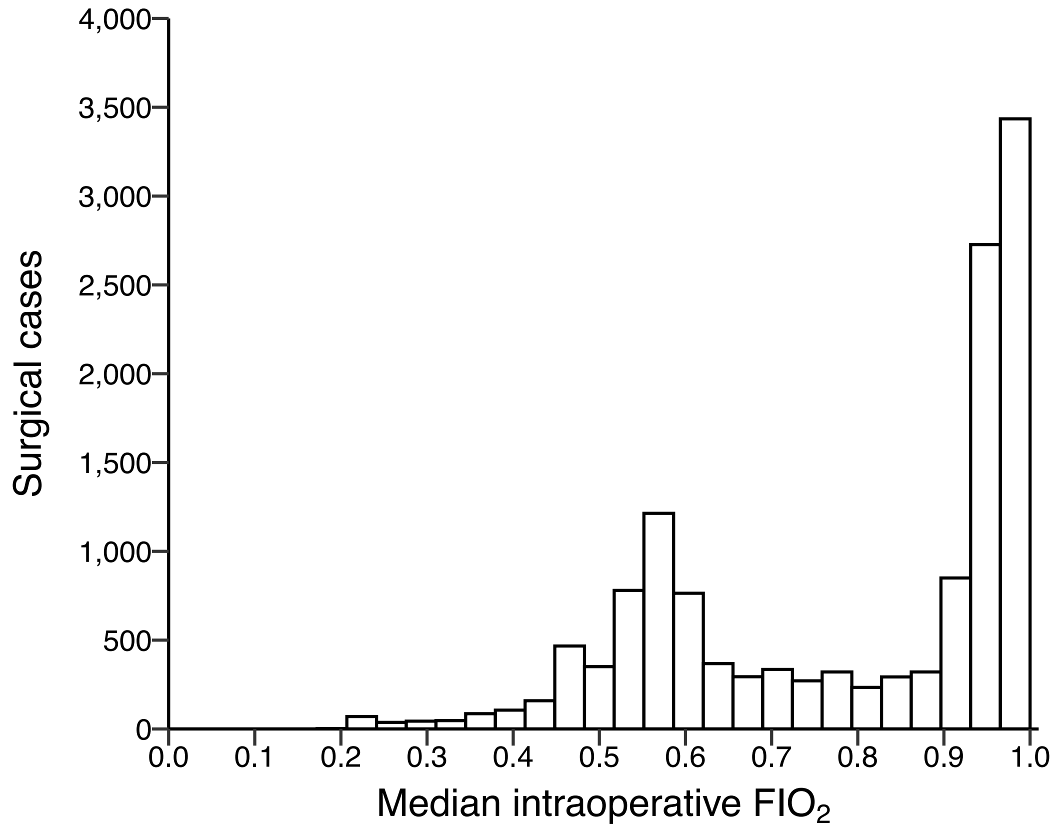
Procedure body region/surgery type	CPT code
Head	00160, 00162, 00164, 00100, 00102, 00170, 00172, 00174, 00176, 00120, 00124, 00126, 00103, 00140, 00142, 00144, 00145, 00147, 00148, 00190, 00192, 00210, 00211, 00212, 00214, 00215, 00216, 00218, 00220, 00222, 00104
Neck	00300, 00320, 00322, 00326, 00350, 00352
Spine and spinal cord	00640, 00600, 00604, 00620, 00622, 00625, 00626, 00630, 00632, 00634, 00635, 00670
Open heart	00550, 00560, 00561, 00562, 00563, 00566, 00567, 00580
Intrathoracic	00500, 00520, 00522, 00524, 00528, 00529, 00539, 00540, 00541, 00546, 00548, 00542, 00530, 00532, 00534, 00537
Extrathoracic	00400, 00410, 00402, 00404, 00406, 00450, 00452, 00454, 00470, 00472, 00474
Upper abdomen	00700, 00702, 00730, 00731, 00732, 00740, 00750, 07520, 00754, 00756, 00790, 00792, 00794, 00796, 00797, 00770
Lower abdomen	00800, 00802, 00820, 00810, 00811, 00812, 00813, 00830, 00832, 00834, 00836, 00840, 00844, 00848, 00866, 00902, 00904, 00880, 00882
Gynecologic	00842, 00948, 00950, 00952, 00846, 00851, 00942, 00944, 00906, 00940
Pelvic	01112, 01130, 01160, 01120, 01140, 01150, 01170, 01173, 01180, 01190
Urologic	00862, 00868, 00864, 00870, 00872, 00873, 00865, 00908, 00910, 00912, 00914, 00916, 00918, 00860
Male reproductive system	00921, 00922, 00924, 00926, 00928, 00930, 00932, 00934, 00936, 00938, 00920
Lower extremity	01200, 01220, 01340, 01380, 01390, 01420, 01462, 01490, 01202, 01210, 01212, 01214, 01215, 01230, 01232, 01234, 01250, 01320, 01360, 01382, 01392, 01400, 01402, 01404, 01464, 01470, 01472, 01474, 01480, 01482, 01484, 01486, 01260, 01270, 01272, 01274, 01430, 01432, 01440, 01442, 01444, 01500, 01502, 01520, 01522
Upper extremity	01620, 01680, 01682, 01730, 01820, 01860, 01610, 01622, 01630, 01634, 01636, 01638, 01710, 01712, 01714, 01716, 01732, 01740, 01742, 01744, 01756, 01758, 01760, 01810, 01829, 01830, 01832, 01650, 01652, 01654, 01656, 01670, 01770, 01772, 01780, 01782, 01840, 01842, 01844, 01850, 01852
Radiologic	01916, 01920, 01922, 01924, 01925, 01926, 01930, 01931, 01932, 01933, 01935, 01936
Burn	01951, 01952, 01953
Obstetric	01958, 01960, 01961, 01968, 01967, 01962, 01963, 01969, 01964, 01965, 01966
Other	01990, 01991, 01992, 01995, 01996, 01999

4. **Supplementary Figure 1.** Directed Acyclic Graph showing the relationships among factors and median fraction of inspired oxygen (FIO_2). There were five groups of factors: medical center, anesthesiologist provider, in-room anesthesia provider, patient, and procedure. Anesthesiologists, in-room providers, and patients are nested within medical center. Arrows represent potential causal associations between groups of factors. For each group of factors, we estimated their effects on intraoperative median FIO_2 independent from the effects of all other factors.



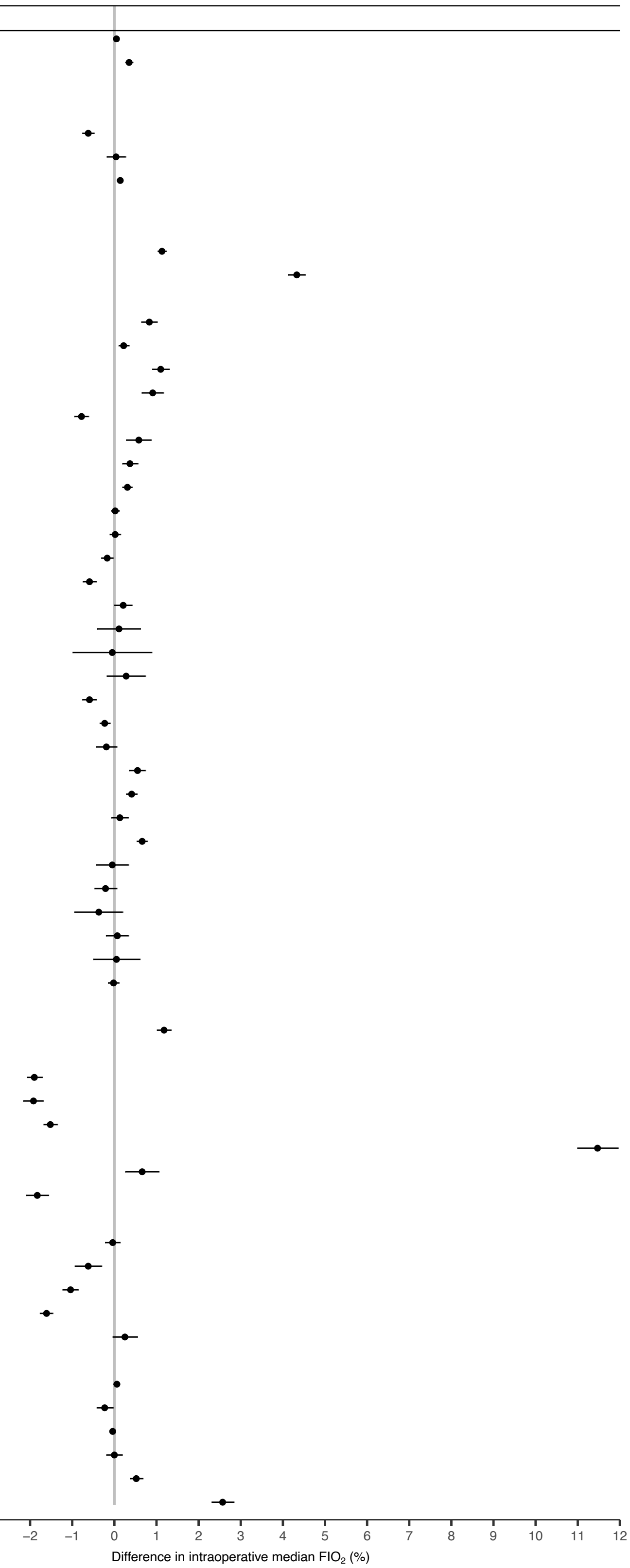
[*] AHRQ Elixhauser comorbidities included congestive heart failure, arrythmia, valvular disease, pulmonary circulation disorder, peripheral vascular disease, paralysis, other neurologic disorders, chronic pulmonary disease, hypertension, diabetes, hypothyroidism, renal failure, liver disease, peptic ulcer disease, AIDS/HIV, lymphoma, metastatic cancer, solid tumor without metastasis, rheumatoid arthritis/collagen disease, coagulopathy, obesity, weight loss, fluid and electrolyte imbalance, blood loss anemia, deficiency anemia, alcohol abuse, drug abuse, psychoses, and depression, each treated as a unique covariate in the model. [†] Surgery procedure categories including the following categories: head, neck, spine and spinal cord, open heart, intrathoracic (non-open heart), extrathoracic, upper abdomen, lower abdomen, gynecologic/pelvic, urologic/male reproductive, extremity, or other (burn, obstetric, radiologic), modeled as one covariate. [‡] SpO_2 desaturation was categorized as an ordinal variable of four categories of incrementally lower nadir SpO_2: all SpO_2 values $\geq$ 96% (i.e., no desaturation), all $SpO_2 \geq$ 93%, all $SpO_2 \geq$ 90%, and some SpO_2 < 90%

5. **Supplementary Figure 2.** Distribution of intraoperative median fraction of inspired oxygen (FIO_2) in patients who received open heart surgery (N=13,576).

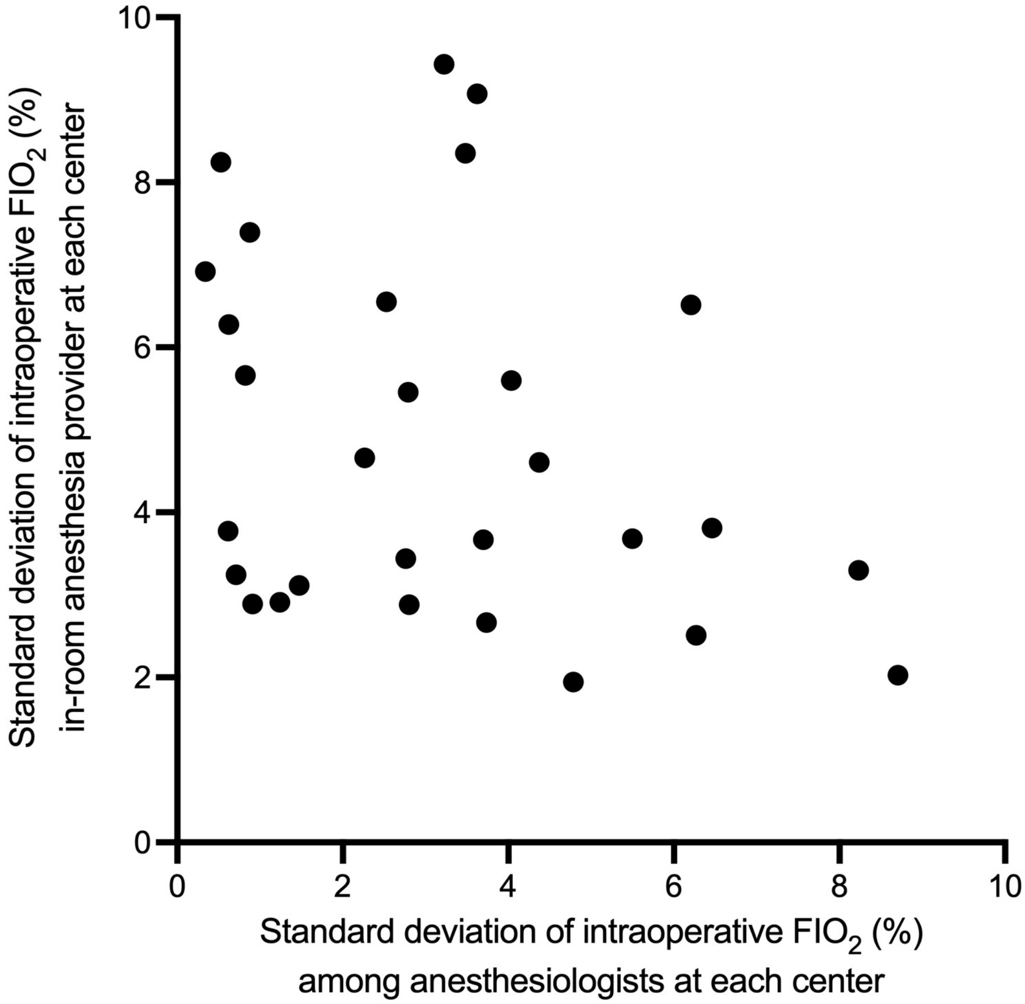


6. **Supplementary Figure 3.** Patient and procedure factors and their independent associations with intraoperative fraction of inspired O_2 (FIO_2). Compared to the primary model, *this model does not contain intraoperative factors*. Model estimates with 95% confidence intervals (CI) represent the change in median intraoperative FIO_2 associated with each factor, independent of all other factors.

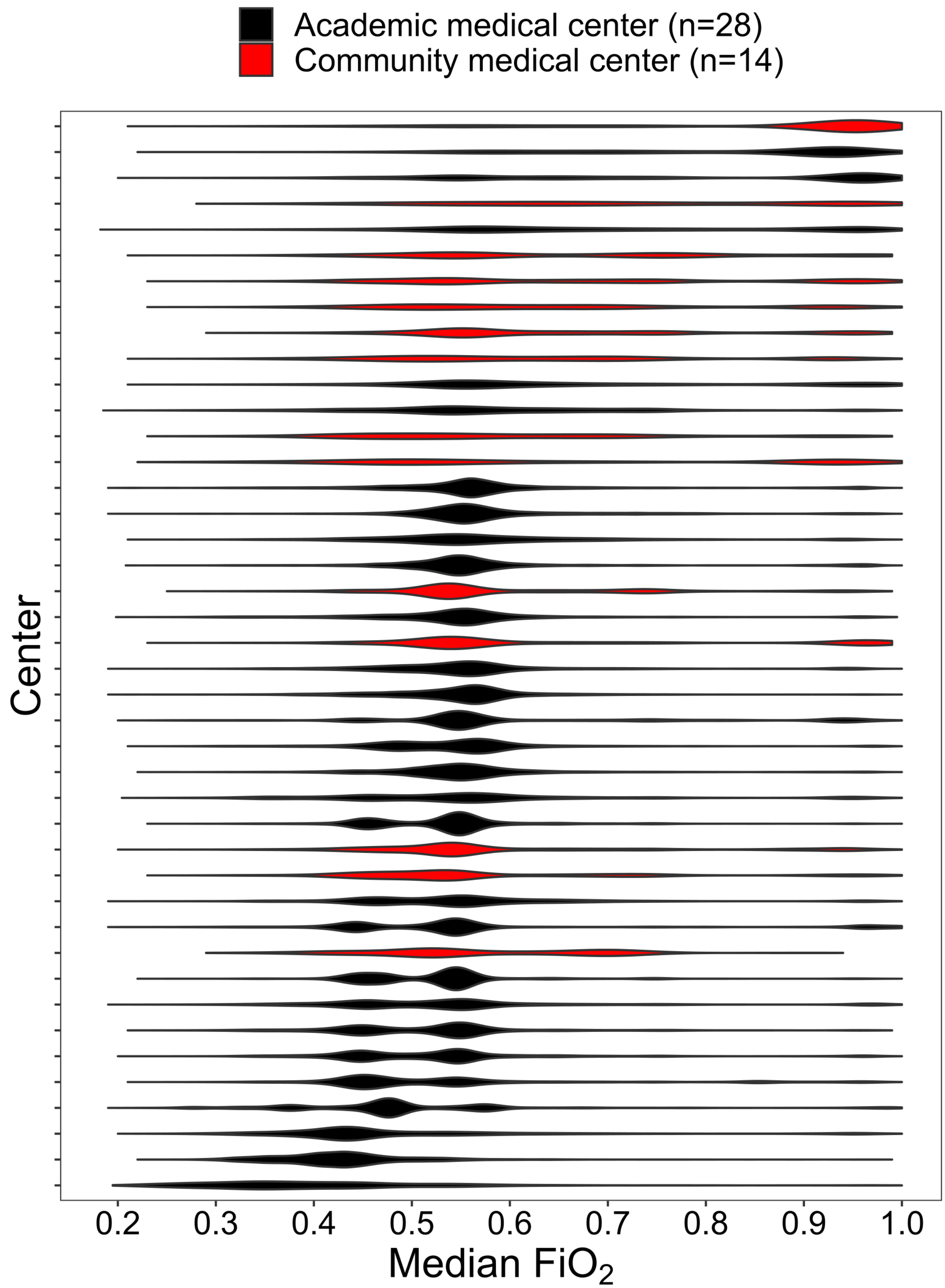
Characteristic	Estimate (95% CI)
Age, year	0.05 (0.05, 0.05)
Sex, female	0.35 (0.26, 0.44)
Race	
White (reference group)	
Black	−0.62 (−0.76, −0.48)
Other	0.04 (−0.18, 0.27)
Body mass index, kg/m2	0.14 (0.13, 0.14)
Medical history	
ASA class 1 or 2 (reference group)	
ASA class 3	1.13 (1.03, 1.23)
ASA class >= 4	4.33 (4.12, 4.54)
Elixhauser comorbidities	
Congestive heart failure	0.83 (0.64, 1.02)
Arrhythmia	0.22 (0.10, 0.35)
Valvular disease	1.10 (0.90, 1.31)
Pulmonary circulation disorder	0.91 (0.65, 1.17)
Peripheral vascular disease	−0.78 (−0.95, −0.61)
Paralysis	0.58 (0.28, 0.88)
Other neurologic disorders	0.37 (0.19, 0.56)
Chronic pulmonary disease	0.31 (0.19, 0.43)
Hypertension	0.02 (−0.08, 0.12)
Diabetes	0.02 (−0.11, 0.15)
Hypothyroidism	−0.17 (−0.31, −0.03)
Renal failure	−0.59 (−0.75, −0.42)
Liver disease	0.21 (0.00, 0.42)
Peptic ulcer disease	0.11 (−0.41, 0.62)
AIDS/HIV	−0.05 (−0.99, 0.89)
Lymphoma	0.28 (−0.18, 0.74)
Metastatic cancer	−0.59 (−0.76, −0.42)
Solid tumor without metastases	−0.23 (−0.35, −0.10)
Rheumatoid arthritis/collagen vascular disease	−0.19 (−0.44, 0.06)
Coagulopathy	0.55 (0.35, 0.74)
Obesity	0.41 (0.28, 0.54)
Weight loss	0.13 (−0.07, 0.33)
Fluid and electrolyte disorder	0.66 (0.53, 0.79)
Blood loss anemia	−0.05 (−0.44, 0.34)
Deficiency anemia	−0.21 (−0.47, 0.06)
Alcohol abuse	−0.37 (−0.95, 0.20)
Drug abuse	0.07 (−0.20, 0.34)
Psychoses	0.05 (−0.50, 0.61)
Depression	−0.02 (−0.15, 0.11)
Surgery characteristics	
Emergency surgery	1.18 (1.01, 1.35)
Surgery procedure category	
Head	−1.90 (−2.08, −1.71)
Neck	−1.92 (−2.16, −1.68)
Spine and spinal cord	−1.52 (−1.68, −1.35)
Open heart	11.47 (10.99, 11.96)
Intrathoracic (non−open heart)	0.66 (0.26, 1.06)
Extrathoracic	−1.83 (−2.09, −1.56)
Upper abdomen (reference group)	
Lower abdomen	−0.04 (−0.22, 0.14)
Gynecologic/Pelvic	−0.62 (−0.94, −0.30)
Urologic/male reproductive	−1.04 (−1.23, −0.85)
Extremity	−1.61 (−1.77, −1.46)
Other (include burn, obstetric, radiologic)	0.25 (−0.04, 0.55)
Baseline labs	
Hemoglobin, g/dl	0.06 (0.03, 0.09)
Hemoglobin measured preoperatively	−0.23 (−0.42, −0.03)
Creatinine, mg/dl	−0.04 (−0.08, 0.01)
Creatinine measured preoperatively	0.00 (−0.19, 0.19)
Lactate measured preoperatively	0.52 (0.37, 0.68)
Troponin measured preoperatively	2.57 (2.31, 2.84)



7. **Supplementary Figure 4.** Scatterplot showing the standard deviation of FIO2 among anesthesiologists versus the standard deviation of FIO2 among in-room anesthesia providers within each medical center and independent of patient and procedure factors. Each dot represents one medical center. There was no correlation between the variability of intraoperative oxygen administration among anesthesiologists and among anesthesia in-room providers across medical centers (r=-0.30, P=0.12).



8. **Supplementary Figure 5.** Distribution of median FIO_2 for each case within each medical center. The height of the shaded region corresponds with the proportion of patients who received FIO_2 at that level. Centers are displayed in descending order of overall median FIO_2 for the center.



9. **Supplementary Table 2**. Variance (95% confidence interval) expressed as percent of total variance in intraoperative FIO_2 administration explained by patient and procedure factors (covariates modeled as fixed effects), and medical center, anesthesiologist, and in-room anesthesia provider (covariates modeled as random effects) in the primary model, the sensitivity analysis that excluded intraoperative factors, and the sensitivity analysis that examined intraoperative *mean* instead of *median* FIO_2.

Factor Categories	Primary model	No intraoperative factors	Mean FIO_2
Patient	3.5 (3.5, 3.5)	3.5 (3.5, 3.5)	3.4 (3.4, 3.4)
Procedure	4.4 (4.2, 4.6)	3.0 (2.9, 3.2)	5.2 (5.0, 5.5)
Medical Center	23.3 (22.4, 24.2)	24.5 (23.6, 25.4)	27.2 (26.2, 28.1)
Anesthesiologist provider	7.7 (7.2, 8.2)	7.6 (7.1, 8.2)	8.3 (7.8, 8.7)
In-room provider	8.1 (7.8, 8.4)	8.0 (7.7, 8.3)	8.6 (8.4, 8.9)
Unexplained	53.0 (52.4, 53.6)	53.5 (52.8, 54.1)	47.7 (47.0, 48.4)