Revised statistical analysis plan for:

Cohort study of intraoperative lung protective ventilation trends in a large Canadian health authority

Changes to this statistical analysis plan compared to original study plan;

- Change to the study title to be more encompassing of all objectives of the study
- Change to the model building methods (part III of analysis) to reflect the exploratory nature of the model, in response to initial editor comments (1).

Note that study objectives, data range, and data source have not changed.

All changes compared to original study protocol are in blue on this document.

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Objectives

1. Identify rates of compliance with lung protective ventilation (LPV) guidelines in the Fraser Health Authority in the Province of British Columbia, Canada. Compliance with ventilation guidelines is defined as meeting two criteria. The first is that their average tidal volume is 6-8 mL/kg IBW and the second is that the average positive end expiratory pressure (PEEP) is at least 5 cm H_2O. Patients ventilated according to only one or neither of the above criteria will not be considered to have been ventilated according to the guidelines.
2. To elucidate time trends and shifts in LPV compliance from the pre-COVID to 2020s era.
3. To evaluate whether any time trends and shifts in LPV compliance in the 2020s era are sustained.
4. To elucidate predictors of compliance with LPV practice among providers. These predictors may help inform the design of educational efforts and systemic changes to tackle areas of deficiency.

Definition of LPV:

LPV is defined as an average tidal volume of 6-8 mL/kg ideal body weight and an average positive end expiratory pressure (PEEP) of at least 5 cmH2O.

Population:

Patients undergoing non-cardiac, non-thoracic surgery in Fraser Health Authority from 2014 – 2023 requiring general anesthesia with intubation.

Exclusion criteria: age < 18 years, cardiac or thoracic surgery, ASA 6 (organ donor), surgical procedure related to an occurrence or complication of prior procedure during the same admission/within 30 days, multiple National Surgical Quality Improvement Program (NSQIP) assessed cases within 30 days only for same patient, cases in electronic anesthesia record that are unable to be linked to NSQIP data or vice versa.

Data collection

Ventilation and other intraoperative data were obtained from the electronic anesthetic record, whereas perioperative data were obtained from the NSQIP database.

Part I: Patterns of compliance to LPV and relationship with default ventilator settings

- Descriptive statistics for compliance to LPV will be calculated for the entire dataset
- Among the non-compliance cases, the % attributable to the following will be calculated. This analysis is useful for determining areas of intervention/education required:
  - Low PEEP
  - Inappropriate (both too high or too low) tidal volume
  - Too low tidal volume
  - Too high tidal volume
  - Both low PEEP and inappropriate tidal volume

Part II: Investigation of time trends to compliance

A Shewhart control chart (p chart) of LPV compliance will be presented to investigate time trends of LPV compliance as correlated to the COVID pandemic, and to identify special-cause variation in LPV compliance throughout the pandemic. The following rules to look for trends and shifts will be employed (2):

- 1 point is outside the control limits.
- 2 out of 3 consecutive points are more than 2 sigmas from the center line in the same direction.
- 4 out of 5 consecutive points are more than 1 sigma from the center line in the same direction.
- 8/9 points on the same size of the center line.
- 6 consecutive points are steadily increasing or decreasing.
- 14 consecutive points are alternating up and down.
- 15 consecutive points are within 1 sigma of the center line.
- 8 consecutive points on either side of the center line with not within 1 sigma.

Part III: Predictors of compliance to LPV

Our list of hypothesized predictors to LPV use include:

- Age

- Biological sex
- Height
- Obesity of any class (body mass index > 30)
- Emergency case
- ASA classification
- Surgical duration
- Chronic obstructive pulmonary disease
- Congestive heart failure
- Surgical subspecialty
- Pre-COVID era v.s. 2020s era
- After-hours surgery (weekends, or between 1900 and 0700, based on local anesthesiology practitioner and nursing shift structure)
- Academic site (presence of established residency rotation)
- Neuromuscular blockade given
- Laparoscopic surgery
- NB: We considered before January 2020 as the pre-COVID era, and after June 2020 as the 2020s era. The former cutoff was chosen as January 2020 contained the first COVID case in BC. The latter cutoff was chosen as it constitutes three months after March 2020, when the World Health Organization announced COVID's pandemic status, and BC announced a state of emergency with the start of isolation policies. We hypothesized that any impact of the COVID pandemic on LPV compliance patterns would unlikely to have occurred prior COVID's arrival in BC, but would likely be in full swing three months after initiation of widespread social isolation, a very palpable event in society.
- NB2: parameters such as oxygen saturation, end-tidal carbon dioxide, and peak inspiratory pressures may be affected by use of LPV, and therefore will not be included as candidate predictors due to high likelihood of reverse causation (3). Mode of ventilation has been shown to correlate with LPV compliance(3), but this is unfortunately not recorded in our dataset.

We performed bivariate analysis to obtain unadjusted odds ratios for each hypothesized predictor to LPV non-compliance, using Chi-squared test for categorical predictors and bivariate logistic regression for continuous predictors. Fisher exact test was used if contingency table cell frequencies were < 5. For multi-level categorical predictors, we performed bivariate logistic regression to obtain odds ratios for each level if the chi-squared test for that predictor was statistically significant. We calculated adjusted odds ratios for each predictor via exploratory logistic regression including all hypothesized confounders, recognizing the exploratory nature of this approach (1). We used Bonferroni method for p-value adjustment for multiple comparisons. Lastly, we hypothesized that academic sites, defined as sites with an established residency rotation, may have increased compliance to published practice guidelines, including LPV compliance. Therefore, a subgroup analysis with only patients at academic sites was conducted to test this hypothesis.

<u>Sensitivity analyses, subgroup analyses, and other supplemental analyses</u>

- In the 2020s era, for tidal volumes from 400-600mL, we will plot the % of patients in whom tidal volume satisfies LPV criteria. This will inform any required change to the default tidal volume ventilator setting to maximize the number of patients satisfying LPV criteria if the tidal volume setting were left unchanged. In the same simulation, we will model changing the default PEEP setting on anesthesia machines from PEEP = off to PEEP = 5.

- We will perform subgroup analysis for academic hospital sites only for the identification of predictors of LPV non-compliance. Academic hospital sites are defined by the presence of an established residency rotation.
- We will perform the following sensitivity analyses for part III:
    - Inclusion of the 6 month transition period between pre-COVID and 2020s era
    - Night hours only for definition of off-hours surgery

References:

1. Thorpe KE. How to construct regression models for observational studies (and how NOT to do it!). Canadian Journal of Anesthesia/Journal canadien d'anesthésie. 2017;64(5):461-70.
2. Montgomery. Introduction to Statistical Quality Control. 6 ed. USA2009.
3. Walkey AJ, Wiener RS. Risk factors for underuse of lung-protective ventilation in acute lung injury. Journal of critical care. 2012;27(3):323. e1-. e9.