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Airway driving pressure is associated with postoperative pulmonary complications after major abdominal surgery: a multicentre retrospective observational cohort study

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Abstract

Background: High airway driving pressure is associated with adverse outcomes in critically ill patients receiving mechanical ventilation, but large multicentre studies investigating airway driving pressure during major surgery are lacking. We hypothesised that increased driving pressure is associated with postoperative pulmonary complications in patients undergoing major abdominal surgery.

Methods: In this preregistered multicentre retrospective observational cohort study, the authors reviewed major abdominal surgical procedures in 11 hospitals from 2004 to 2018. The primary

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Appendix A. Supplementary data
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outcome was a composite of postoperative pulmonary complications, defined as postoperative pneumonia, unplanned tracheal intubation, or prolonged mechanical ventilation for more than 48 h. Associations between intraoperative dynamic driving pressure and outcomes, adjusted for patient and procedural factors, were evaluated.

Results: Among 14 218 qualifying cases, 389 (2.7%) experienced postoperative pulmonary complications. After adjustment, the mean dynamic driving pressure was associated with postoperative pulmonary complications (adjusted odds ratio for every 1 cm H_2O increase: 1.04; 95% confidence interval [CI], 1.02–1.06; $P<0.001$). Neither tidal volume nor PEEP was associated with postoperative pulmonary complications. Increased BMI, shorter height, and female sex were predictors for higher dynamic driving pressure (β=0.35, 95% CI 0.32–0.39, $P<0.001$; β=−0.01, 95% CI −0.02 to 0.00, $P=0.005$; and β=0.74, 95% CI 0.63–0.86, $P<0.001$, respectively).

Conclusions: Dynamic airway driving pressure, but not tidal volume or PEEP, is associated with postoperative pulmonary complications in models controlling for a large number of risk predictors and covariates. Such models are capable of risk prediction applicable to individual patients.

Keywords

abdominal surgery; driving pressure; lung protective ventilation; postoperative pulmonary complications; predictive models; ventilation-induced lung injury

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Mechanical ventilation of the lungs is a necessary supportive therapy for critically ill patients and those undergoing major surgical procedures; however, repeated inflation/deflation cycles under positive pressure exposes alveoli to mechanical stresses, potentially resulting in clinically significant ventilator-induced lung injury[1] and may contribute to the development of postoperative pulmonary complications. Numerous lung protective ventilation strategies have been proposed to limit alveolar overdistension, prevent atelectasis, and prevent oxygen toxicity through the application of smaller tidal volumes, use of PEEP, and avoidance of excessive oxygen concentration.[2] However, many lung protective ventilation studies in surgical patients have investigated a bundled ventilation strategy, limiting the ability to resolve the contribution of any individual ventilation variable to the overall strategy.[3-5] When studies of single interventions, such as variation of tidal volume[6 7] or PEEP[8 9] alone, have been performed they often have not been found to be associated with benefit. Recent studies in both the ICU[10 11] and the operating room[5,12-14] suggest that driving pressure may be the ventilation variable most strongly associated with adverse clinical outcomes in some, but not all, surgical scenarios.[15]

Airway driving pressure is a potentially unifying variable which reflects the interaction of respiratory system factors and the ventilation strategy and is thus affected by ventilation variables, the degree of lung recruitment, and respiratory system elastance. However, prior work examining the relationship between driving pressure and adverse outcomes related to mechanical ventilation after a major surgery has been limited by heterogeneous patient cohorts and small sample sizes, limiting statistical power and the ability to control for confounding effects of other variables that may predispose to high driving pressure delivery.[12 16 17]

The primary objective of this multicentre observational study is to examine the association between dynamic driving pressure and postoperative pulmonary complications. Additionally, this study (1) examines the association between dynamic driving pressure and a secondary outcome of pulmonary complications, major morbidity, and 30-day mortality; (2) compares the relative protective contribution of driving pressure with tidal volume and PEEP; and (3) evaluates the potential impact of patient variables, including those factors shown to predict higher tidal volume ventilation[18] on exposure to higher driving pressure.

Methods

Study design

University of Virginia Institutional Review Board (21039) approval was obtained for this observational study. The Institutional Review Board of each contributing organisation also approved aggregation of this limited dataset. Informed patient consent was waived because no patient care interventions were involved in the conduct of the study. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) guidelines were followed.[19] Study methods including data collection, outcomes, and statistical analyses were established before accessing data and presented at the Multicenter Perioperative Outcomes Group (MPOG) peer-review committee on 13 August 2018, with an *a priori* final analytical plan approved and registered on 14 February 2019.[20]

Study population

Inclusion criteria were adult patients (≥18 yr of age) who underwent a major abdominal surgical procedure (mechanical ventilation ≥120 min) at an MPOG institution between 2004 and 2018 and had clinical data available in the integrated American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) surgical outcomes registry.[21] Eleven academic and private centres were included based upon availability of complete data as relevant to this study (Supplementary Information, Appendix 1). Admission type and hospital admission were not included in the definition of major abdominal surgical procedure. Mechanical ventilation ≥120 min was selected to ensure clinically significant exposure to intraoperative mechanical ventilation, an independent risk factor for postoperative pulmonary complications.[4]

Patients with missing (or non-valid) ventilation data and those with incomplete covariate data were excluded from our study. If multiple surgical procedures occurred within 30 days, only the initial procedure was considered. Patients requiring mechanical ventilation at presentation for surgery were also excluded. The derivation of our study cohort is detailed in Fig 1.

Data sources

We collected study data from two sources: the MPOG electronic database[22] and the ACS NSQIP registry.[23] The MPOG research team has developed processes to extract data from the perioperative record and to then transform those data into a standardised, de-identified format that can be used for both research and quality improvement.[22] Physiological monitors including vital signs and ventilator settings are automatically collected every 60 s throughout a procedure. In addition, templated script elements are recorded and time-stamped.[5] MPOG data undergo rigorous validation, including limited clinician adjudication, and standardised approaches to ensure data integrity and quality.[22]

The ACS NSQIP programme is a nationally validated registry of surgical data. Each participating hospital has a trained surgical clinical reviewer who collects preoperative and postoperative data on surgical patients, and a surgeon 'champion' leads and oversees implementation and quality at each institution.[24] Data quality is validated and audited to ensure reliability.

Primary outcome: postoperative pulmonary complications

The primary outcome was a composite of postoperative pulmonary complications, defined as any one or more of the following occurring within 30 days postoperatively: pneumonia, requirement of ventilatory support for any reason (unplanned tracheal intubation, failure to wean from ventilator support within 48 h from the end of surgery), or both. The primary outcome was curated from standardised postoperative complications tracked within ACS NSQIP. A data dictionary detailing the individual complications comprising each outcome can be found in Supplementary Information, Appendix 2.

Secondary outcome: composite of primary outcome, major morbidity, or 30-day mortality

A composite outcome including postoperative pulmonary complications, major morbidity, and/or 30-day mortality was also assessed. Complications included in the major morbidity outcomes were: pulmonary embolism, renal insufficiency or acute renal failure, urinary tract infection, cerebrovascular accident, myocardial infarction, cardiac arrest, graft/prosthesis/flap failure, deep vein thrombosis/thrombophlebitis, sepsis, septic shock, return to the operating room within 30 days, hospitalisation beyond 30 days, unplanned readmission, and unplanned reoperation. A detailed description of each complication can be found in Supplementary Information, Appendix 2.

Exposure variable – dynamic driving pressure

Peak inspiratory pressure and plateau pressure are variably recorded based upon individual settings at each MPOG institution. Therefore, we calculated two driving pressure variables: (1) driving pressure (ΔP=plateau pressure–PEEP) and (2) dynamic driving pressure ($d\Delta P$=peak inspiratory pressure–PEEP). As dynamic driving pressure has been shown to be an acceptable proxy for driving pressure when plateau pressure is unavailable,[5,13 15 25-27] our analytical plan called for both peak inspiratory pressure and plateau pressure to be queried. We calculated the Pearson correlation coefficient between the two driving pressure variables (driving pressure and dynamic driving pressure) to determine the degree of association. Ultimately, dynamic driving pressure was selected as the driving pressure variable used in subsequent analyses based on greater availability in our dataset.

We then calculated the mean dynamic driving pressure value for the *initial period of mechanical ventilation* (10-min epoch beginning 20 min after the initiation of ventilation). This initial period was selected *a priori* to provide a representative indication of driving pressure, independent of artifactual changes at case initiation and completion. In addition, surgical factors (such as positioning changes and pneumoperitoneum) have been shown to alter elastance and the resulting association with airway driving pressure.[15 28 29] Mean dynamic driving pressure from the initial ventilation period was selected as the primary exposure variable *a priori* to minimise variability and missing data that occurs with induction and emergence, and avoid artifacts from surgical and positional factors, which potentially alters driving pressure.[28]

Additional ventilation variables

In addition, tidal volume and PEEP were collected on a minute-by-minute basis as previously described.[5 13] Using the ventilation data collected, we also calculated: tidal volume per predicted body weight (V_T/PBW) for the initial period of ventilation. Predicted body weight was calculated as 50.0+(0.91×[height in cm–152.4]) for men; 45.5+(0.91×[height in cm–152.4] for women.[30]

Preoperative variables

Variables which represented clinical characteristics that would be known before the induction of anaesthesia were queried and collected. General categories queried included: (1) patient characteristics (age, sex, race, height, weight, admission type, ASA physical classification status), (2) social history, and (3) comorbidities (based upon ACS NSQIP designations).[31] A full list of available preoperative variables can be found in Supplementary Information, Table S1.

Procedural variables

We collected procedural details (general anaesthetic, emergency surgery, surgical classification, and laparoscopic approach) censored to the point of initial exposure to mechanical ventilation (Supplementary Information, Table S1). Intraoperative factors occurring after the initial ventilator exposure (for example: blood transfusion, total surgical duration) and therefore downstream within the causal pathway were not included in the multivariable model developed. The surgical procedure was further identified by surgical Current Procedural Terminology (CPT) code into the following classifications: (1) colorectal, (2) foregut, (3) general surgery, (4) hepatobiliary, (5) urologic, and (6) vascular–abdominal; and classification of CPTs as minimally invasive or not (Supplementary Information, Appendix 3).

Statistical analyses

Perioperative and intraoperative characteristics were summarised using medians and inter-quartile ranges for continuous variables, and counts and percentages for categorical covariates. Comparisons of continuous data were made using Mann–Whitney *U*-tests and categorical data were compared using Pearson χ^2 tests. A *P*-value <0.05 was selected *a priori* to denote statistical significance because driving pressure was asserted as the variable of primary interest.[5]

Multivariable logistic regressions

We use mixed-effects logistic regression models, clustered by institution, for multivariable assessment of the primary and secondary outcomes, with additional covariates selected *a priori*. We used a convenience sample of all available MPOG linked with NSQIP data. Statistical analysis was performed in R version 4.1.0 (*lme4* with *boot* for bootstrap confidence intervals) (R Foundation for Statistical Computing, Vienna, Austria). Discrimination was assessed with the *c*-statistic.

Risk factors for ventilation with elevated driving pressure

To test the hypothesis that the patient population most susceptible to ventilation with elevated tidal volume are also susceptible to ventilation with elevated dynamic driving pressure, we created an additional linear regression model with dynamic driving pressure as the outcome (Model 3). To confirm accepted risk factors, we also repeated the regression with tidal volume as the outcome of interest (Model 4).

Sensitivity analyses

Additional sensitivity analyses were performed as described above using two alternative definitions for our primary exposure variable: (1) dynamic driving pressure over the entire case duration (instead of the initial ventilation period) and (2) true driving pressure (from centres submitting plateau pressure data).

Results

Of the 41 906 surgical cases initially reviewed from 11 MPOG institutions with linked NSQIP data, 16 519 non-abdominal surgery cases were excluded. Of the remaining 25 400 cases, 9109 lacked the required ventilator data to calculate dynamic driving pressure. An additional 2060 cases were missing other covariate data. The total cohort meeting full inclusion criteria was 14 218 abdominal surgical procedures (Fig 1). Missing data are described in Supplementary Table S2.

Study population – baseline characteristics and univariate analyses

The median patient age was 57 (inter-quartile range, 46–67) yr, and 57.8% were female (Table 1). Of the surgical procedures, 51.7% used a minimally invasive approach and 4.1% were emergent (Supplementary Information, Table S3). The most common procedures included: *laparoscopy, surgical, with total hysterectomy, for uterus 250 g or less* (CPT code: 58571; 913 cases, 6.4%); *laparoscopy, surgical; colectomy, partial, with anastomosis, with coloproctostomy (low pelvic anastomosis)* (CPT code: 44207; 669 cases, 4.7%); and *laparoscopy, surgical; colectomy, partial, with anastomosis* (CPT code: 44204; 561 cases, 3.9%) (Supplementary Information, Appendix 3). The mean procedure duration was 212 (162–287) min with median driving pressure of 16 (12–21) cm H_2O (Supplementary Information, Table S3).

Outcomes

Among 14 218 qualifying cases, 389 (2.7%) experienced a postoperative pulmonary complication, and 2202 (15.5%) experienced a non-respiratory complication. Patient mortality was 66 (0.5%), with 2311 (16.3%) experiencing a composite outcome (postoperative pulmonary complications, major morbidity, or 30-day mortality). The breakdown of individual complications can be found in Table 2.

Patients developing postoperative pulmonary complications tended to be older (65 [56–74] yr compared with 57 [46–67] yr, $P<0.001$) and male (57.1% compared with 41.8%, $P<0.001$). A greater proportion of postoperative pulmonary complication occurred in patients with partially or totally dependent (6.7% compared with 1.2%, $P<0.001$) functional status. (ACS-NSQIP functional status scale – *Independent*: Does not require assistance from another person for any activities of daily living, including one who functions independently with the use of prosthetics, equipment, and/or devices. *Partially Dependent*: Requires some assistance from another person for activities of daily living regardless of use of prosthetics, equipment, and/or devices. *Totally Dependent*: Requires total assistance for all activities of daily living.) A greater proportion smoked (20.6% vs 14.0%, $P<0.001$), and had comorbidities including congestive heart failure (15.4% *vs* 2.8%, $P<0.001$), chronic obstructive pulmonary disease (25.7% *vs* 13.0%, $P<0.001$), renal insufficiency (16.7% *vs* 4.2%, $P<0.001$), and sepsis (20.3% *vs* 2.9%, $P<0.001$). Postoperative pulmonary complications occurred more frequently after emergent cases (17.7% *vs* 4.2%, $P<0.001$) and were less likely after minimally invasive surgery (19.8% *vs* 51.5%, $P<0.001$). Full details can be found in Table 1.

Selection of exposure variable – driving pressure

We derived plateau pressure data on 4165 and peak inspiratory pressure data on 16 449 unique abdominal surgical procedures. For the 3245 cases where both plateau pressure and peak inspiratory pressure data were available, the correlation co-efficient between driving pressure and dynamic driving pressure during the initial ventilation period (10-min epoch beginning 20 min after the initiation of mechanical ventilation) was 0.945. The correlation plot can be found in Supplementary Information, Figure S1A. Ultimately, based upon the high correlation, documented clinical utility,[5 13 25] and larger availability of qualifying cases – we selected dynamic driving pressure as the primary measure driving pressure variable. The primary exposure variable was mean dynamic driving pressure during the 10-min epoch beginning 20 min after mechanical ventilation (*initial ventilation period*). The correlation coefficient between dynamic driving pressure during the initial ventilation period and dynamic driving pressure for the entire case was 0.806 and the accompanying correlation plot can be found in Supplementary Information, Figure S1B.

Descriptive statistics on driving pressure and other ventilation variables

The median dynamic driving pressure was 16 (12–21) cm H_2O, V_T was 489 ml (439–567), V_T PBW was 8 (7–9) ml kg^{-1} and PEEP was 5 (2–5) cm H_2O (Table 1). Dynamic driving pressure had a right-skewed distribution. PEEP notably had a very narrow distribution, with the majority of cases receiving 5 cm H_2O. Notably, 3132 (22.0%) received PEEP <2 cm H_2O and 2002 (14.1%) received zero PEEP. Histograms displaying dynamic driving pressure, tidal volume, and PEEP can be found in the Supplementary Information, Figure S2.

Multivariable logistic regression models

Primary outcome – postoperative pulmonary complications (model 1)— Dynamic driving pressure was associated with postoperative pulmonary complications in the generalised linear model (adjusted odds ratio [OR]=1.04; 95% confidence interval [CI], 1.02–1.06; *P*<0.001). Neither PEEP (adjusted OR=1.02; 95% CI, 98–1.07; *P*=0.400) nor tidal volume (adjusted OR=0.98; 95% CI, 0.92–1.04; *P*=0.452) was associated with postoperative pulmonary complications. Age (in decades), male sex, higher ASA physical status classification (IV or V), dependent functional status, and current tobacco use were patient factors associated with postoperative pulmonary complications. The comorbidities – congestive heart failure, chronic obstructive pulmonary disease, renal failure, and preoperative sepsis – were also associated with postoperative pulmonary complications. Intraoperative details, including emergency surgery and open (as opposed to minimally invasive) surgical approach, were also highly significant. Vascular surgery was associated with increased risk of postoperative pulmonary complications, whereas gynaecological surgery was associated with decreased risk. The model had strong discrimination (*c*-statistic=0.815; 95% CI, 0.792–0.838). (Interpretation of the *c*-statistic [discrimination]: 0.5, none; >0.7, good; >0.8, strong; 1.0, perfect.) The estimated variance of the MPOG institution as a random effect for this model was 0.020 (standard error=0.113). The full details of Model 1 can be found in Table 3. The predicted probability of developing a postoperative pulmonary complication increased as a function of mean dynamic driving pressure, more than doubling over the examined range of this variable. The predicted probability curve for a representative patient can be found in Fig 2.

Composite outcome – postoperative pulmonary complication, major morbidity, or 30-day mortality (model 2)—Dynamic driving pressure was not found to be associated with our composite outcome (adjusted OR=1.01; 95% CI, 1.00–1.02; *P*=0.131). Similar risk factors were associated with the composite outcome as with the pulmonary complication model, including age, higher ASA physical status classification, dependent functional status, and comorbidities including congestive heart failure, chronic obstructive pulmonary disease, renal failure, and sepsis. Model 2 had a markedly worse performance when compared with Model 1 (*c*-statistic=0.685, 95% CI 0.673–0.698 *vs* 0.815, 95% CI 0.792–0.838). Full details of Model 2 can be found in Supplementary Information, Table S4.

Risk factors for ventilation with elevated driving pressure (model 3)—Next, we created a multivariable linear regression model with driving pressure as the outcome to assess whether the traditional risk factors for non-protective ventilation were associated with high driving pressures (Model 3). In this model, we confirmed that increased BMI (kg m^{-2} (β=0.35; 95% CI, 0.32–0.39; *P*<0.001), decreased height (cm) (β=−0.01; 95% CI, −0.02 to 0.00; *P*=0.005), and female sex (β=0.74; 95% CI, 0.63–0.86; *P*<0.001) were all associated with dynamic driving pressure (Supplemental Information, Table S5A). This means that dynamic driving pressure increases by 0.35 cm H_2O, for every 1 kg m^{-2} increase in BMI and dynamic driving pressure increases by 0.01 cm H_2O for every cm decrease in height. In addition, emergency surgery, laparoscopic approach, and current tobacco use were also associated with elevated driving pressure.

We also confirmed the previously described[18] association between BMI (β=0.07; 95% CI, 0.05–0.08; $P<0.001$), decreased height (β=−0.08; 95% CI, −0.08 to −0.07; $P<0.001$), and female sex (β=0.07; 95% CI, 0.01–0.14; $P=0.022$) with tidal volume (Supplemental Information, Table S5B).

Sensitivity analyses

When dynamic driving pressure was considered over the extended case duration (as opposed to the initial ventilation period), the significant association with the primary outcome remained (adjusted OR=1.05; 95% CI, 1.02–1.08; $P=0.002$) (Supplemental Information, Table S6). Additional sensitivity analyses showed that true driving pressure (P_{PLAT}–PEEP) predicts postoperative pulmonary complications after abdominal surgery (adjusted OR=1.05; 95% CI, 1.01–1.10; $P=0.027$) (Supplemental Information, Table S7).

Discussion

We report results of a large multicentre retrospective observational study evaluating dynamic airway driving pressure exposures in patients undergoing mechanical ventilation for major abdominal surgery to characterise the relationship between dynamic driving pressure and the risk of postoperative pulmonary complications. Using robust, validated observational databases, we report an overall postoperative pulmonary complication risk (pneumonia, reintubation, or prolonged ventilation) of 2.7% after abdominal surgery. Dynamic driving pressure was associated with postoperative pulmonary complications. Notably, for tidal volume and PEEP, two components of traditional lung protective ventilation,[3 4 32] the null hypothesis of no effect was not rejected. In addition, we found that larger BMI, smaller height, and female sex – known risk factors for ventilation with high tidal volume[18] – are also risk factors for receiving high dΔP.

Comparison with previous studies

Our findings are in general agreement with prior smaller studies[16 33] including a small meta-analysis of postoperative pulmonary complications after general anaesthesia for a number of different surgery types,[12] which demonstrated driving pressure, but not tidal volume, to be associated with postoperative pulmonary complications. We assessed the impact of driving pressure in a much larger and more procedurally homogeneous cohort than previously described.[12] Direct comparison with other studies of airway driving pressure and postoperative pulmonary complication risk is limited by differences in the composition of the composite primary outcome. In this study, postoperative pulmonary complications were defined as events of high clinical importance (pneumonia or requirement of ventilatory support) – which could explain the lower incidence compared with previous studies, which used a much broader definition of postoperative pulmonary complications including atelectasis and oedema.[34] In addition we were able to identify additional risk factors including: (1) age, (2) higher ASA status, and (3) dependent functional status that were not significant in the prior meta-analysis.[12] Comorbidities and social history was assessed in more detail than previous studies, providing additional discrimination.

Our finding that tidal volume was not associated with postoperative pulmonary complications in abdominal surgery is consistent with recent randomised trials which examined the impact of an isolated decrease in tidal volume in surgical patients (6 *vs* 10 ml kg^{-1})[6] and a recent patient-level meta-analysis that showed high intraoperative PEEP with recruitment manoeuvres during low tidal volume ventilation does not reduce postoperative pulmonary complications.[35] Our finding that increased BMI, short stature, and female sex were associated with increased driving pressure is consistent with, and extends upon, prior work showing these patients to be at greater risk for receiving ventilation with higher tidal volumes.[18]

Limitations of study methodology

Our study has notable strengths, and several limitations. First, this large, multicentre study was well positioned to assess the impact of varied practice patterns across different regions and institutions (estimated variance of institution as a random effect was 0.020 with standard error of 0.113). Abstractor adjudicated standardised outcome is another methodological strength. The large and relatively homogeneous cohort enabled us to include a number of relevant covariates and risk predictors, effectively controlling for potentially confounding variables. However, the retrospective nature of the study has inherent limitations including the possibility of yet unidentified confounding variables. An additional limitation is the wide period of data collection (2004–18) and resulting change of practice patterns over time, which may introduce unaccounted covariates. Abnormal respiratory mechanics are also markers of poorer lung function at the onset of mechanical ventilation, which is likely a stronger predisposing factor to postoperative pulmonary complications than tidal lung strain in normal lungs. This is important because modifications in ventilator management may not modify the risk of complications, although the importance of driving pressure as a risk predictor remains. Accruing evidence appears to support a strong relationship between driving pressure, perhaps as a surrogate of dynamic strain, and the development of postoperative pulmonary complications in abdominal surgery.[16 17]

An additional strength of the current study is that we confined our primary analysis to abdominal surgery, in contrast to other studies which assessed more heterogeneous surgical cohorts[15 33 36 37] and also controlled for surgical type and approach (specifically open *vs* laparoscopic). Future studies are necessary to understand how surgical approach influences driving pressure and the subsequent association with postoperative pulmonary complications. Recent studies have demonstrated that increased driving pressure has a larger impact in laparoscopic compared with open abdominal procedures (closed: adjusted OR=1.13 [95% CI, 1.12–1.14], $P<0.001$ *vs* open: adjusted OR=1.07 [95% CI, 1.05–1.10], $P<0.001$).[16]

Another limitation is the large number of cases excluded owing to either missing ventilation data (35.8%) or missing covariate data (8.1%) (Supplemental Information, Table S2); however, the omitted cases do not appear to have been excluded in a biased manner. Of note, the majority (95.5%) of the data excluded for missing ventilation data were from a single institution, suggesting an issue with electronic capture of ventilation data. Because plateau pressure data were incomplete, dynamic driving pressure (using peak inspiratory pressure) was used as a proxy for driving pressure. To account for this limitation, we demonstrated strong correlation (0.945) between dynamic and true airway driving pressures for the 4150 cases where both plateau pressure and peak inspiratory pressure data were available and confirmed the association between true driving pressure and the primary outcome (Supplementary Information, Table S7). Another limitation is that outcome measures were not specifically confirmed by the study investigators, relying upon institutional reporting to ACS-NSQIP, a surgeon-led reporting programme, utilising clinical reviewers who undergo standardised training, and database auditing from the American College of Surgeons to ensure data reliability. In addition, the outcome *requirement of ventilatory support* does not specifically confirm pulmonary aetiology which would be necessary to diagnose respiratory failure. Finally, any data reduction where driving pressure is simply expressed as a mean value over time may not capture the complexity required to fully model this phenomenon.

Clinical correlation

Driving pressure, but not tidal volume or PEEP, was associated with a markedly increased risk of postoperative pulmonary complications after major abdominal surgery. Based originally upon results from the Acute Respiratory Distress Syndrome Network, ventilation with low tidal volumes has comprised the cornerstone of protective ventilation strategies used clinically in both critically ill patients and those undergoing major surgery.[3 4 30] However, both observational studies[38 39] and prospective trials[6] in the perioperative arena have consistently failed to implicate tidal volume as the aetiological agent in lung injury or postoperative pulmonary complications. The greater influence of driving pressure as compared with either tidal volume or PEEP is consistent with our evolving understanding of the pathogenesis of postoperative pulmonary complications and may be the variable most carefully monitored and titrated intraoperatively. Although driving pressure appears to be the ventilatory factor most strongly associated with postoperative pulmonary complications, we cannot infer causation. However, results of the current study appear generally consistent with those of small prospective studies which demonstrate that efforts to minimise driving pressure by PEEP titration result in diminished rates of atelectasis and postoperative pulmonary complications after abdominal surgery.[17 40]

Collectively, these data would support clinical efforts to monitor airway driving pressure during perioperative ventilation of abdominal surgery patients and to consider minimising driving pressures by individualisation of PEEP. Numerous patient and procedural characteristics associated with increased risk for postoperative pulmonary complications were also identified in this study. Providers caring for certain patients – specifically those with (1) higher ASA status, (2) dependent functional capacity, (3) current tobacco use, (4) comorbidities such as sepsis and congestive heart failure, or (5) those undergoing emergency surgery – may need to exercise greater vigilance in their ventilation strategy, given both the greater likelihood of delivering higher driving pressures and the increased risk of postoperative pulmonary complications. Although the incremental increase in risk (per 1 cm H_2O in driving pressure) appears relatively small, we have shown more than a doubling of risk for a representative patient (Fig 2) over the range of driving pressures seen in the study.

Conclusions

In this multicentre, retrospective observational cohort study, we integrated robust data sources from varied perioperative sources, to study the impact of ventilatory variables on pulmonary complications and demonstrated that driving pressure, but not tidal volume or PEEP, was associated with a marked increased risk of postoperative pulmonary complications after major abdominal surgery. We also demonstrated the feasibility of modelling driving pressure related risk for individual patients and further identified patient variables – short stature, high BMI, and female sex – which are associated with higher driving pressure exposure. Notably, female sex was associated with higher dynamic driving pressure but lower incidence of our primary outcome, postoperative pulmonary complications. In addition, we quantified both the incremental increase in risk associated with increasing driving pressure and the individual contributions of key ventilatory variables, which have often been studied only in a bundled approach.[3-5 15] The results of this study also confirm the utility of a 'big data' approach to evaluation of perioperative exposures and clinically relevant outcomes utilising high-fidelity perioperative databases and suggest that such approaches may be helpful in informing rational design of future randomised trials. Future studies, including RCTs, will be required to provide further insight into the relationship between driving pressure and postoperative pulmonary complications, including a potential causal mechanism and whether modifications in driving pressure reduce the risk for postoperative pulmonary complications.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data sharing

The dataset is governed by the MPOG Data Use Agreement (DUA) which allows it only to be shared with other MPOG DUA holders. A limited dataset would be available to other parties after publication upon execution of a Data Use Agreement and fulfilment of other regulatory requirements (including IRB approval).

Appendix B.: Non-author collaborators part of the group

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Abbreviation

ACS-NSQIP	American College of Surgeons National Surgical Quality Improvement Program
ASA	American Society of Anesthesiologist
BMI	Body mass index
cm	Centimetres
COPD	Chronic Obstructive Pulmonary Disease
CHF	Congestive heart failure
CPT	Current Procedural Terminology
ΔP	Driving pressure
Cdyn	Dynamic compliance
dΔP	Dynamic driving pressure
FAER	Foundation for Anesthesia Education and Research
LPV	Lung protective ventilation
MPOG	Multicenter Perioperative Outcomes Group
NHLBI	National Heart, Lung, and Blood Institute
PEEP	Positive end-expiratory pressure
PBW	Predicted Body Weight
PPCs	Pulmonary complications

RECORD	REporting of studies Conducted using Observational Routinely-collected health Data
Cs	Static compliance
VT	Tidal volume
VILI	Ventilator-induced lung injury

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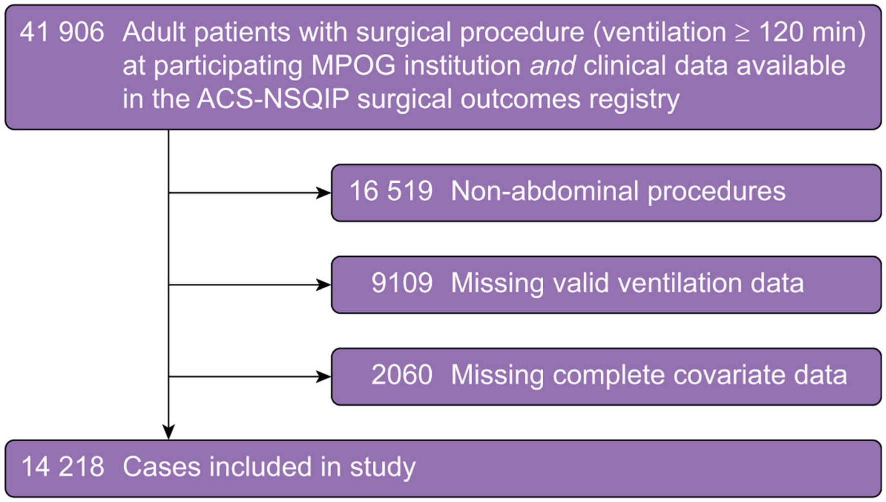

Fig. 1.

Derivation of study cohort. ACS-NSQIP, American College of Surgeons National Surgical Quality Improvement Program; MPOG, Multicenter Perioperative Outcomes Registry. Abbreviations: ACS-NSQIP = American college of surgeons national surgical quality improvement program; Min = Minutes; MPOG = Multicenter perioperative outcomes registry.

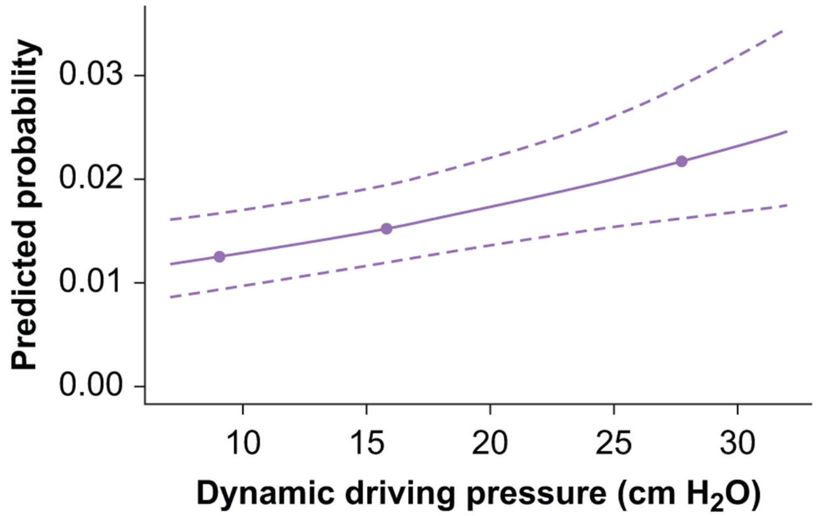

Fig. 2.

Predicted probability of developing postoperative pulmonary complication as a function of dynamic driving pressure. The plot shows the estimated probability of developing a postoperative pulmonary complication by modified driving pressure for a 59-yr-old female patient, with ASA class 3, independent functional status, no comorbidities, non-smoker, who underwent a non-emergent upper abdominal surgery, lasting 220 min, and receiving 2.4 L of crystalloid, but no blood transfusion. The dots on the graph are at the 5th, 50th, and 95th percentiles of dynamic driving pressures.

Table 1

Patient and procedural characteristics of patients developing and not developing postoperative pulmonary complications. *P*-values from skewed continuous data are calculated using a rank sum test because there is little loss even with normal data. For robustness, we also report median [q1, q3] for all continuous variables. SD, standard deviation; IQR, inter-quartile range.

	Entire cohort		Postoperative pulmonary complication				P-value	
	n=14 218		No, *n*=13 829 (97.3%)		Yes, *n*=389 (2.7%)		χ^2	Mann-Whitney/ Wilcoxon
	n, mean, or median	Percent, SD, IQR	*n*, mean, or median	Percent, SD, IQR	*n*, mean, or median	Percent, SD, IQR		
Patient characteristics								
Age	57	[46, 67]	57	[46, 67]	65	[56, 74]		<0.001
Female sex	8222	57.8	8055	58.2	167	42.9	<0.001	
BMI (kg m^{-2})	28	[24, 34]	28	[24, 33]	28	[24, 33]		0.050
Comorbidities								
Congestive heart failure	448	3.2	388	2.8	60	15.4	<0.001	
Chronic obstructive pulmonary disease	1893	13.3	1793	13.0	100	25.7	<0.001	
Renal insufficiency	639	4.5	574	4.2	65	16.7	<0.001	
Sepsis	485	3.4	406	2.9	79	20.3	<0.001	
Emergent surgery	582	4.1	513	3.7	69	17.7	<0.001	
Peak inspiratory pressure (cm H_2O)	19	[16, 24]	19	[16, 24]	21	[17, 25]		0.001
PEEP (cm H_2O)	5	[2, 5]	5	[2, 5]	4	[2, 5]		0.649
Dynamic driving pressure (cm H_2O)	16	[12, 21]	16	[12, 21]	17	[13, 22]		<0.001
Tidal volume (ml)	489	[439, 567]	489	[439, 567]	490	[435, 565]		0.583
Tidal volume PBW (ml kg^{-1})	8	[7, 9]	8	[7, 9]	8	[7, 9]		0.097
Dynamic compliance (ml cm H_2O^{-1})	32	[26,40]	32	[26,40]	30	[24, 38]		<0.001

Table 2

Incidence of complications comprising primary and composite outcomes. The outcomes table contains data on those patients included in the regression model, with complete data on all covariates. OR, operating room.

Complication			Patient population (n=14 218)	
			n	**(%)**
Primary outcome (postoperative pulmonary complication)			389	2.7
	Pneumonia		187	1.3
	Unplanned intubation		192	1.4
	Ventilation >48 h		194	1.4
Morbidity (non-respiratory complication)	Non-respiratory complications		2202	15.5
		Pulmonary embolism	79	0.6
		Renal insufficiency or acute renal failure	148	1.0
		Urinary tract infection	413	2.9
		Cerebrovascular accident	17	0.1
		Myocardial infarction	44	0.3
		Cardiac arrest	57	0.4
		Graft/prosthesis/flap failure	1	0.0
		Deep venous thrombosis/thrombophlebitis	37	0.3
		Sepsis/septic shock	633	4.5
		Return to OR within 30 days	728	5.1
		Hospitalisation beyond 30 days	155	1.1
		Unplanned readmission	984	6.9
Mortality	30-day mortality		66	0.5
Composite outcome (morbidity or mortality)			2311	16.3

Table 3

Risk factors for primary outcome (postoperative pulmonary complications). CI, confidence interval; COPD, chronic obstructive pulmonary disease; aOR, adjusted odds ratio.

Model 1. Postoperative pulmonary complications (*c*-statistic=0.815; 95% CI, 0.792–0.838)			
	aOR	**95% CI**	***P*-value**
Ventilation variable			
Dynamic driving pressure (cm H_2O)	1.04	1.02 1.06	<0.001
PEEP (cm H_2O)	1.02	0.98 1.07	0.400
Tidal volume (ml kg^{-1} of predicted body weight)	0.98	0.92 1.04	0.452
Preoperative variables			
Age (decades)	1.22	1.13 1.31	<0.001
Female sex	0.58	0.42 0.81	0.001
Height (cm)	0.98	0.96 1.00	0.115
BMI (kg m^{-2})	1.00	0.99 1.01	0.916
ASA class			
1–2	0.61	0.46 0.81	0.001
3	Reference		
4–5	1.72	1.20 2.45	0.003
Functional status			
Independent	Reference		
Partially/totally dependent	1.61	1.23 2.10	0.001
Current smoker	1.21	1.02 1.43	0.030
Comorbidities			
Congestive heart failure	2.17	1.63 2.90	<0.001
COPD	1.38	0.95 2.01	0.090
Renal failure	1.84	1.27 2.67	0.001
Sepsis	3.79	2.45 5.86	<0.001
Laboratory values			
Initial haematocrit <0	1.01	0.66 1.54	0.978
Procedural details			
Emergency surgery	1.46	1.11 1.91	0.006
Surgical type			
Colorectal	Reference		
Foregut	1.32	0.70 2.52	0.394
General surgery	0.72	0.47 1.10	0.130
Gynaecological	0.45	0.35 0.57	<0.001
Hepatobiliary	1.12	0.85 1.46	0.425
Urological	0.87	0.57 1.33	0.511
Vascular	2.74	2.06 3.64	<0.001
Vascular–abdominal	1.77	1.18 2.64	0.006
Laparoscopic	0.37	0.28 0.48	<0.001