A Description of Intraoperative Ventilator Management in Patients with Acute Lung Injury and the Use of Lung Protective Ventilation Strategies

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ABSTRACT

Background: The incidence of acute lung injury (ALI) in hypoxic patients undergoing surgery is currently unknown. Previous studies have identified lung protective ventilation strategies that are beneficial in the treatment of ALI. The authors sought to determine the incidence and examine the use of lung protective ventilation strategies in patients receiving anesthetics with a known history of ALI.

Methods: The ventilation parameters that were used in all patients were reviewed, with an average preoperative Pa_{CO_2}/F_{IO_2} ratio of ≤ 300 between January 1, 2005 and July 1, 2009. This dataset was then merged with a dataset of patients screened for ALI. The median tidal volume, positive end-expiratory pressure, peak inspiratory pressures, fraction inhaled oxygen, oxygen saturation, and tidal volumes were compared between groups.

Results: A total of 1,286 patients met criteria for inclusion; 242 had a diagnosis of ALI preoperatively. Comparison of patients with ALI *versus* those without ALI found statistically yet clinically insignificant differences between the ventilation strategies between the groups in peak inspiratory pressures and positive end-expiratory pressure but no other category. The tidal volumes in cc/kg predicted body weight were approximately 8.7 in both groups. Peak inspiratory pressures were found to be 27.87 cm H_2O on average in the non-ALI group and 29.2 in the ALI group.

Conclusion: Similar ventilation strategies are used between patients with ALI and those without ALI. These findings suggest that anesthesiologists are not using lung protective ventilation strategies when ventilating patients with low Pa_{CO_2}/F_{IO_2} ratios and ALI, and instead are treating hypoxia and ALI with higher concentrations of oxygen and peak pressures.

What We Already Know about This Topic

- Anesthesiologists typically increase F_{IO_2} and positive end-expiratory pressure intraoperatively when patients become hypoxemic during anesthesia.

What This Article Tells Us That Is New:

- For patients with a preoperative diagnosis of acute lung injury anesthesiologists still increased F_{IO_2}, tolerated higher peak inspiratory pressures, and used lower positive end-expiratory pressure than guidelines recommend intraoperatively. Anesthesiologists do not appear to use low tidal volume ventilation intraoperatively.

RELATIVE hypoxia and decreasing Pa_{O_2}/F_{IO_2} (P/F) ratios are common conditions during general anesthesia.[1] Because atelectasis is a common reason for relative hypoxemia in the surgical setting, tidal volumes of 10–12 ml/kg have been traditionally advocated.[2] Acute lung injury (ALI) is a clinical syndrome that is defined as the rapid onset of hypoxia with a P/F ratio ≤ 300 and bilateral pulmonary infiltrates in the absence of left atrial hypertension.[3] The overall in-hospital 90-day mortality of patients with ALI is more than 30%.[4] There are data suggesting ventilation strategies may influence the postoperative incidence of ALI after pneumonectomy, but to date, the incidence of ALI in hypoxic patients undergoing surgical anesthesia has not been described.[5–7] Intensive care unit (ICU) ventilator management of patients with ALI involves minimizing ventilator-associated lung injury by using lower tidal volumes (V_T) of 6 ml/kg predicted body weight (PBW) and limiting plateau pressures to less than 30 cm H_2O combined with moderate positive end-expiratory pressure (PEEP) in a lung protective ventilation strategy (LPVS).[8–9] In addition, aggressive PEEP

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and recruitment maneuvers have been successfully used to improve oxygenation while reducing potential oxygen toxicity and alveolar shear stress, although they have not been found to provide mortality benefit.[10–11]

In our previous work, we demonstrated that patients with a low intraoperative P/F ratio were typically managed using increased FIO_2 and peak airway pressures.[12] However, this study did not take into account the preoperative hypoxic status of the patient, the etiology of the low P/F ratio, the incidence of ALI in the population with a low intraoperative P/F ratio, or the mortality of the population. Therefore, we sought to determine the incidence of preexisting ALI in patients undergoing surgery and examine the intraoperative management of preoperatively hypoxemic patients using a separate database of patients with known ALI. Furthermore, we sought to determine if the management of patients with a low P/F ratio because of ALI was fundamentally different from those who had a low P/F ratio because of some other etiology and to examine the mortality rates between these two groups. Using a large, multiyear set of automatically collected intraoperative data, we examined preoperative arterial blood gas (ABG) values along with the intraoperative V_T, PEEP, FIO_2, and peak inspiratory pressures (PIP) that were used in the surgical setting. Specifically, we explored if there were differences in mechanical ventilation strategies in patients with known ALI compared with those of patients with hypoxia from other causes. We hypothesized that anesthesia providers would not routinely implement LPVS in hypoxemic patients or in patients with known ALI.

Materials and Methods

Institutional Review Board approval was obtained for this cohort study at The University of Michigan Medical Center in Ann Arbor, a large, tertiary care facility. All adult operations performed between January 1, 2005 and July 1, 2009 with at least one ABG value in the 24 h before proceeding to the operating room (OR) were examined. In the event multiple ABG values were obtained, the average values of all validated blood gases were used to generate an average P/F ratio. Patients with average P/F ratios less than 300 were included in the study.

Preoperative data were collected from routine clinical documentation that was entered into the institutional anesthesia information system (Centricity, General Electric Healthcare, Waukesha, WI). The record includes a structured preoperative history and physical examination allowing for coded entry and free text where required. Data obtained from the preoperative history included age, sex, American Society of Anesthesiologists classification, and height. From the height variable, PBW was calculated using the formula 50 + 2.3 (height [in] – 60) for men and 45.5 + 2.3 (height [in] – 60) for women.

The values for the intraoperative blood gases examined were manually entered by the anesthetic team into the structured electronic anesthesia information system (Centricity, General Electric Healthcare). Preoperative ABGs were obtained from an automated laboratory interface that connected to the anesthesia information system. Intraoperative physiologic and ventilator data were acquired using an automated, validated electronic interface from the anesthesia machine (Aisys, General Electric Healthcare) and physiologic monitors (Solar 9500; General Electric Healthcare). FIO_2, PIP, V_T, PEEP, oxyhemoglobin saturation (SpO_2), and end-tidal carbon dioxide ($EtCO_2$) values from the time of incision to the end of anesthesia were obtained and analyzed for median values to eliminate spurious and isolated values. Preoperative ABG values were excluded if $0.21 > FIO_2 > 1.00$. From the recorded intraoperative PaO_2 values and median FIO_2 the P/F ratio was calculated for each blood gas value. The cc/kg PBW was calculated from the median V_T and the PBW. The values for intraoperative PaO_2, $PaCO_2$, and pH were analyzed if available. Values with 45 mmHg $> PaO_2 >$ 600 mmHg, 20 mmHg $> PaCO_2 >$ 110 mmHg, $6.79 > pH > 7.99$, $0.21 > FIO_2 > 1.00$ or associated with a median 20 mmHg $> EtCO_2 >$ 110 mmHg, P/F ratio > 600 were excluded because of the high probability of venous origin of the blood sample or erroneous data entry. Blood gases with abnormal characters were also removed from the dataset. Cases with patients younger than 18 yr, a documented height of less than 55 inches, or a documented height greater than 80 inches were also excluded. Case times were validated as having started and ended by electronically documented heart rate from electrocardiogram or electronically documented start, incision, and end times in the event electrocardiogram data were not available. Cases with negative or undocumented times were excluded. Cases from patients graded as American Society of Anesthesiologists classification 6 were also excluded because the ventilation strategy implemented may have been designed to favor perfusion to other organs.

To identify the subpopulation of hypoxemic patients who actually had ALI compared with those with other causes for hypoxia, patients in this dataset were merged with a dedicated preexisting research dataset of all patients on ventilators at the University of Michigan Medical Center who were screened for entry into ALI studies. In this research dataset, it was ultimately determined if a patient had ALI by analyzing the patient's ventilator status, ABG, chest x-ray, and clinical documentation. Patients were included in this dataset if they were on a ventilator, had bilateral infiltrates on chest x-ray as determined by a clinician, had a P/F ratio ≤ 300, and had minimal evidence of fluid overload. If identical onset and OR dates were present for a patient, the chest x-ray, ABG, and anesthesia start time were analyzed by one of the authors to determine if the criteria for ALI were met before or after administration of anesthesia. Patients were assigned as either having or not having ALI before anesthesia was administered. Hence, only patients who were receiving mechanical ventilation before anesthesia were considered to possibly have ALI.

To determine the percentage of patients receiving mechanical ventilation and the associated settings before their anesthetic was administered, a respiratory therapy random check database was merged with the dataset. The ventilator settings from this dataset were obtained within the 24 h before the patient's procedural start time. Patients without any ventilator settings (V_T, PIP, plateau pressure, or PEEP), but with a recorded FIO_2 were considered to be spontaneously ventilated. Comparisons were made between the preoperative and intraoperative ventilator setting from this dataset.

This combined dataset was then merged with an institutional death registry. Patients were categorized as being alive or dead at 90 days. In order to avoid the effect of multiple surgeries and anesthetics on patient outcome, patients who had more than one surgical procedure were excluded from the dataset for univariate analysis for mortality at 90 days.

Statistical Analysis

Statistical analysis was performed using SPSS version 17 (SPSS Inc., Chicago, IL) and R version 2.12 (R Foundation for Statistical Computing, Vienna, Austria). Patients were divided into those with ALI and those without ALI. The mean value and SD for each group was calculated for cc/kg PBW, PIP, PEEP, FIO_2, PaO_2, $PaCO_2$, pH, age, and American Society of Anesthesiologists classification. The groups were compared using either an independent sample Student *t* test for parametric distributions or the Mann–Whitney U test for nonparametric distributions. Comparisons between preoperative and intraoperative ventilator settings were made using the paired Student *t*-test for parametric distributions, and the Wilcoxon signed-rank test for nonparametric distributions. Boolean analysis was completed using chi-square analysis. Statistically significant values were considered to have *P* values $\leq$0.05 using two-tailed tests. Univariate analysis was completed on predictors of mortality at 90 days.

Results

A total of 1,286 surgical cases with preoperative hypoxemia were identified and met inclusion criteria. Surgical cases that were excluded are shown in figure 1. Of the patients, 64% were male and the average age was 55.3 yr. Preoperative ventilation data were available on 730 cases (56.8%). Fifteen of the 730 cases (2.1%) were found not to be undergoing mechanical ventilation. Six of 155 cases in the ALI group were spontaneously ventilated at the time of the spot check, and 9 of 575 not in the ALI group were spontaneously ventilated at the time of the spot check. Table 1 shows the demographic, preoperative, and average preoperative arterial blood gas data obtained for the cases included in the analysis. In an effort to determine if there was a statistical difference between the groups of patients with preoperative ventilation data compared with those without these data, table 2 was generated. There were statistically different yet clinically insignificant values found for the weight, preoperative pH, and preoperative $PaCO_2$. This is validated by the fact that the body mass index and preoperative P/F ratios are statistically insignificant, and the pH values differ by 0.01.

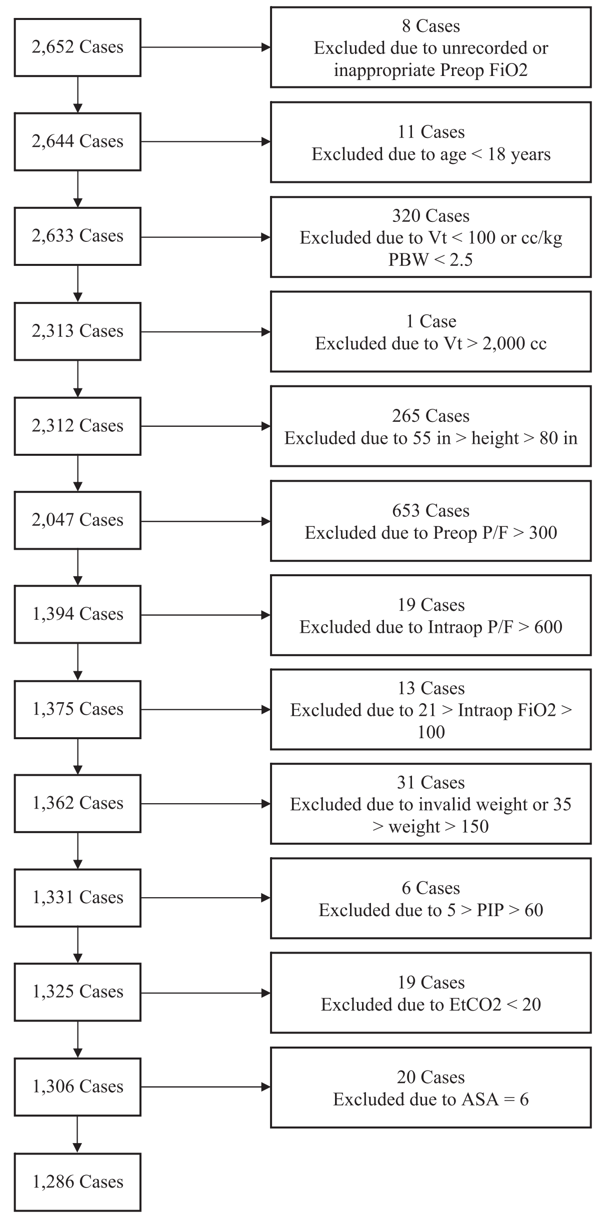

Fig. 1. Method of case exclusion: Intraoperative arterial blood gas (ABG) values with 40 mmHg > $PaCO_2$ > 600 mmHg, 20 mmHg > $PaCO_2$ > 110 mmHg, 6.99 > pH > 7.99, 0.21 > fraction inspired oxygen (FIO_2) > 1.00, associated with a median 20 mmHg > end-tidal (Et) CO_2 (carbon dioxide) > 110 mmHg, P/F ratio > 600, or a combined partial pressure of oxygen ($PaCO_2$) < 55 mmHg with a median SpO_2 value more than 93% were excluded. ASA = American Society of Anesthesiologists; $EtCO_2$ = end-tidal carbon dioxide; FIO_2 = fraction inspired oxygen; $PaCO_2$ = partial pressure of carbon dioxide; $PaCO_2$ = partial pressure of oxygen; PBW = predicted body weight; P/F = PaOC/FIO_2; PIP = peak inspiratory pressure; SpO_2 = Pulse Oximeter Oxygen Saturation; Vt = tidal volume.

Of the 1,286 cases meeting criteria, 242 (19%, 95% CI 16.7–21.0) were found to have preoperative ALI. Table 3 displays the average and SD of the ventilator parameters for each group of patients while in the OR. Boxplots were gen-

Table 1. Preoperative Demographics and ABG Values for Patients with and without ALI

	No ALI			ALI			
	N	Mean	SD	N	Mean	SD	*P* Value
Age	1,044	56.07	14.99	242	54.14	16.32	0.17
% Male	662	63.4	NA	157	64.9	NA	0.67
Weight (kg)	1,044	87.95	22.09	242	85.95	22.50	0.21
Height (in)	1,044	67.59	4.12	242	67.29	4.26	0.31
BMI	1,044	29.85	7.36	242	29.49	7.80	0.50
PBW	1,044	65.82	11.07	242	65.19	11.28	0.43
ASA status	1,042	3.70	.64	242	3.68	.59	0.76
Preop pH	1,044	7.42	.07	242	7.42	.06	0.04
Preop Pa_{O_2} (mmHg)	1,044	102.34	39.05	242	86.79	20.29	< 0.01
Preop Pa_{CO_2} (mmHg)	1,043	39.03	6.82	242	41.86	9.68	< 0.01
Preop F_{IO_2}	1,044	53.71	20.20	242	47.09	13.96	< 0.01
Preop P/F ratio	1,044	201.26	56.99	242	194.44	52.19	0.04
Preop Vt	559	555.92	115.99	144	535.53	131.25	0.07
Preop cc/kg PBW	559	8.45	1.64	144	8.25	1.97	0.20
Preop PIP	530	26.04	5.81	138	27.83	6.48	0.01
Preop Pplat	397	20.66	4.80	89	21.12	5.13	0.41
Preop PEEP	555	6.56	2.46	140	6.82	2.39	0.12
Preop F_{IO_2}	573	53.30	22.93	153	47.88	14.96	0.46

Demographic, preoperative ABG values, and preoperative ventilator settings for hypoxic patients before the start of anesthesia.

ABG = arterial blood gas; ALI = acute lung injury; ASA = American Society of Anesthesiologists; BMI = body mass index; F_{IO_2} = fraction of inspired oxygen; NA = not applicable; Pa_{CO_2} = partial pressure of carbon dioxide; Pa_{O_2} = partial pressure of oxygen; PBW = predicted body weight; PEEP = positive end expiratory pressure; P/F = PaOC/F_{IO_2}; PIP = peak inspiratory pressure; Pplat = plateau pressure; Preop = preoperative; Vt = tidal volume.

erated displaying the average PIP, PEEP, F_{IO_2}, and V_T for patients with and without ALI (fig. 2). There was a statistically significant difference in the ventilatory parameters between the two groups with the cc/kg PBW, PEEP, and PIP administered; however, these differences were clinically insignificant.

In order to determine if patients were indeed being managed differently in the OR than in the ICU, we compared the preoperative and intraoperative ventilator settings. The results of this comparison are shown in table 4. There were statistically significant differences in the F_{IO_2}, PIP, VT, and PEEP administered. To examine only the patients with ALI, preoperative and intraoperative ventilator settings were compared with patients with a preoperative diagnosis of ALI. Differences were found in the F_{IO_2}, PIP, and PEEP applied. There were increased intraoperative tidal volumes in both total V_T and cc/kg PBW, but these did not meet statistical significance. The results of this analysis are shown in table 5. We then examined the preoperative management of patients who were receiving less than 7 ml/kg PBW preoperatively with known ALI. Thirty-four patients were identified with an average V_T of 5.92 ml/kg PBW preoperatively. Intraoperatively, these patients received 7.5 ml/kg PBW ($P = 0.002$) with increased PIP (25.52 cm H_2O *versus* 28.7 cm H_2O, $P = 0.026$).

Table 2. Preoperative Demographics and ABG Values for Patients with and without Preoperative Ventilation Data

	Without Data			With Data			
	N	Mean	SD	N	Mean	SD	*P* Value
Age	556	56.49	15.36	730	55.11	15.16	0.11
% Male	344	0.62	NA	475	0.65	NA	0.24
Weight	556	86	22.5	730	88.77	21.86	0.03
Weight in	556	67.33	4.09	730	67.69	4.19	0.13
BMI	556	29.38	7.46	730	30.08	7.43	0.09
PBW	556	65.15	11.01	730	66.11	11.17	0.12
ASA	555	3.7	0.64	729	3.69	0.62	0.77
Preop pH	556	7.41	0.07	730	7.42	0.06	< 0.01
Preop Pa_{CO_2}	555	39.78	7.28	730	39.4	7.7	0.37
Preop P/F	556	199.13	56.52	730	200.62	55.92	0.64

Preoperative demographics and ABG values for patients with and without preoperative ventilation data. As shown, there is minimal difference between groups.

ABG = arterial blood gas; ASA = American Society of Anesthesiologists; BMI = body mass index; Pa_{CO_2} = partial pressure of carbon dioxide; Pa_{O_2} = partial pressure of oxygen; PBW = predicted body weight; P/F = Pa_{O_2}/F_{IO_2}; Preop = preoperative.

Table 3. Intraoperative Parameters for Patients with and without ALI

	No ALI			ALI			
	N	Mean	SD	N	Mean	SD	*P* Value
Average pH	723	7.39	.08	87	7.38	.07	0.38
Average Pa_{O_2}	718	183.22	93.49	86	151.40	66.73	0.01
Average Pa_{CO_2}	720	41.94	7.92	87	43.07	7.02	0.20
Median FI_{O_2}	1,033	81.76	19.95	236	80.78	19.27	0.36
Average P/F	711	227.67	111.73	85	198.68	104.86	0.02
cc/kg PBW	1,044	8.69	2.02	242	8.67	2.19	0.89
Median PEEP	1,044	4.70	3.51	242	5.45	3.65	0.01
Median PIP	1,044	27.87	6.12	242	29.81	6.17	< 0.01
Median V_T	1,044	562.46	121.28	242	557.07	140.21	0.55
Median ET_{CO_2}	1,039	33.94	5.24	238	35.67	6.18	< 0.01
Case duration (min)	1,044	185.25	147.98	242	111.28	77.56	< 0.01

Intraoperative ABG and ventilatory parameters for hypoxic patients.

ABG = arterial blood gas; ALI = acute lung injury; $EtCO_2$ = end tidal carbon dioxide; FI_{O_2} = fraction inspired oxygen; Pa_{CO_2} = partial pressure of carbon dioxide; Pa_{O_2} = partial pressure of oxygen; PBW = predicted body weight; PEEP = positive end expiratory pressure; P/F = Pa_{O_2}/FI_{O_2}; PIP = peak inspiratory pressure; V_T = tidal volume.

Univariate analysis was then completed on the predictors of 90-day mortality on the reduced dataset that consisted of patients who underwent only one surgery. A total of 791 patients were included in this dataset, of whom 17% had a diagnosis of ALI before anesthetic was administered. The overall 90-day mortality for the population was 21%, and the ALI group mortality was 32% compared to 19% for the non-ALI population. Results of the univariate analysis are shown in table 4. Of note, significant predictors for mortality preoperatively included pH and P/F ratio, body mass index, American Society of Anesthesiologists status, and age. Intraoperative ventilatory predictors of mortality included PEEP and PIP.

Discussion

We have previously demonstrated that patients who became hypoxic intraoperatively were typically managed using increased FI_{O_2} and increased PIP, and had a marginal increase in the amount of PEEP delivered from 2.86 cm H_2O to 5.48 cm H_2O.[12] In the most severely hypoxic patient population, this was accompanied by a clinically trivial yet statistically significant reduction in V_T on average from 9.05 to 8.64 ml/hg PBW. However, this previous study did not take into account the preoperative P/F ratio of patients or the preexisting incidence of ALI.

In this new series, approximately 20% of patients presenting to the OR with a preexisting P/F ratio ≤ 300 were identified as meeting criteria for a diagnosis of ALI. From the data collected, it appears the typical management of a preexisting hypoxic patient by the anesthesiologists is to use increased FI_{O_2}, tolerate high PIP, and use lower amounts of PEEP than are prescribed by the ARDSnet (ARMA and ALVEOLI) trials regardless of the etiology of the hypoxia. The average Vt observed was 8.7 (2) cc/kg PBW with an average PEEP of approximately 5 cm H_2O. It did appear that anesthesiologists limited PIP to less than 30 cm H_2O on average. The Vt delivered in the OR was very much in line with the Vt provided in the ICU before the patient's procedure. These data suggest that most anesthesiologists do not implement strict ARDSnet LPVS when hypoxic patients come to the OR regardless if they have ALI or some other cause of hypoxia, and they tend to use preexisting ventilator settings that are similar to those found in the ICU. However, when looking at a subset receiving ≤ 76 ml/kg PBW tidal volumes preoperatively with known ALI, the volumes were increased intraoperatively. This finding is of interest because there is considerable evidence suggesting ALI outcomes are improved if patients are managed using LPVS while in the ICU.[9,13] Further investigation is required to determine whether this practice is more common in other medical centers, as well as whether the evidence for improved ALI outcomes from LPVS from the ICU generalizes to mechanical ventilation practices in the operating room.

In the ARDSnet ARMA trial, 861 patients were randomized to receive ventilation with either 6 ml/kg PBW or 12 ml/kg PBW of ventilation when a diagnosis of ALI was made. Overall the actual mortality difference was 9% in favor of the lower tidal volume group, despite the fact that oxygenation was better in the higher tidal volume group. In the ALVEOLI trial, patients with ALI received 6 ml/kg PBW ventilation with either an aggressive PEEP, "open lung" strategy or the conventional PEEP dictated by ARMA. This study did not show a mortality benefit, but it did show slightly reduced ventilator days. These two well-conducted studies provide evidence that increased oxygenation does not lead to reduced mortality in the ALI population. However, from our study, it appears anesthesiologists are favoring increased oxygenation over a proven modality in the treatment of ALI. This is shown by the increased intraoperative Pa_{O_2} compared with the preoperative Pa_{O_2}.

There has been a concern in the anesthesia community about the potential downsides of using LPVS in the operat-

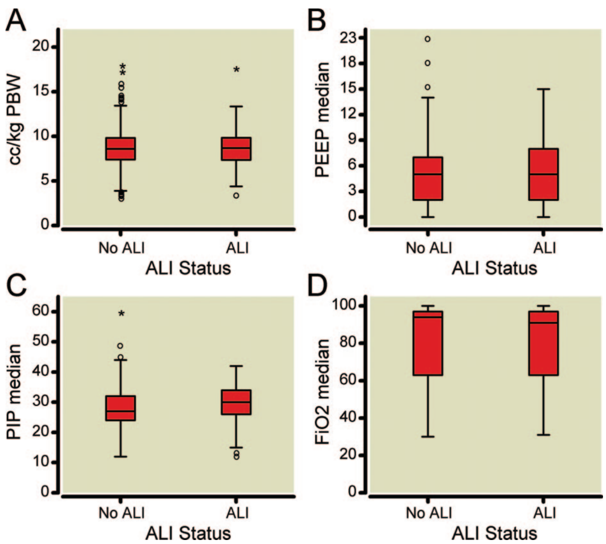

Fig. 2. (*A–D*) Distribution of ventilator settings by ALI status. (*A*) cc of ventilation per kg PBW by ALI status. *Solid lines* represent median values, *boxes* represent the interquartile range, *T bars* represent 95% of total sample, ○ represent outliers (1.5–3 X box length), * represent extreme outliers (more than 3 X box length). (*B*) Median positive end-expiratory pressure (PEEP) by ALI status. *Solid lines* represent median values, *boxes* represent the interquartile range, *T bars* represent 95% of total sample, ○ represent outliers (1.5–3 X box length), * represent extreme outliers (more than 3 X box length). (*C*) Median PIP by ALI status. *Solid lines* represent median values, *boxes* represent the interquartile range, *T bars* represent 95% of total sample, ○ represent outliers (1.5–3 X box length), * represent extreme outliers (more than three times box length). (*D*) Median F_{IO_2} by ALI status. *Solid lines* represent median values, *boxes* represent the interquartile range, *T bars* represent 95% of total sample, ○ represent outliers (1.5–3 X box length), * represents extreme outliers (more than 3 X box length). ALI = acute lung injury; F_{IO_2} = fraction inspired oxygen; PBW = predicted body weight; PEEP = positive end expiratory pressure; PIP = peak inspiratory pressure.

ing room because these ventilator settings potentially result in increased atelectasis and hence decreased oxygenation. It has been demonstrated that LPVS does not result in increased atelectasis when used in patients undergoing general anesthesia. Cai *et al.* performed computed tomography scans on healthy volunteer patients before induction, after induction, and after mechanical ventilation with patients treated with either low V_T ventilation or normal V_T.[2] In this study there was no difference in the amount of atelectatic lung, regardless of the V_T provided, based on computed tomography.

There may be some concerns by anesthesiologists that LPVS would be harmful because of potentially increased cytokines from increased PEEP and potential hypercapnia in patients who do not have ALI. It has been shown that LPVS does not increase biologic markers of lung injury in normal lung. Wrigge *et al.* have shown that LPVS or a high Vt/low PEEP strategy showed equivalent or minimal elevation in the amounts of pulmonary and systemic levels of inflammatory markers after thoracic, intraabdominal, or cardiac surgery in patients with a normal lung.[14–15] These data may support the decision of providers to avoid using LPVS in routine patients because it is equivocal and better oxygenation may be provided using non-LPVS ventilator settings. However, in patients with previously injured lung, there appeared to be an association with increased plasma cytokines after high Vt mechanical ventilation.[16] As the incidence or development of ALI in a particular patient may not be known before an OR course, it would seem reasonable for the anesthesiologist to consider the use of LPVS in the hypoxic patient if it was believed that there was a high likelihood of the patient having or developing ALI.

Some may contend that the short duration of high pressure/high volume ventilation endured during a surgery will not lead to worse outcome in the overall care of a critically ill patient. Licker *et al.* described the intraoperative management and postoperative incidence of ALI in a cohort of 879 patients undergoing lung resection for cancer and found that postoperative ALI was diagnosed in 37 patients (4.2%) and

Table 4. Preoperative and Intraoperative Ventilator Settings for All Patients

		Preoperative		Intraoperative		
	N	Mean	SD	Mean	SD	*P* Value
F_{IO_2}	719	52.13	21.56	81.61	20.14	< .001
PIP	668	26.41	5.99	28.18	6.16	< .001
V_t	703	551.74	119.46	564.06	124.66	.009
cc/kg PBW	703	8.41	1.71	8.64	1.99	.002
PEEP	695	6.61	2.45	5.20	3.71	< .001

A comparison of preoperative and intraoperative ventilator settings for all patients using the paired Student *t* test or Wilcoxon signed-rank test.

F_{IO_2} = fraction inspired oxygen; PBW = predicted body weight; PEEP = positive end expiratory pressure; PIP = peak inspiratory pressure; V_T = tidal volume.

Table 5. Preoperative and Intraoperative Ventilator Settings for Patients with Preoperative ALI

		Preoperative		Intraoperative		
	N	Mean	SD	Mean	SD	*P* Value
F_{IO_2}	149	47.99	15.06	82.38	18.63	<.001
PIP	138	27.83	6.47	30.17	6.19	<.001
V_T	144	535.53	131.25	556.31	146.28	.092
cc/kg PBW	144	8.25	1.97	8.58	2.18	.098
PEEP	140	6.82	2.39	5.86	3.72	< .001

A comparison of preoperative and intraoperative ventilator settings for ALI patients using the paired Student *t* test or Wilcoxon signed-rank test.

ALI = acute lung injury; F_{IO_2} = fraction of inspired oxygen; PBW = predicted body weight; PEEP = positive end expiratory pressure; PIP = peak inspiratory pressure; V_T = tidal volume.

acute respiratory distress syndrome in 17 patients (1.5%).[5] After multivariate analysis, it was concluded that the ventilatory hyperpressure index was an independent predictor of development of ALI with an odds ratio of 3.2. Fernandez-Perez *et al.* described the occurrence of ALI after elective surgery as 1.8%.[17] In the multivariate analysis, increased PIP was a significant predictor of postoperative ALI with an odd ratio of 1.07. These data suggest that short intervals of high pressure do indeed have a small but demonstrable correlation with the development of ALI. In our data, we found the PIP to be associated with increased mortality. This finding may be simply a marker of increased illness, or it may be indicative of active injury to the lung. The current data do not provide an answer to this question.

This study has several limitations. First, the data were collected as part of the clinical care delivered and from a research study screening database. As a result, the data reflects the electronic anesthetic record, and no additional detail is available. There were no rigorous processes to validate the entry of data, although the use of automated collection of physiologic data has been accepted in many previous studies.[18–20] However, this methodology is devoid of the Hawthorne effect and provides insight into the actual modalities that are used by anesthesiologists for patients with preexisting low P/F ratios. Second, the data are from a single tertiary care center and may not serve as a representative sample of patients throughout the world. Next, because of the data resources available, some patients who were not ventilated preoperatively may indeed have ALI. Hence, it is possible there were patients in the non-ALI group who should have been included in the ALI registry and the incidence may indeed be even higher than what we identified. To address this concern, we attempted to examine a defined set of patients of which their preoperative ventilatory status was known from our respiratory therapy database. However, data were not available on all patients and it is possible that this population was different from the entire population studied. To determine if there was a difference between groups with and without preoperative ventilation data, we conducted five rounds of multiple imputations on missing values, understanding there are limitations on the utility of imputing values that are determined by clinicians. The results showed new statistically significant differences in preoperative absolute Vt, plateau pressure, FiO2, and intraoperative Pa_{CO_2} because of increased power. However, these imputed values were not substantially changed from the actual values reported in table 1, and there was no statistical difference in the Vt in cc/Kg PBW or P/F ratio, suggesting that the patients with complete data reasonably represent the preoperative ventilation and comorbidities of all patients. Next, our dataset focused on PIP rather than plateau pressures. Although these values differ in their nature, from the data presented, the trend is consistent in that increasing PIP correlated with increasing plateau pressures. Finally, there is the possibility of type-1 error in the analysis because we conducted more than 50 inferences with a significant P value <0.05. We realize that we have a small sample size and the number of inferences performed may in fact lead to the possibility that some inferences will be significant.

In conclusion, the incidence of ALI in patients undergoing anesthesia with preoperative P/F ratios $\leq$ 300 in our institution is approximately 20%. These patients are managed in a similar format that does not use LPVS regardless of the etiology of their hypoxia, and the Vt settings appear to mirror the ventilator settings provided to patients in the ICU. Overall, it appears risk factors for mortality at 90 days include increased PIP and preexisting ALI. Further study is required to determine if the use of LPVS intraoperatively has a substantive impact in reducing mortality of hypoxic patients who undergo surgery both with and without ALI.

References

1. Strachan L, Noble DW: Hypoxia and surgical patients–prevention and treatment of an unnecessary cause of morbidity and mortality. J R Coll Surg Edinb 2001; 46:297–302
2. Cai H, Gong H, Zhang L, Wang Y, Tian Y: Effect of low tidal volume ventilation on atelectasis in patients during general anesthesia: A computed tomographic scan. J Clin Anesth 2007; 19:125–9
3. Bernard GR, Artigas A, Brigham KL, Carlet J, Falke K, Hudson L, Lamy M, Legall JR, Morris A, Spragg R: The American-European Consensus Conference on ARDS. Definitions, mechanisms, relevant outcomes, and clinical trial coordination. Am J Respir Crit Care Med 1994; 149:818–24
4. Phua J, Badia JR, Adhikari NK, Friedrich JO, Fowler RA, Singh JM, Scales DC, Stather DR, Li A, Jones A, Gattas DJ, Hallett D, Tomlinson G, Stewart TE, Ferguson ND: Has mortality from acute respiratory distress syndrome decreased over time?: A systematic review. Am J Respir Crit Care Med 2009; 179:220–7
5. Licker M, de Perrot M, Spiliopoulos A, Robert J, Diaper J, Chevalley C, Tschopp JM: Risk factors for acute lung injury after thoracic surgery for lung cancer. Anesth Analg 2003; 97:1558–65
6. Jeon K, Yoon JW, Suh GY, Kim J, Kim K, Yang M, Kim H, Kwon OJ, Shim YM: Risk factors for post-pneumonectomy acute lung injury/acute respiratory distress syndrome in primary lung cancer patients. Anaesth Intensive Care 2009; 37:14–9
7. Dulu A, Pastores SM, Park B, Riedel E, Rusch V, Halpern NA: Prevalence and mortality of acute lung injury and ARDS after lung resection. Chest 2006; 130:73–8
8. Dos Santos CC: Advances in mechanisms of repair and remodelling in acute lung injury. Intensive Care Med 2008; 34:619–30
9. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. The Acute Respiratory Distress Syndrome Network. N Engl J Med 2000; 342:1301–8
10. Gattinoni L, Vagginelli F, Chiumello D, Taccone P, Carlesso E: Physiologic rationale for ventilator setting in acute lung injury/acute respiratory distress syndrome patients. Crit Care Med 2003; 31:S300–4
11. Mercat A, Richard JC, Vielle B, Jaber S, Osman D, Diehl JL, Lefrant JY, Prat G, Richecoeur J, Nieszkowska A, Gervais C, Baudot J, Bouadma L, Brochard L, Expiratory Pressure (Express) Study Group: Positive end-expiratory pressure setting in adults with acute lung injury and acute respiratory distress syndrome: A randomized controlled trial. JAMA 2008; 299:646–55

12. Blum JM, Fetterman DM, Park PK, Morris M, Rosenberg AL: A description of intraoperative ventilator management and ventilation strategies in hypoxic patients. Anesth Analg 2010; 110:1616–22
13. Brower RG, Lanken PN, MacIntyre N, Matthay MA, Morris A, Ancukiewicz M, Schoenfeld D, Thompson BT, National Heart, Lung, and Blood Institute ARDS Clinical Trials Network: Higher *versus* lower positive end-expiratory pressures in patients with the acute respiratory distress syndrome. N Engl J Med 2004; 351:327–36
14. Wrigge H, Uhlig U, Zinserling J, Behrends-Callsen E, Ottersbach G, Fischer M, Uhlig S, Putensen C: The effects of different ventilatory settings on pulmonary and systemic inflammatory responses during major surgery. Anesth Analg 2004; 98:775–81
15. Wrigge H, Uhlig U, Baumgarten G, Menzenbach J, Zinserling J, Ernst M, Drömann D, Welz A, Uhlig S, Putensen C: Mechanical ventilation strategies and inflammatory responses to cardiac surgery: A prospective randomized clinical trial. Intensive Care Med 2005; 31:1379–87
16. Wrigge H, Zinserling J, Stüber F, von Spiegel T, Hering R, Wetegrove S, Hoeft A, Putensen C: Effects of mechanical ventilation on release of cytokines into systemic circulation in patients with normal pulmonary function. ANESTHESIOLOGY 2000; 93:1413–7
17. Fernández-Perez ER, Sprung J, Afessa B, Warner DO, Vachon CM, Schroeder DR, Brown DR, Hubmayr RD, Gajic O: Intraoperative ventilator settings and acute lung injury after elective surgery: A nested case control study. Thorax 2009; 64:121–7
18. Nafiu OO, Kheterpal S, Morris M, Reynolds PI, Malviya S, Tremper KK: Incidence and risk factors for preincision hypotension in a noncardiac pediatric surgical population. Paediatr Anaesth 2009; 19:232–9
19. Kheterpal S, O'Reilly M, Englesbe MJ, Rosenberg AL, Shanks AM, Zhang L, Rothman ED, Campbell DA, Tremper KK: Preoperative and intraoperative predictors of cardiac adverse events after general, vascular, and urological surgery. ANESTHESIOLOGY 2009; 110:58–66
20. Kheterpal S, Tremper KK, Englesbe MJ, O'Reilly M, Shanks AM, Fetterman DM, Rosenberg AL, Swartz RD: Predictors of postoperative acute renal failure after noncardiac surgery in patients with previously normal renal function. ANESTHESIOLOGY 2007; 107:892–902