ANESTHESIOLOGY

Driving Pressure during Thoracic Surgery

A Randomized Clinical Trial

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ABSTRACT

Background: Recently, several retrospective studies have suggested that pulmonary complication is related with driving pressure more than any other ventilatory parameter. Thus, the authors compared driving pressure–guided ventilation with conventional protective ventilation in thoracic surgery, where lung protection is of the utmost importance. The authors hypothesized that driving pressure–guided ventilation decreases postoperative pulmonary complications more than conventional protective ventilation.

Methods: In this double-blind, randomized, controlled study, 292 patients scheduled for elective thoracic surgery were included in the analysis. The protective ventilation group (n = 147) received conventional protective ventilation during one-lung ventilation: tidal volume 6 ml/kg of ideal body weight, positive end-expiratory pressure (PEEP) 5 cm H_2O, and recruitment maneuver. The driving pressure group (n = 145) received the same tidal volume and recruitment, but with individualized PEEP which produces the lowest driving pressure (plateau pressure–PEEP) during one-lung ventilation. The primary outcome was postoperative pulmonary complications based on the Melbourne Group Scale (at least 4) until postoperative day 3.

Results: Melbourne Group Scale of at least 4 occurred in 8 of 145 patients (5.5%) in the driving pressure group, as compared with 18 of 147 (12.2%) in the protective ventilation group ($P = 0.047$, odds ratio 0.42; 95% CI, 0.18 to 0.99). The number of patients who developed pneumonia or acute respiratory distress syndrome was less in the driving pressure group than in the protective ventilation group (10/145 [6.9%] *vs.* 22/147 [15.0%], $P = 0.028$, odds ratio 0.42; 95% CI, 0.19 to 0.92).

Conclusions: Application of driving pressure–guided ventilation during one-lung ventilation was associated with a lower incidence of postoperative pulmonary complications compared with conventional protective ventilation in thoracic surgery.

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EDITOR'S PERSPECTIVE

What We Already Know about This Topic

- Driving pressure (plateau minus end-expiratory airway pressure) is a target in patients with acute respiratory distress syndrome, and is proposed as a target during general anesthesia for patients with normal lungs. It has not been reported for thoracic anesthesia where isolated, inflated lungs may be especially at risk.

What This Article Tells Us That Is New

- In a double-blinded, randomized trial (292 patients), minimized driving pressure compared with standard protective ventilation was associated with less postoperative pneumonia or acute respiratory distress syndrome.

One-lung ventilation during thoracic surgery is prone to volutrauma, barotrauma, atelectrauma, and oxygen toxicity, which are the important aspects of ventilator-induced lung injury.[1–3] Direct surgical injury and one-lung ventilation are also associated with a profound inflammatory cytokine release because of abundant immune cells on the lung endothelium and alveolus.[4] Excessive neutrophils recruited in response to the proinflammatory cytokines increase pulmonary vascular permeability in both dependent and nondependent lungs.[5] These reactions often precede systemic inflammatory response syndrome, acute respiratory distress syndrome (ARDS), pneumonia, or catabolic pathway, which slows the recovery of the patient.[6–8] Therefore, lung protection is of utmost importance, and protective ventilation is strongly recommended during thoracic surgery.[9,10]

Protective ventilation—that is, using low tidal volume (V_T), positive end-expiratory pressure (PEEP) with the recruitment maneuver, and limiting inspiratory pressure[1,2,11]—has been applied in thoracic surgery by using V_T 5 to 6 ml/kg of ideal body weight and PEEP 5 cm H_2O with the recruitment maneuver at 20 cm H_2O for 15 to 20 s during one-lung ventilation.[9,10,12–14] However, a high incidence of postoperative pulmonary complications is still being observed even with a protective ventilatory strategy,[3,13,15–17] and mild postoperative pulmonary complications such as atelectasis, pleural effusion, or even the need for prolonged oxygen therapy are related to increased poor outcomes.[15]

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Recently, an interesting meta-analysis on ARDS patients was published, which may change our ventilation strategy.[18] This study introduced a concept of driving pressure and insisted that high driving pressure was most strongly associated with worse survival. V_T and PEEP were not related to patient outcomes, or only related when they influenced the driving pressure.[18] Driving pressure is defined as V_T divided by respiratory system compliance and can be easily calculated as plateau pressure minus PEEP.[18] Thus, we considered that driving pressure–guided ventilation might be another technique to reduce postoperative pulmonary complications and improve recovery in thoracic surgery patients.

Previous studies on driving pressure are rare and mostly retrospective studies that report risk-predictive value of driving pressure.[18–20] Thus, prospective, randomized trials to assess the independent role of driving pressure in clinical outcomes have been requested.[21]

Therefore, we conducted a large-scale, randomized, controlled trial in thoracic surgery and compared clinical outcomes between conventional protective ventilation and driving pressure–guided ventilation. Our primary endpoint was postoperative pulmonary complications based on the Melbourne Group Scale until postoperative day 3. The Melbourne Group Scale is widely used for the diagnosis of postoperative pulmonary complications and outperformed other scales in terms of postoperative pulmonary complication recognition after thoracotomy.[22] We hypothesized that driving pressure–guided ventilation during one-lung ventilation decreases postoperative pulmonary complications compared with conventional protective ventilation in thoracic surgery.

Materials and Methods

Study Population

This prospective, randomized, double-blind, parallel groups study was approved by our Institutional Review Board (SMC 2016-05-107) and registered with Clinicaltrials.gov (NCT02851238, Principal Investigator: Hyun Joo Ahn, Date of Registration and last update: August 11, 2016 and October 8, 2018; The registration was corrected to reflect the blinding destination: https://clinicaltrials.gov/ct2/show/NCT02851238). Written informed consent was obtained from all of the participants. The study was performed from August 2016 to August 2017 at the Samsung Medical Center (Seoul, Korea). A total of 322 patients undergoing elective pulmonary resection or esophagectomy were assessed for eligibility, and 312 patients were enrolled by study staff. The inclusion criteria were age of at least 19 yr, and undergoing one-lung ventilation for thoracic surgery. The exclusion criteria were the American Society of Anesthesiologists (ASA) Physical Status of at least IV, patients who are contraindicated with application of PEEP (high intracranial pressure, bronchopleural fistula, hypovolemic shock, right ventricular failure), and patients who refused being enrolled in the study. Drop-out criteria were change of surgery to the simple wedge resection, interruption of study protocol, bleeding (greater than 500 ml), or severe hypotension (mean blood pressure less than 55 mm Hg with vasopressor/inotrope) during the operation.

Blinding Methods

Randomization was done by computer-generated random numbers with a fixed block size of 4 and a 1:1 ratio, and the allocation was sealed in an opaque envelope. An attending anesthesiologist who was not involved in the study opened the sealed envelope just before anesthesia and provided the designated ventilator setting according to the group assignment. The group designation was blinded during the data collection and analysis. The corresponding author and coauthors collected data on blood gas, ventilatory parameters, and postoperative complications by retrieving blinded study logs; attending anesthesiologists who were not involved in the study recorded the blood gas results and ventilator parameters. The Melbourne Group Scale and lung complications were checked by intensive care unit physicians and hospitalists who were not involved in the study during daily routine assessment. A chest x-ray was taken every day in the morning and examined by the blinded physician.

Study Protocol of Each Ventilator Strategy

For the protective ventilation group, mechanical ventilation during one-lung ventilation was maintained with fraction of inspired oxygen (F_{IO_2}) 1.0, V_T 6 ml/kg of ideal body weight at PEEP 5 cm H_2O, and volume-controlled ventilation with an inspiratory pause of 30% and inspiration to expiration ratio of 1:2. The ventilation rate was adjusted in the range of 10 to 15 beats per minute to maintain end-tidal CO_2 between 35 to 40 mm Hg. For driving pressure–guided ventilation, patients received the same F_{IO_2} and V_T, but individualized lowest driving pressure was applied during one-lung ventilation. Driving pressure was calculated as plateau pressure minus PEEP. Trial for the lowest driving pressure was started at 5 min of one-lung ventilation by increasing PEEP from 2 to 10 cm H_2O incrementally. V_T and respiratory rate were fixed at 6 ml/kg and 12 beats per minute during PEEP trial. Each PEEP level (2, 3, 4, 5, 6, 7, 8, 9, 10 cm H_2O) was maintained for 10 respiratory cycles, and the driving pressure of the last cycle was recorded at each PEEP level. Then the PEEP level that produced the lowest driving pressure was chosen and maintained throughout one-lung ventilation. Trial for the lowest driving pressure was performed in the lateral position before incision and took 450 s. All patients received the same ventilation protocol before and after the study period, which was F_{IO_2} 0.5, V_T of 6–8 ml/kg ideal body weight with 5 mm Hg PEEP, and volume-controlled ventilation with an inspiratory pause of 30% and inspiration to expiration ratio of 1:2. Recruitment was performed

twice for both groups: at the commencement of one-lung ventilation to the dependent lung by squeezing the bag at 20 cm H_2O for 15 to 20 s[10] and at the restart of two-lung ventilation by squeezing the bag at 30 to 40 cm H_2O for 15 to 20 s. A ventilatory monitor (Primus Infinity Empowered, Dräger, Germany) continuously displayed peak inspiratory pressure, plateau pressures, and PEEP.

Anesthesia and Surgery

For induction of anesthesia, a propofol 1.5- to 2.5-mg/kg bolus with remifentanil continuous infusion was used. Intubation was performed using a double-lumen tube after a bolus injection of rocuronium 1.0 mg/kg, and the position of the tube was confirmed by fiberoptic bronchoscopy. A radial arterial catheter was placed for blood sampling and continuous hemodynamic monitoring. During surgery, anesthesia was maintained with sevoflurane, remifentanil, and rocuronium. Sevoflurane was titrated to maintain a bispectral index of 40 to 60 during surgery. The maintenance fluid was lactated Ringer's solution, infused at a rate of 3 to 5 $ml \cdot kg^{-1} \cdot h^{-1}$ Patients undergoing video-assisted thoracoscopic surgery received intravenous patient-controlled analgesia (IV-PCA). Open thoracotomy and esophagectomy patients received patient-controlled thoracic epidural analgesia or IV-PCA, which was decided by each surgeon's preference and the existence of contraindications for regional analgesia. A thoracic epidural catheter was placed between the T4 and T6 interspaces before surgery. The epidural solution was a mixture of ropivacaine (0.15%) plus hydromorphone (8 μg/ml) and infused at a basal rate of 5 ml/h with 3 ml of bolus and a 15-min lockout interval. The mean duration of epidural analgesia was 3 days. According to our postoperative protocol, the patients who receive lobectomy or more extensive lung resection stayed in the intensive care unit for 1 day and esophagectomy patients stayed in the intensive care unit for 2 days. Maintenance fluid was administered at a rate of 2 to 3 $ml \cdot kg^{-1} \cdot h^{-1}$ until postoperative day 1 and 0.5 to 1 $ml \cdot kg^{-1} \cdot h^{-1}$ on postoperative day 2 and 3. The patient was encouraged to ambulate from postoperative day 1 and received a daily physiotherapy program that included deep-breathing exercises, incentive spirometry, and chest physiotherapy by physiotherapists and attending nurses during the intensive care unit and ward stays.

Measurements

For the assessment of postoperative pulmonary complications, the Melbourne Group Scale was used (chest x-ray findings of atelectasis or consolidation; raised white cell count [greater than 11.2×10^6 /ml] or administration of respiratory antibiotics postoperatively, in addition to prophylactic antibiotics; temperature greater than 38°C; signs of infection on sputum microbiology; purulent sputum different from preoperative status; oxygen saturation less than 90% on room air; physician diagnosis of pneumonia; and prolonged intensive care unit stay [longer stay than 1 and 2 days for lung and esophagus surgery, respectively] or readmission to the intensive care unit).[17] Postoperative pulmonary complications were defined as positive when patients presented with four or more of the eight dichotomous factors.

ARDS was defined according to the Berlin definition: (1) acute onset over 1 week or less; (2) bilateral opacities consistent with pulmonary edema; (3) a ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen ($Pa_{O_2}/F_{I_{O_2}}$) less than 300 mm Hg with a minimum of 5 cm H_2O PEEP (or continuous positive airway pressure); (4) must not be fully explained by cardiac failure or fluid overload in the physician's best estimation using available information.

Data on postoperative pulmonary complications and extra-pulmonary complications were collected during the hospital stay. The primary outcome was the incidence of postoperative pulmonary complications defined by Melbourne Group Scale within postoperative day 3, assuming that postoperative pulmonary complications related to intraoperative ventilation techniques occur early.[23,24] Secondary outcomes were partial pressure of oxygen in arterial blood during surgery and extrapulmonary complications.

Statistical Analysis

In a previous study, the incidence of postoperative pulmonary complications by Melbourne Group Scale was 14%.[17] We expected a greater than 10% point decrease in postoperative pulmonary complications in driving pressure group, with 18% dropout or ineligibility. A total of 312 patients were required for a two-sided alpha of 5% and 80% power (Pearson chi-square test).

Categorical variables are reported as the number and percentage. Continuous variables are expressed as the mean ± SD, or median (interquartile). The normal distribution of data was evaluated with the Kolmogorov–Smirnov test or the Shapiro Wilk test. The primary outcome (pulmonary complications defined by Melbourne Group Scale) was evaluated with the chi-square test, and the secondary outcomes (partial pressure of oxygen in arterial blood and extrapulmonary complications) were evaluated using independent samples *t* test and the chi-square test, respectively. Demographic data, perioperative data, and clinical outcomes between the two groups were examined with the chi-square test or Fisher exact test for categorical variables and independent samples *t* test or Mann–Whitney *U* test for continuous variables. All of the analyses were performed using SAS version 9.4 (SAS Institute, Cary, North Carolina, USA) and SPSS (version 24, Chicago, Illinois, USA). Two-sided alpha of 0.05 was used for all of the statistical tests.

Results

Three hundred twenty two patients were assessed for eligibility, and 312 patients were entered into the study. Six

and seven patients in each protective ventilation and driving pressure group were dropped out because of change of surgery and interruption of study protocol. Finally, 147 and 145 patients in each protective ventilation and driving pressure group were analyzed (fig. 1).

There were no differences in demographic or operational data between groups (tables 1 and 2). For the primary endpoint, postoperative pulmonary complications based on Melbourne Group Scale of at least 4 occurred in 8 of 145 patients (5.5%) in the driving pressure group, as compared with 18 of 147 (12.2%) in the protective ventilation group within postoperative day 3 ($P = 0.047$, odds ratio, 0.42; 95% CI, 0.18 to 0.99). Overall incidence of postoperative pulmonary complications was 8.9% (26 of 292).

ARDS was less common in the driving pressure group than in the protective ventilation group (0 of 145 *vs.* 5 of 147, $P = 0.025$) within postoperative day 3. Pneumonia occurred in 10 of 145 (6.9%) and 17 of 147 (11.6%) in the driving pressure group and the protective ventilation group, respectively ($P = 0.157$) within postoperative day 3. The total number of patients who developed pneumonia or ARDS within postoperative day 3 was less in the driving pressure group than in protective ventilation group (10 of 145 [6.9%] *vs.* 22 of 147 [15.0%], $P = 0.028$; odds ratio, 0.42; 95% CI, 0.19 to 0.92; fig. 2). The number of patients whose pneumonia or ARDS continued until postoperative day 7 was 9 (6.2%) and 14 (9.5%) in the driving pressure group and the protective ventilation group, respectively ($P = 0.277$).

Figure 3 shows the distribution of driving pressure during one-lung ventilation. The driving pressure was different between the two groups (median [interquartile range]: 9 [8 to 10] cm H_2O *vs.* 10 [9 to 11] cm H_2O, driving pressure group *vs.* protective ventilation group, $P < 0.001$). In the driving pressure group, the median PEEP was 3 (interquartile range, 2 to 5) cm H_2O compared with 5 cm H_2O in the protective ventilation group ($P < 0.001$). The peak inspiratory pressure and plateau pressure were lower in the driving pressure group than in the protective ventilation group during one-lung ventilation. Laboratory findings

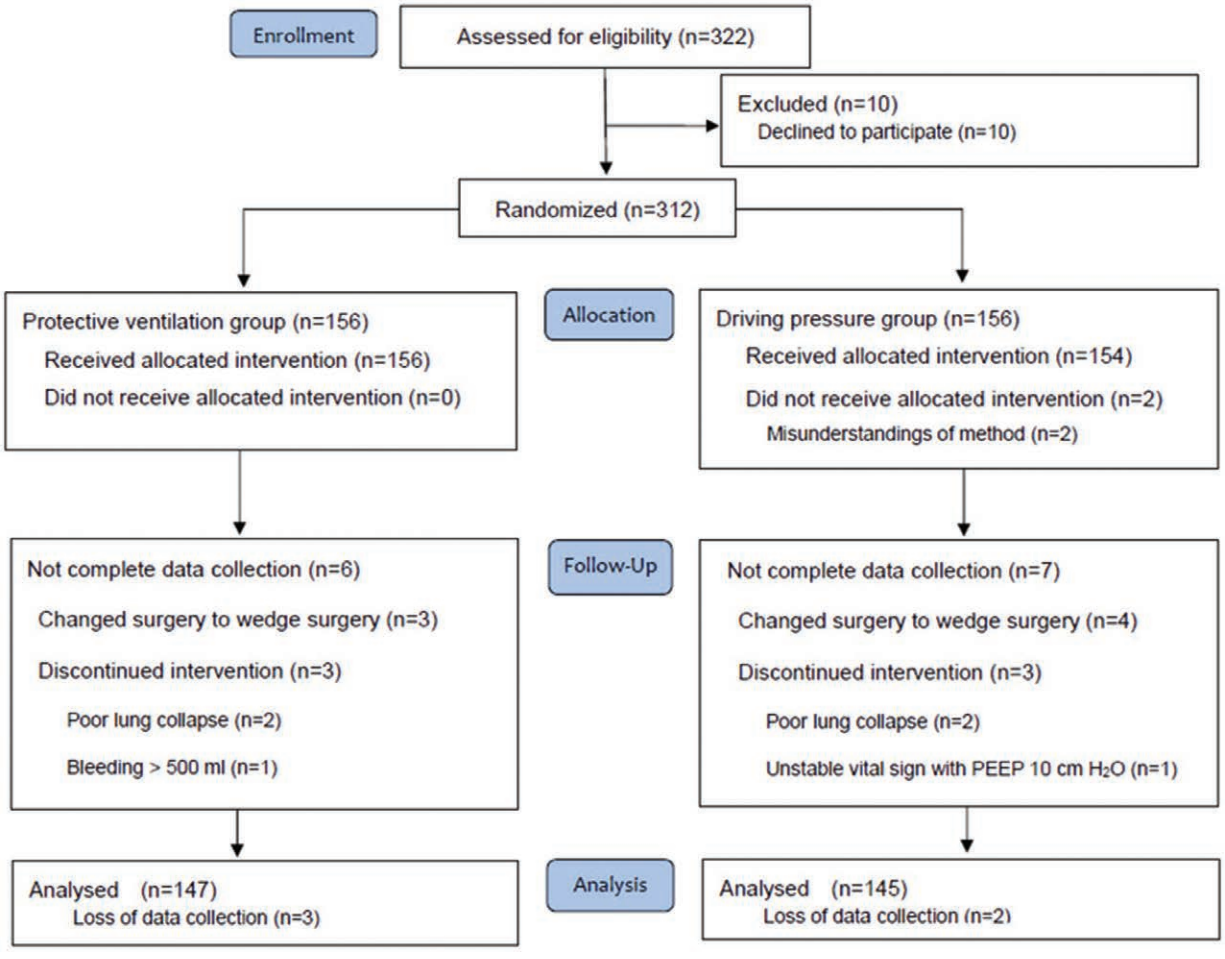


Fig. 1. Flow diagram of patient selection. PEEP, positive end-expiratory pressure.

Table 1. Characteristics of Patients

Characteristic	Protective Ventilation Group	Driving Pressure Group
Age, yr	63 ± 10	64 ± 9
Sex, F(M)	81(66)	86(59)
Weight, kg	61.4 ± 10.1	64.1 ± 11.4
Height, cm	160.9 ± 8.6	163.3 ± 9.2
BMI	23.6 ± 3.0	23.9 ± 3.2
ASA (I/II/III)	20/117/10	16/121/8
Underlying disease		
Hypertension	51	67
Diabetes mellitus	25	29
COPD or old Tb	27	28
Coronary vessel disease	5	6
Previous chemotherapy & radiotherapy	27	29
Alcohol, no/social/heavy*	92/45/10	78/55/12
Smoking		
No	70	63
Stop more than 6 month	43	39
Stop within 6 month	22	25
Current smoker	12	18
Creatinine, mg/dl	0.85 ± 0.21	0.88 ± 0.26
Hemoglobin, d/dl	12.8 ± 0.7	13.0 ± 0.7
Left ventricle ejection fraction, %	64.1 ± 6.3	65.1 ± 6.3
Preoperative FVC, L	3.40 ± 0.82	3.45 ± 0.86
Preoperative FEV1/FVC, %	72.0 ± 9.2	73.5 ± 9.0
Preoperative FEV1, %	86.7 ± 15.0	87.5 ± 15.0
$DLCO_2$, %	87.2 ± 16.1	84.6 ± 15.1

*Heavy drinking is consuming 15 drinks or more per week for men or 8 drinks or more per week for women as defined by the Centers for Disease Control and Prevention. Values are numbers or mean ± SD. ASA, American Society of Anesthesiologist physical status; BMI, body mass index; COPD, chronic obstructive pulmonary disease; DLCO, diffusing capacity of carbon monoxide; FEV1, forced expiratory volume; FVC, forced vital capacity; Tb, tuberculosis.

Table 2. Characteristics of Surgery

Characteristics	Protective Ventilation Group (n = 147)	Driving Pressure Group (n = 145)
Type of surgery		
Esophagus/Lung	12/135	16/129
Lobectomy, right/left	60/59	69/52
Bilobectomy, right	3	7
Sleeve lobectomy	2	1
Video-assisted thoracoscopic surgery/thoracotomy	101/46	95/50
Double lumen tube		
Right/Left	43/104	44/102
Surgeon 1/2/3/4/5/6/7	50/26/6/9/42/8/5	49/29/13/4/40/4/6
Intraoperative fluid amount, ml	1039 ± 415	1032 ± 442
Intraoperative bleeding, ml	100 [50, 200]	100 [50, 150]
Intraoperative urine output, ml	200 [135, 295]	230 [120, 330]
Duration of one-lung ventilation, min	104 [84, 140]	105 [79, 137]
Duration of anesthesia, min	188 [156, 240]	190 [161, 228]
Duration of operation, min	132 [103, 187]	136 [112, 178]
Patient-controlled analgesia (intravenous/epidural)	129/18	121/24
Postoperative fluid amount, ml (for 3 days)	3523 ± 965	3797 ± 1112

Values are numbers, mean ± SD or median [interquartile range], or as otherwise noted.

such as Pa_{O_2}, $PaCO_2$, and pH were not different between the two groups throughout surgery (table 3).

There were two in-hospital deaths in the protective ventilation group and one death in the driving pressure group. The durations of intensive care unit stay (median [interquartile range]: 21 [18 to 25] h *vs.* 22 [18 to 25] h) and hospital stay (median [interquartile range]: 6 [5 to 9] days *vs.* 6 [5 to 9] days) did not differ between protective ventilation group and driving pressure group. However, the durations of intensive care unit and hospital stays significantly differed between those who were and were not classified with postoperative pulmonary complications based on Melbourne Group Scale (median [interquartile range]: 74 [25 to 165] h *vs.* 21 [18 to 24] h, $P = 0.003$ and 14 [9 to 19] days *vs.* 6 [5 to 7] days, $P < 0.001$).

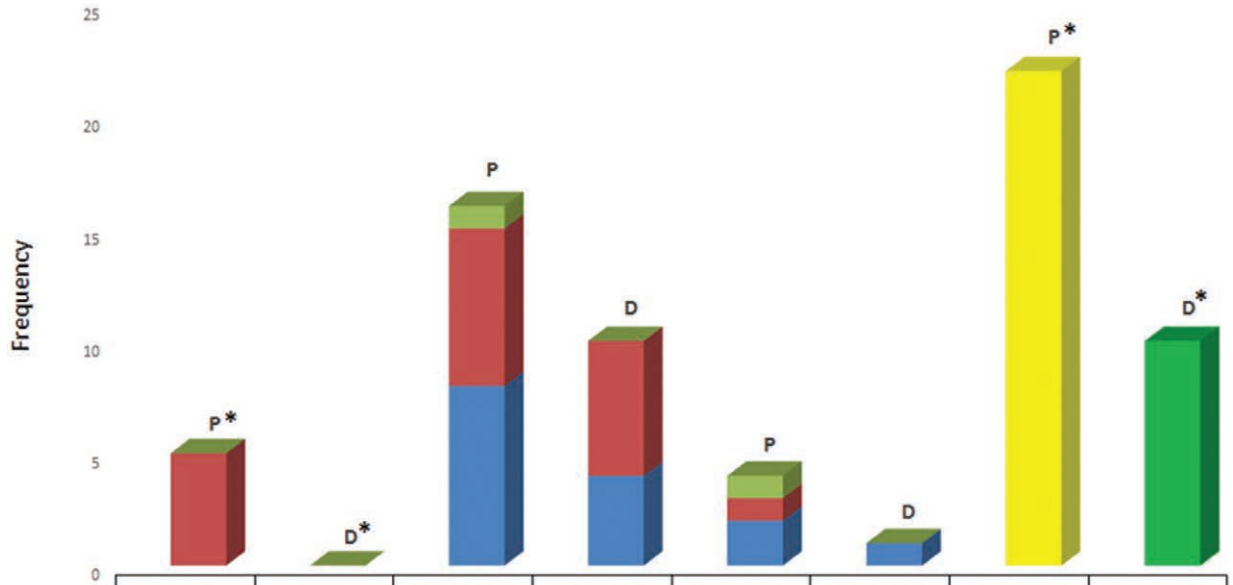
Complications in other organs did not differ between the two groups; postoperative atrial fibrillation was present in 23 of 147 (16%) and 19 of 145 (13%) in the protective ventilation group and the driving pressure group, respectively. Cerebral ischemic events (transient ischemic attack or stroke) occurred in 4 of 147 (2.7%) and 4 of 145 (2.8%) in the protective ventilation group and the driving pressure group, respectively.

Discussion

The incidence of postoperative pulmonary complications defined by the Melbourne Group Scale of at least 4 was reported around 13%[22] to 14.5%[17] in thoracic surgery. In our study, the incidence of postoperative pulmonary complications based on the Melbourne Group Scale was 12.2% with conventional protective ventilation and 5.5% with driving pressure–guided ventilation. Pneumonia or ARDS were less frequent in the driving pressure group than in the protective ventilation group (6.9% *vs.* 15.0%).

Driving pressure is defined as V_T divided by respiratory system compliance and can be easily calculated as plateau pressure minus PEEP.[18] In recent retrospective studies, driving pressure was suggested as being more strongly associated with survival than V_T and PEEP in ARDS patients.[20,25] In addition, individual changes in V_T, PEEP, or plateau pressures were not independently associated with survival; they were only associated if they were among the changes that led to reductions in driving pressure.[18] Subsequent retrospective study on ARDS patients supported that the driving pressure is closely related to hospital mortality even among patients who received protective ventilation,[19] and protective ventilation alone was not associated with an improved rate of survival.[1,19]

For surgical patients, a meta-analysis from 17 randomized, controlled trials of protective ventilation was recently published. In these multivariable analyses, driving pressure was associated with the development of postoperative pulmonary complications, whereas no association was found for V_T and PEEP.[20]



	ARDS	ARDS	Pneumonia-operated lung	Pneumonia-operated lung	Pneumonia-ventilated lung	Pneumonia-ventilated lung	Pneumonia and/or ARDS	Pneumonia and/or ARDS
POD1	0	0	1	0	1	0		
POD2	5	0	7	6	1	0		
POD3	0	0	8	4	2	1	22	10

Fig. 2. The onset and frequency of lung lesions. *Chi-square test for comparing variables, $P < 0.05$. ARDS, acute respiratory distress syndrome; D, driving pressure group; P, protective ventilation group; POD 1, postoperative day 1; POD 2, postoperative day 2; POD 3, postoperative day 3.

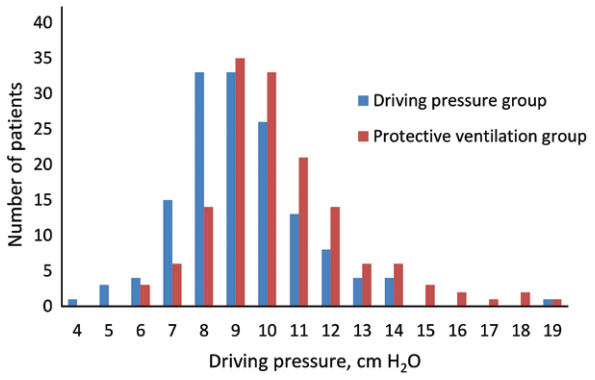


Fig. 3. The driving pressure of both groups during one-lung ventilation.

Previous studies on driving pressure are mostly retrospective studies and reported risk-predictive value of driving pressure.[18–20] Thus, prospective, randomized trials to assess the independent role of driving pressure in clinical outcomes have been requested.[21] Our study was designed to answer that question and showed that driving pressure–guided ventilation is related to the reduction of postoperative pulmonary complications in thoracic surgery.

We assume that postoperative pulmonary complications were reduced because the patients were ventilated according to their "functional lung size" in driving pressure group. "Functional lung size" is the volume of aerated lung available for tidal ventilation.[26] Both are harmful to over-distend (barotrauma) or under-ventilate (atelectasis) lungs than functional size. Respiratory system compliance (C_{RS}) is the highest when the lungs are ventilated according to their functional lung size.[26] Driving pressure is defined as V_T/C_{RS}. Therefore, ventilation at the lowest driving pressure is to ventilate a patient according to his/her "functional lung size" while avoiding under- or over-distension.[18]

There are no established techniques for driving pressure–guided ventilation yet. We used the PEEP which produces the lowest driving pressure and subsequently the highest C_{RS} in the current study.[21,27] A similar approach was used in a pilot study for abdominal surgery.[28] Patients who present for thoracic surgery usually have underlying differences in their respiratory system compliance because of mass size or site or frequently accompanying lung disease. Under such conditions, fixed-setting ventilation may over-distend lungs of small functional size or under-ventilate lungs of large functional size. Therefore, it may be beneficial to perform "functional size-based" ventilation.

The cut-off value of driving pressure has not been identified yet, but 15 cm H_2O is being suggested for

Table 3. Characteristics of Ventilator Parameters and Intraoperative Arterial Blood Gas Analysis

	Protective Ventilation Group			Driving Pressure Group			*P* Value		
Characteristics	$TLV_{baseline}$	OLV_{15}	TLV_{10}	$TLV_{baseline}$	OLV_{15}	TLV_{10}	$TLV_{baseline}$	OLV_{15}	TLV_{10}
Tidal volume, mL	459 ± 76	359 ± 53	445 ± 70	472 ± 69	365 ± 52	458 ± 83	0.125	0.334	0.161
PEEP, cm H_2O	5	5	5	5	3[2,5]	5		< 0.001	
Plateau pressure, cm H_2O	13[12,15]	15[14,16]	14[12,16]	13[11,14]	12[11,14]	13[11,15]	0.261	< 0.001	0.031
Peak inspiratory pressure, cm H_2O	16[15,18]	21[19,23]	17[15,19]	16[14,18]	20[17,22]	16[14,19]	0.909	0.041	0.178
Driving pressure, cm H_2O		10[9,11]			9[8,10]			< 0.001	
PaO_2, mm Hg		224.2 ± 102.7	249.8 ± 105.1		240.2 ± 114.1	238.3 ± 97.5		0.210	0.335
$PaCO_2$, mm Hg		36.1 ± 2.4	36.5 ± 4.0		35.7 ± 2.9	35.9 ± 2.9		0.864	0.201
pH		7.4 ± 0.1	7.4 ± 0.1		7.4 ± 0.1	7.4 ± 0.1		0.292	0.303

Values are mean ± SD or median interquartile range. *P* values are for the comparison between the two groups at each time point. OLV_{15}, one-lung ventilation 15 min; PEEP, positive end-expiratory pressure; $TLV_{baseline}$, total lung ventilation just after induction; TLV_{10}, total lung ventilation 10 min after one-lung ventilation.

ARDS patients.[29] Several patients in the protective ventilation group showed driving pressure more than 15 cm H_2O (1/145 *vs.* 9/147, driving pressure group *vs.* protective ventilation group, $P = 0.011$, in fig. 3). However, interestingly, the median difference of driving pressure between the two groups was only 1 cm H_2O (median [interquartile range]: 9 [8 to 10] cm H_2O *vs.* 10 [9 to 11] cm H_2O, driving pressure group *vs.* protective ventilation group, $P < 0.001$). In our study, the key point of driving pressure–guided ventilation was an individualized ventilation[30] using different PEEP. A small difference in median values of driving pressure indicates that individualized ventilation is more important than the absolute number of driving pressure itself.

However, several studies have also reported that even a small increase in driving pressure brings a difference in clinical outcomes. In a previous retrospective study on ARDS patients, each unit of driving pressure (1 cm H_2O) was associated with a 3.4% increase in the risk for major morbidity.[13] For surgical patients, a meta-analysis from 17 randomized, controlled trials of protective ventilation showed the odds ratio for postoperative pulmonary complications is 1.16 for each 1 cm H_2O increase in driving pressure (95% CI, 1.13 to 1.19; $P < 0.001$).[20]

The optimum PEEP is the PEEP level that results in the greatest respiratory system compliance (the lowest driving pressure).[1,31] The median optimum PEEP was 3 (interquartile range, 2 to 5) cm H_2O in our study (driving pressure group), and this was a new finding considering that PEEP 5 to 6 cm H_2O has been recommended for thoracic surgery.[9,10,12,13] We assumed the reason for this finding is that patients undergoing thoracic surgery usually develop intrinsic PEEP of 2 to 6 cm H_2O[10,32] during one-lung ventilation. Patients with no intrinsic PEEP will show an increase in lung compliance from a moderate (5 to 6 cm H_2O) extrinsic PEEP. However, if patient has intrinsic PEEP, a lower amount of extrinsic PEEP is required to shift the expiratory equilibration point toward the lower inflection point of the compliance curve.[10] Our findings may explain why studies of higher PEEPs did not show consistent survival benefits.[33,34] In our study, Pa_{O_2}, $PaCO_2$, and pH did not differ throughout surgery between the two groups, and this shows that adequate ventilation was delivered in the driving pressure group despite lower PEEP.

There are several limitations in our study. First, each ventilatory strategy was applied only in the period of one-lung ventilation. Longer application may have resulted in more difference in postoperative pulmonary complications. Second, we did not measure intrinsic PEEP. The majority of patients undergoing thoracic surgery develop an intrinsic PEEP during one-lung ventilation.[35] The presence of intrinsic PEEP may have under- or overestimated the actual driving pressure. Third, we used increment PEEP instead of decrement PEEP to determine the optimal PEEP.[36] These two methods may result in different optimal PEEP and driving pressure. Forth, lung compliance may have increased during the stepwise increase in PEEP in the driving pressure group. However, usually a stepwise increase in PEEP up to 20 cm H_2O is required to increase lung compliance (open lung technique).[28] Our PEEP trial went up only to 10 cm H_2O; thus, its effect on lung compliance were considered limited. Fifth, we used high F_{IO_2} during one-lung ventilation for both groups. This may expose patients to oxidative stress lung injury.[37,38] Finally, we applied V_T 6 ml/kg of ideal body weight. This was selected based on our previous study,[9] and a guideline of protective ventilation in thoracic surgery.[10] Lower V_T may have to be applied in future studies.

In conclusion, driving pressure–guided ventilation during one-lung ventilation was related to a reduced incidence of postoperative pulmonary complications compared with conventional protective ventilation in thoracic surgery. Application of the patient's specific PEEP, which can reduce driving pressure, may be recommended for thoracic surgery patients.

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Competing Interests

The authors declare no competing interests.

Reproducible Science

Full protocol available at: dukiduck.park@samsung.com.
Raw data available at: dukiduck.park@samsung.com.

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