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#### **Research Article**

# Relationship between Acute Lung Injury and the Pressure-Flow Curve

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#### Abstract

**Background:** Recently, the open-lung concept has been used in the respiratory care of patients with Acute Lung Injury (ALI), however, the expiratory phase in ALI patients has not yet been studied in detail. In this study, we paid attention to the pressure-flow curves that can be generated using the P/V tool on the Hamilton-G5 mechanical ventilator.

**Methods:** We conducted a comparative analysis of the Maximum Expiratory Flow Rate (MEFR), pressure at MEFR, etc., in 5 adult control patients who were scheduled to undergo surgery, and 13 ALI patients, including 5 with postoperative respiratory failure, 5 with pneumonia, 2 with interstitial pneumonia, and 1 with acute pancreatitis. The P/V loops were recorded after the induction of anesthesia in the control subjects and after the diagnosis of ALI in the ALI patients.

**Results:** At the time of the P/V loop measurement, the compliance (31.8 and 78.2 ml/hPa in the ALI and control groups, respectively), MEFR (-169.4 and -404.0 ml/s, respectively), and pressure at MEFR (10.6 and 4.2 hPa, respectively) were significantly different between the ALI and control groups.

**Conclusion:** Thus, analysis of pressure-flow curves may be helpful in grasping the pathogenesis of ALI.

#### **ABBREVIATIONS**

ALI: Acute Lung Injury; MEFR: Maximum Expiratory Flow Rate; PEEP: Positive End-Expiratory Pressure; ARDS: Acute Respiratory Distress Syndrome; FRC: Functional Residual Capacity; LIP: Lower Inflection Point; UIP: Upper Inflection Point: APRV; Airway Pressure Release Ventilation; OLC: Open Lung Concept; ICU: Intensive Care Unit; P/F ratio: PaO<sub>2</sub>/FiO<sub>2</sub> ratio; RMs: Recruitment Maneuvers; CPAP: Continuous Positive Airway Pressure

#### **INTRODUCTION**

The optimal level of Positive End-Expiratory Pressure (PEEP) in the ventilatory management of patients with Acute Respiratory Distress Syndrome (ARDS) is still widely debated. However, the use of PEEP during mechanical ventilatory support causes re-expansion of collapsed alveoli and an increase of the Functional Residual Capacity (FRC), by which improved oxygenation can be expected. In the case of ARDS patients, PEEP must always be maintained to prevent lung collapse at end-

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#### **Keywords**

- P/V loop
- ALI
- Open-lung concept
- APRV

expiration and atelectrauma [1]. Pressure-volume curves have been used to determine appropriate levels of PEEP [2]. It has also been reported that ventilation parameters can be appropriately set by grasping the Lower and Upper Inflection Points (LIP and UIP) from pressure-volume curves [3]. In recent years, airway pressure release ventilation (APRV) based on the Open-Lung Concept (OLC) has been more commonly used than ventilation with lower tidal volumes, which are set based on LIP and UIP, in the respiratory care of Acute Lung Injury (ALI) and other patients. However, there are still problems that need to be resolved in APRV, such as determination of the high PEEP values.

The airway pressure can be gradually increased using the P/V tool on the Hamilton-G5 mechanical ventilator (Hamilton Medical AG, Bonaduz/Switzerland) during mechanical ventilatory support while measuring the ventilatory volume and flow rate, to obtain pressure-volume and pressure-flow curves. In the actual procedure, the pressure is increased by 3 hPa per second to 35 hPa and then decreased by 3 hPa per second to 0 hPa. The measurement takes approximately 23 seconds. Figure

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1 shows the pressure-flow curves drawn using Microsoft Excel (Microsoft Japan Co., Ltd., Tokyo/Japan) from the data obtained using the P/V tool and imported into a personal computer. The curves indicate that the expiratory waveforms differ between normal and ALI patients and that the expiratory pressure at the Maximum Expiratory Flow Rate (MEFR) is higher in the ALI patients. Namely, alveolar collapse is speculated to occur at a higher pressure in patients with ALI. By setting the PEEP at a higher value than this pressure in APRV, alveolar collapse may be prevented. Therefore, MEFR, pressure at MEFR, and the interval between the start of expiration and MEFR were investigated in ALI patients from the G5 pressure-flow curves.

#### **MATERIALS AND METHODS**

The controls were 5 healthy adults who were scheduled to undergo surgery and gave consent for participation in this study on the day before surgery. The mean age of the subjects was 49.4  $\pm$  12.4 years (mean  $\pm$  SD), the male: female ratio was 3:2, the mean height was 164.6  $\pm$  6.7 cm, and the mean weight was 65.7  $\pm$  10.5 kg. After induction of anesthesia with propofol (1 to 2 mg/kg) and rocuronium bromide (0.6 mg/kg), anesthesia was maintained with propofol (4 to 6 mg/kg/h) and remifentanil (0.1  $\mu$ g/kg/min), and when the circulation stabilized, the measurement using the P/V tool on the Hamilton-G5 was performed.

The ALI group consisted of 13 patients admitted to the ICU who were diagnosed as having ALI by blood gas analysis and chest radiography who were admitted to the Intensive Care Unit (ICU) of Tohoku University Hospital between September 2010 and March 2012. The purpose of this study was explained to the families of the patients, and after obtaining their consent, the patients were placed on mechanical ventilator support with Hamilton-G5. The patients were sedated with propofol to a Ramsay sedation score of approximately 3 to 4, however, 0.6 mg/kg of rocuronium bromide was also injected intravenously to prevent spontaneous breathing and body movements. In addition, the cuff pressure was increased to 35 cm  $H_2O$  to prevent cuff leak. Then the measurement using the P/V tool of Hamilton-G5 was performed immediately before extubation in 7 of the 9 patients who survived (not including 1 patient who could not be

extubated and 1 patient in whom APRV was discontinued due to blood pressure reduction). The P/V tool data were recorded on a personal computer, and the MEFR, pressure at MEFR, etc., were compared from the pressure-flow curves generated. The Stat View-j 5.0 statistical software (SAS Institute USA) was used for the statistical analysis. The Mann-Whitney U test was used for comparison between groups, with the significance level set at p < 0.05. This study was conducted with the approval of the Ethics Committee of Tohoku University.

#### **RESULTS AND DISCUSSION**

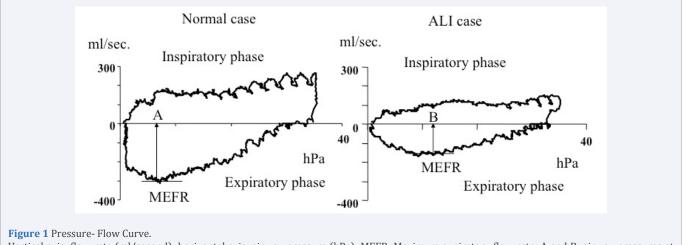
#### Results

In the normal control group, the mean age was  $49.4 \pm 12.4$  years (mean ± SD), the male: female ratio was 3:2, the mean height was  $164.6 \pm 6.7$  cm, and the mean weight was  $65.7 \pm 10.5$  kg. In the ALI patients, the mean age was  $68.3 \pm 16.2$  years, the male: female ratio was 7:6, the mean height was  $158.6 \pm 9.1$  cm, and the mean weight was  $62.4 \pm 13.8$  kg (Table 1). The ALI group included 5 patients diagnosed as having postoperative respiratory failure, 5 with pneumonia, 2 with interstitial pneumonia, and 1 with acute pancreatitis. The PaO<sub>2</sub>/FiO<sub>2</sub> (P/F) ratio was  $133.8 \pm 43.4$  mm Hg immediately before the P/V loop measurement. The mortality rate in the ICU was 30%.

At the time of the P/V loop measurement, the lung compliance was significantly lower (p = 0.014) in the ALI group (31.8 ± 8.8 ml/hPa) than that in the control group (78.2 18.0 ml/hPa).

The MEFR was significantly lower (p = 0.014) in the ALI group (-169.4 ± 44.0 ml/s) than that in the control group (-403.0 ± 77.1 ml/s). The MEFR immediately before extubation was still significantly lower in the ALI group (-222.8 ± 34.9 ml/s; p = 0.045) than that in the control group, but significantly higher (p = 0.012) than the value recorded at the initial P/V loop measurement (Figure 2).

The pressure at MEFR was significantly higher (p = 0.019) in the ALI group (10.6 ± 2.6 hPa) than that in the control group (4.2 ± 2.2 hPa). The pressure at MEFR immediately before extubation was almost the same in the ALI group as that in the control group (Figure 3).



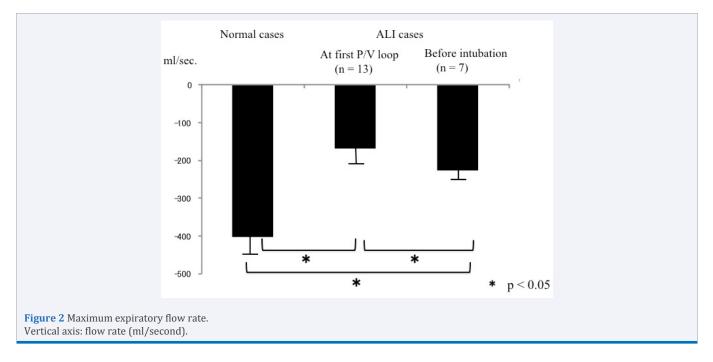
Vertical axis: flow rate (ml/second); horizontal axis: airway pressure (hPa); MEFR: Maximum expiratory flow rate; A and B: airway pressures at MEFR.

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	:	Demographic	data.
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Case	Age (years)	Sex	FIO <sub>2</sub>	PEEP (hPa)	P/F ratio (mmHg)	High PEEP (hPa)	ICU outcome
After aortic replacement	62	female	1.0	10	65.3	30	alive
After aortic replacement	45	male	1.0	5	96.1	26	Alive $\cdot$ discontinued
After aortic replacement	78	male	0.5	5	165.8	28	death
Intestinal necrosis	81	female	0.8	7	148.7	20	alive
Intestinal necrosis	67	female	0.5	5	175	22	alive
Pneumonia	74	male	0.5	5	174	28	alive
Pneumonia	40	male	0.6	10	163	24	death
Pneumonia	76	male	1.0	5	117	28	alive
Pneumonia	81	male	1.0	5	90.3	26	death • discontinued
Pneumonia	72	Female	1.0	5	69.9	24	alive • could not be extubated
Interstitial pneumonia	83	female	1.0	5	113	30	alive
Interstitial pneumonia	71	female	1.0	5	181	22	alive
Acute pancreatitis	58	male	0.5	5	180.6	30	death
Mean ± SD	68.3±16.8		0.8±0.2	5.9±1.2	137.8±43.4	26.0±3.4	

Discontinued: APRV was discontinued due to blood pressure reduction.



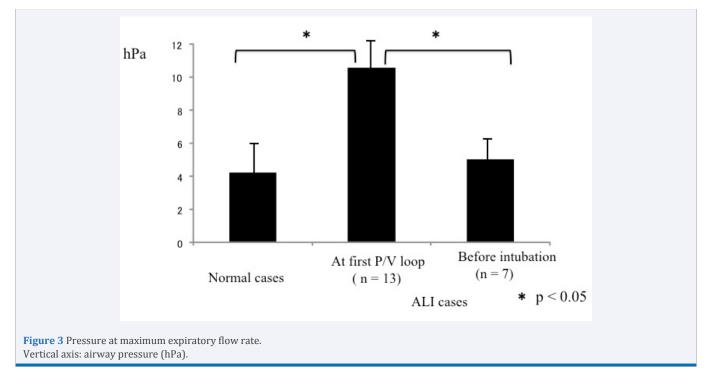
The interval between the start of expiration and MEFR was significantly shorter (p = 0.014) in the ALI group (8.22 ± 0.86 seconds) than that in the control group (11.87 ± 2.90 seconds).

#### Discussion

Impaired oxygenation in ALI patients is mainly caused by increased intrapulmonary shunting and increased ventilationperfusion mismatch [4]. Alveolar collapse leads to shunting, and collapse of the dorsal alveoli is prominent in ALI patients [5]. In addition, interstitial edema, reduced compliance, increased pulmonary vascular resistance, etc.,cause abnormal distribution of the pulmonary blood flow and ventilation, to increase the ventilation-perfusion mismatch.

Recruitment Maneuvers (RMs) are used to improve lung collapse. There are at present no standard RMs, however, it is said that the higher the pressure and the longer the pressure is maintained at a high level, the greater the effect [6]. For pneumatizing areas where pneumatization cannot be accomplished by mechanical ventilation, RMs using airway pressures higher than the peak airway pressure are necessary during mechanical ventilation. The safety of RMs using peak airway pressures as high as 60 cm H<sub>2</sub>O has been reported [7].

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In general, RMs appears to be safe, although the potential for transient decrease of the blood pressure exists. Another issue is that heavy sedation or even paralysis may be needed in some patients requiring the use of RMs for a prolonged duration.

The Continuous Positive Airway Pressure (CPAP) (Phigh) phase of APRV ensures an appropriate lung capacity and is equivalent to RMs, and the short-time Low-pressure release phase (Plow) promotes spontaneous breathing [8]. APRV is different from other RMs in that the pressure used to expand the alveoli is itself used for the maintenance. However, without proper setting of a High Pressure (Phigh), it is difficult to open the alveoli. In general, for opening alveoli, maintenance of the Phigh at a value higher than the appropriate plateau pressure is necessary [9]. In the present study also, the pressure at MEFR was higher in the ALI group than that in the control group, confirming the speculation that the alveoli start to collapse at higher pressures in ALI patients. In addition, the P/V tool on the Hamilton-G5 allows decrease of the pressure at 1-second intervals, and the start of alveolar collapse at higher pressures means that the alveoli start to collapse earlier.

The time constant is said to be the product of airway resistance and compliance, and in general, the time required to complete expiration is 4 times the time constant. In ALI, the lung compliance is low [10] and the time constant is small. In this study also, it can be speculated that the lung compliance in the ALI patients was very low and that the time constant was small. It is said that the expiratory Time (T low) in APRV must be set shorter than the time required completing the expiration to prevent alveolar collapse [11]. Such a study carried out in greater detail may be useful for proper setup of the expiratory time, etc.

### CONCLUSION

This study revealed reduced MEFR, higher pressure at MEFR, and shorter time to MEFR as characteristic findings in the ALI

patients. These results may be helpful for better grasping the pathogenesis of ALI.

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