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Revised manuscript

Effect of age on pulmonary gas exchanges during laparoscopy in the Trendelenburg-lithotomy position

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A short title: Pulmonary gas exchange and age in laparoscopy

Abstract

Background: There is a possibility that physiological changes in respiratory mechanics caused by aging lead to deterioration of pulmonary gas exchanges and an increase in (A-a)D_{O₂} and to a difference between Pa_{CO₂} and PET_{CO₂} (P(a-ET)_{CO₂}) during laparoscopy in the Trendelenburg-lithotomy position (TLP).

Methods: The subjects were 51 gynecological patients. Pressure-controlled ventilation was used to maintain PET_{CO₂} measured by the side stream method within the range of 4 to 4.67 kPa. During laparoscopy with CO₂ insufflation in the TLP, tidal volume was increased to keep PET_{CO₂} within $\pm 20\%$ of the preinsufflation value. Subjects were divided into three groups by age: a young group (Y: < 45 y.o.), a middle age group (45 y.o. \leq < 64 y.o.) and an elderly group (E: \geq 65 y.o.).

Results: Before pneumoperitoneum (PPN), significant differences were found between the Y and the E groups in Pa_{O₂}, (A-a)D_{O₂}, Pa_{CO₂} and P(a-ET)_{CO₂}. In all groups, peak inspiratory pressure (PIP) and Pa_{CO₂} were increased progressively during PPN in the TLP. P(a-ET)_{CO₂} increased gradually after starting CO₂ insufflation in the TLP only in the E group.

Conclusions: Increase in P(a-ET)_{CO₂} was seen during PPN in the TLP in the elderly group. With CO₂ insufflation in the TLP, the setting of mechanical ventilation based on the value of PET_{CO₂} measured by the side stream method should be determined with caution in elderly patients.

Key words: laparoscopy, Trendelenburg position, pulmonary gas exchange, side stream method, age

Monitoring of arterial carbon dioxide (CO_2) tension (Pa_{CO_2}) as expired end-tidal CO_2 tension (PET_{CO_2}) measured by capnometry is thought to be useful to determine the appropriate mechanical ventilation setting during anesthesia management. The side stream method to evaluate PET_{CO_2} is considered to be valuable in clinical management because this method enables simultaneous measurements of PET_{CO_2} and anesthetic gases. Several factors have been reported to affect PET_{CO_2} determined by the side stream method (1) and to increase the difference of arterial-end tidal carbon dioxide tension ($\text{P(a-ET)}_{\text{CO}_2}$). Advanced age has been reported to one of the factors contributing to an increase in $\text{P(a-ET)}_{\text{CO}_2}$. Cephalad shift of the diaphragm during laparoscopy in the Trendelenburg-lithotomy position (TLP) would decrease functional residual capacity (FRC) and increase dead space ventilation, factors that are thought to affect pulmonary gas exchanges. There is a possibility that physiological changes in lung and respiratory mechanics caused by aging lead to exaggeration of pulmonary oxygenation capacity and an increase in $\text{P(a-ET)}_{\text{CO}_2}$ during laparoscopy in the TLP. This also implies poor reliability of PET_{CO_2} monitoring in elderly patients undergoing laparoscopy in the TLP. Therefore, we investigated the effect of age on pulmonary gas exchanges during gynecological laparoscopy in the TLP.

Methods

After obtaining our institutional Ethics Committee approval and written informed consent, 51 gynecological patients were enrolled in this study. Patients with thoracic and/or broncho-pulmonary disease, body mass index (BMI: weight (kg) height (m)⁻²) over 27 were excluded from this study.

An epidural catheter was inserted at the Th₁₂/L₁ or L₁/L₂ intervertebral space for intra- and post-operative analgesia. After denitrogenation of the lungs with 100% oxygen, anesthesia was induced with 1-2 mg kg⁻¹ propofol and 0.1 mg kg⁻¹ vecuronium, and the trachea was intubated with a 7.0-mm endotracheal tube. General anesthesia was maintained with sevoflurane in nitrous oxide (N₂O) and oxygen. Inspiratory oxygen concentration (FI_{O2}) was changed within 0.33-0.5 to maintain SpO₂ at over 98%, and fresh gas flow was 3-5 L min⁻¹. Mechanical ventilation was started using pressure-controlled ventilation with a respiratory rate (RR) of 10-12 breaths min⁻¹ to maintain PET_{CO2} within the range of 4 to 4.67 kPa. The inspiratory-to-expiratory ratio was 1:2. Anesthetic gases and PET_{CO2} were monitored using the side stream method (5250 RGM, Ohmeda[®], Englewood Co). The capnograph was calibrated according to manufacturer's recommendations in regard to N₂O concentration before each anesthetic management. Gas was sampled continuously from the apparatus end of the endotracheal tube. Intraoperative monitoring included continuous electrocardiography, pulse oxymetry, capnography, and noninvasive measurements of blood pressure and pharyngeal temperature. Epidural anesthesia with 3-5 ml of 1% or 1.5% lidocaine was used together with general anesthesia.

After induction of general anesthesia, a 22-gauge arterial cannula was introduced into the radial artery. After measuring arterial blood gas in the supine lithotomy position as a control, CO₂ insufflation in the TLP (about 22-25 degrees against the horizontal line) was started.

During laparoscopy, tidal volume (TV) was increased to keep P_{ETCO_2} within $\pm 20\%$ of the control value. Respiratory rate (RR) was increased if peak inspiratory pressure (PIP) exceeded 35 cmH₂O. At 0, 15 and 30 min after insufflation in the TLP, arterial blood samples were analyzed at 37 °C using an ABL™ system 625 (Radiometer Medical A/S, Copenhagen, Denmark) with automatic two-point calibration, and the results were corrected to the patient's pharyngeal temperature (2). Peak inspiratory pressure, P_{aO_2} , (A-a) D_{O_2} , P_{aCO_2} and $P(a-ET)_{CO_2}$ at each time were calculated. For evaluation of (A-a) D_{O_2} , alveolar O₂ tension was calculated using the following formula.

$$PAO_2 = FI_{O_2} \times (760 - P_{aH_2O}) - PaCO_2 \times [FI_{O_2} + (1 - FI_{O_2})/R].$$

Alveolar H₂O vapor pressure was assumed to be 47 mmHg. *R* means respiratory exchange ratio and has been reported to be changed by CO₂ insufflation. We used 0.86 and 1.12 as *R* before and after CO₂ insufflation, respectively (3). Cuffed blood pressure (BP) and ECG were also monitored throughout the anesthetic management.

Subjects were divided into three groups by age: a young (Y: younger than 45 years of age) group, a middle age (M: 45-64 years of age) group and an elderly (E: 65 years of age or older) group. Unless otherwise noted, data are expressed as medians (range). The Kruskal-Wallis test and the Mann-Whitney *U* test were used for comparison between groups, and the Friedman test and Wilcoxon's signed-rank test were used for comparison within each group. A P-value less than 0.05 was considered significant.

Results

There was no significant difference in physical characteristics between the three groups except for height (Table 1). Insufflation pressure did not increase over 15 mmHg throughout the period of insufflation in any of the groups.

Hemodynamic data were the same in three groups before peritoneal insufflation. Blood pressure was significantly increased by insufflation in the Y group and the E group, which increase persisted until 30 min after establishing pneumoperitoneum (PPN) in both groups. There was no significant difference in BP between the three groups at each time point. Heart rate was significantly decreased by peritoneal insufflation in the M group (Table 2).

Table 3 shows TV, RR, MV and PIP changes caused by PPN. During preinsufflation in the supine and lithotomy position, there was no difference in each parameter between the three groups except for PIP in the M group. Tidal volume and MV 30 min after establishing peritoneal insufflation was significantly increased only in the E group. There was no significant difference in TV, MV or RR between the three groups. PIP was significantly increased by CO₂ insufflation to maintain PETCO₂ within 20% of preinsufflation values in all three groups, which increase persisted 30 min after starting PPN. PIPs in the M and E groups during PPN in TLP were significantly higher than that in the Y group.

PaO₂ and (A-a)D_{O2} at preinsufflation both in the M and E groups were significantly different from those in the Y group. These differences between groups persisted until 30 min of PPN. There was a significant deterioration in PaO₂ after starting peritoneal insufflation in the TLP in the Y group and the E group (Table 4).

Figure 1 shows PaCO₂ changes caused by peritoneal insufflation in the TLP. During preinsufflation in the supine and lithotomy position, PaCO₂ in the E group was significantly higher than those in the other two groups. Thirty minutes after establishing PPN in the TLP,

the significantly higher value of Pa_{CO_2} in the E group than in the other groups persisted. Pa_{CO_2} in each group was progressively increased by insufflation in the TLP.

During preinsufflation in the supine and lithotomy position, $\text{P(a-ET)}_{\text{CO}_2}$ in the E group was significantly higher than that in the Y group (Figure 2). This difference between these two groups persisted until 30 minutes after establishing PPN. $\text{P(a-ET)}_{\text{CO}_2}$ was significantly increased by peritoneal insufflation in the TLP compared with that before insufflation in the E group alone, which progressively increased during PPN.

Discussion

Before peritoneal insufflation, significant differences were found between the Y group and the E group in Pa_{O_2} , $(A-a)D_{O_2}$, Pa_{CO_2} and $P(a-ET)_{CO_2}$. Pa_{O_2} and $(A-a)D_{O_2}$ in the M group were also significantly different from those in the Y group before peritoneal insufflation. Significant differences in Pa_{CO_2} and $P(a-ET)_{CO_2}$ between the Y group and the E group persisted at 30 min after establishing PPN in the TLP. By this procedure, $P(a-ET)_{CO_2}$ were increased significantly compared with that before insufflation only in the E group, and this changes progressively increased during PPN.

In the present study, there were significant differences in Pa_{CO_2} and $P(a-ET)_{CO_2}$ between the Y group and the E group before intraperitoneal CO_2 insufflation. We determined the ventilation setting initially using the value of PET_{CO_2} . Therefore, we assume that this larger $P(a-ET)_{CO_2}$ in the elderly group resulted in an increase in Pa_{CO_2} in the preinsufflation period. $P(a-ET)_{CO_2}$ has been reported to be correlated with several factors, including systolic BP. There was no difference in systolic BP between the Y and E groups in the preinsufflation period in the present study, and hemodynamic factors could therefore not have contributed to this difference in $P(a-ET)_{CO_2}$. Emphysematous changes with aging and decrease in FRC are expected to increase $P(a-ET)_{CO_2}$ by changes in the ventilation-to-perfusion (V/Q) abnormality of the lung. Elderly patients have progressive increase in alveolar dead space (4), which is thought to be another factor affecting $P(a-ET)_{CO_2}$.

A number of studies have been performed to evaluate $P(a-ET)_{CO_2}$ in adults under general anesthesia, and mean values have been reported to be between 0.31-0.61 kPa (5). In the present study, the median [range] value of $P(a-ET)_{CO_2}$ before peritoneal insufflation in all patients was 0.14 [-0.91~1.28] kPa, a smaller value than those previously reported. Negative $P(a-ET)_{CO_2}$ was seen in 19 of the 51 patients. We measured PET_{CO_2} using the side stream

method. It has been reported that there is a delay in the inspiratory phase of this method by gas transport, and P_{ETCO_2} may be measured as “falsely” elevated and exceed P_{aCO_2} (6). We measured arterial blood gases during the preinsufflation period in the supine lithotomy position (LP), a position that may affect $P(a-ET)_{CO_2}$. Raising the legs in the LP has little effect on respiratory mechanics in awake subjects (7, 8). During general anesthesia, this position may affect FRC and pulmonary blood volume, which would be attributable to a decrease in $P(a-ET)_{CO_2}$. In the supine LP during general anesthesia, $P(a-ET)_{CO_2}$ has been reported to be 0.12 kPa (9).

$P(a-ET)_{CO_2}$ increased after CO_2 insufflation in the TLP only in the E group, which difference increased with prolongation of PPN. Relation between this gradient and the duration of PPN could not be conclusive (3, 10). However, patients were not in the TLP in previous studies. During laparoscopic hysterectomy in 32-61-year-old patients in the TLP, $P(a-ET)_{CO_2}$ was increased by only 0.2 kPa (9). This increase in the gradient was almost the same as that in the Y group in the present study. In the TLP, PIP became higher in all groups. This higher inspiratory pressure may further compress pulmonary blood flow, resulting in a decrease in transport of CO_2 from circulation to the alveolar space and an increase in alveolar dead space.

In the present study, significant deterioration of oxygenation in the M group and the E group was seen before PPN in the TLP. Physiological changes in lung and thoracic functions caused by aging would worsen the oxygenation. Pulmonary O_2 exchange has reported not to be deteriorated by CO_2 insufflation in young patients (3, 11). Even in the elderly group, in the present study, there was no increase in $(A-a)D_{O_2}$ after starting CO_2 insufflation in the TLP.

The acceptable upper limit of alveolar pressure during mechanical ventilation is thought

to be approximately 35 cmH₂O (12). We used pressure-controlled ventilation during the anesthetic management and set the upper limit of airway pressure to less than 35 cmH₂O. In the E group, there were four patients in whom respiratory rate had to be increased at 30 min after insufflation in the TLP. This and the larger difference in P(a-ET)_{CO₂} in elderly patients during laparoscopy in the TLP means that the setting of mechanical ventilation based on the value of PET_{CO₂} should be determined with caution.

There are several limitations in the present study. First, the present clinical study could not be performed in a blind style. All of the anesthesiologists involved in this study knew their patients' demographic data, including age. However, no anesthesiologist was informed about the end point of this study. Second, blood gas analyses were not carried out in supine position or the TLP alone. In our institute, gynecological surgeons performed CO₂ insufflation intraperitoneally before patients were placed in the TLP. Additional time would be needed for blood gas evaluation in the TLP alone, meaning prolongation of anesthesia management. This would not be acceptable ethically. Third, we used the side stream method to measure anesthetic gas agents and expiratory CO₂. Many factors have been reported to affect PET_{CO₂} measured by this method, including the site of gas intake, length of the sampling tube and sampling gas volume (1). In the present study, we tried to maintain the same conditions of gas sampling to minimize the effect of ventilation setting on PET_{CO₂}. Cardiac output (CO) is one of the factors that affect PET_{CO₂} measured by the side stream method (2). It has been reported that P(a-ET)_{CO₂} is considered to be a good estimate of alveolar deadspace, and deadspace ventilation is directly affected by CO (13). We could not measure CO in the present clinical study. Therefore, increase in the gradient shown in the present study may be, in part, attributable to reduction of CO (14). Increase in intraabdominal pressure up to 20 cmH₂O has been reported to an increase (15) or no change

in CO (16). Insufflation pressure in the present study did not exceed 19 cmH₂O, and therefore CO was likely to be increased or at least unchanged even in the E group.

In summary, increase in P(a-ET)_{CO₂} was seen during CO₂ insufflation in the Trendelenburg-lithotomy position in the elderly group. This change was increased with prolongation of pneumoperitoneum. With CO₂ insufflation in the Trendelenburg-lithotomy position, the setting of mechanical ventilation based on the value of PET_{CO₂} should be determined with caution in elderly patients.

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Table 1. Physical characteristics of the patients

	Young Group (N=19)	Middle Group (N=16)	Elderly Group (N=16)
Age; years	34 (19-44)	53 (45-64)	73 (69-89)
Height; cm	157 (144-166)	154.5 (147-163)	148 ^{##§§} (130-156)
Weight; kg	51 (41-67)	51.5 (46-63)	52.5 (36-65)
BMI; kg m ⁻²	21.1 (16.6-24.9)	22.7 (18.4-26.7)	24.5 (16.9-26.7)
Insufflation pressure; mmHg	13 (7-14)	12 (9-14)	12 (9-14)
Degree against horizontal line; degree	23 (14-30)	24.5 (14-32)	23 (13-30)

N: number of patients

BMI: body mass index

Values are medians (range).

P < 0.01 vs Young Group.

§§ P < 0.01 vs Middle Group.

Table 2. Blood pressure and heart rate changes caused by pneumoperitoneum in the Trendelenburg-lithotomy position (TLP)

	Group	Preinsufflation	Insufflation in TLP	15 min after PPN in TLP	30 min after PPN in TLP
sBP (mmHg)	Young	102 (84-146)	122** (86-172)	122** (84-144)	112*** (94-146)
	Middle	105 (84-128)	117 (84-146)	111 (84-156)	111 (78-160)
	Elderly	104 (86-126)	128** (96-174)	123** (96-164)	122* (86-150)
dBP (mmHg)	Young	54 (46-90)	68** (54-98)	64** (54-82)	72***+¶¶ (52-90)
	Middle	57 (42-84)	63 (40-98)	62 (42-102)	64 (38-100)
	Elderly	54 (40-68)	66* (42-100)	65** (52-94)	64** (42-92)
HR (beats min ⁻¹)	Young	74 (46-94)	74 (62-106)	76 (64-90)	72 (62-94)
	Middle	80 (62-94)	79 (58-98)	74*+ (56-88)	73***+ (56-88)
	Elderly	66 (56-86)	70 (58-130)	70 (50-102)	71 (50-104)

PPN: pneumoperitoneum, sBP: systolic blood pressure, dBP: diastolic blood pressure, HR: heart rate

Values are medians (range).

* P < 0.05, ** P < 0.01 vs Preinsufflation of each group.

+ P < 0.05, ++ P < 0.01 vs Insufflation of each group.

¶¶ P < 0.01 vs 15 min after PPN.

Table 3. Changes in tidal volume, respiratory rate, minute ventilation and peak inspiratory pressure caused by pneumoperitoneum in the Trendelenburg-lithotomy position (TLP)

	Group	Preinsufflation	Insufflation in TLP	15 min after PPN in TLP	30 min after PPN in TLP
TV (ml kg ⁻¹)	Young	9.4 (6.0-10.7)	10.0 (5.6-11.3)	9.9 (7.3-11.3)	10.0 (7.3-12.0)
	Middle	9.2 (7.7-12.6)	8.9 (7.7-12.0)	9.3 (6.3-13.7)	9.6 (6.3-13.4)
	Elderly	9.3 (6.9-11.1)	9.6 (5.7-11.2)	9.8 (3.9-12.6)	10.3 ^{**++¶¶} (8.8-13.9)
RR (min ⁻¹)	Young	10 (9-12)	10 (8-12)	12 (8-15)	12 (8-15)
	Middle	10 (9-12)	10 (9-12)	11 (10-17)	11 (10-13)
	Elderly	10 (9-14)	10 (9-14)	10 (10-18)	11 (9-15)
MV (ml kg ⁻¹)	Young	99.2 (60.3-128.2)	100.6 (67.7-134.3)	102.6 (70.6-135.7)	104.9 (86.9-144.0)
	Middle	93.4 (80.4-123.7)	91.9 (81.8-131.0)	99.7 (76.0-164.3)	99.5 (76.0-171.9)
	Elderly	96.1 (68.6-137.4)	98.2 (57.5-137.4)	101.5 (69.7-146.6)	128.8 ^{**++¶¶} (74.3-185.6)
PIP (cmH ₂ O)	Young	15.0 (10-20)	22.0 ^{**} (10-28)	23.0 ^{**++} (14-30)	22.0 ^{**++¶} (14-30)
	Middle	18.5 [#] (12-27)	23.0 ^{**#} (16-34)	25.0 ^{**+##} (20-34)	26.5 ^{**#} (14-35)
	Elderly	16.0 (11-20)	24.0 ^{**} (17-32)	25.0 ^{**+##} (19-35)	29.5 ^{**++##¶¶} (21-35)

TV: tidal volume, RR: respiratory rate, MV: minute ventilation, PIP: peak inspiratory pressure.

PPN: pneumoperitoneum.

Values are medians (range).

** P < 0.01 vs Preinsufflation of each group.

+ P < 0.05, ++ P < 0.01 vs Insufflation of each group.

¶ P < 0.05, ¶¶ P < 0.01 vs 15 min after pneumoperitoneum.

P < 0.05, ## P < 0.01 vs Young group at the same time point.

Table 4. Changes in Pa_O₂ and (A-a)D_O₂ changes caused by pneumoperitoneum in the Trendelenburg-lithotomy position (TLP)

	Group	Preinsufflation	Insufflation in TLP	15 min after PPN in TLP	30 min after PPN in TLP
Pa _O ₂ (kPa)	Young	25.4 (12.9-38.5)	24.0 ^{**} (11.7-33.8)	23.7 [*] (11.8-35.3)	22.7 ^{**¶} (16.0-34.4)
	Middle	21.2 [#] (10.9-32.2)	18.9 [#] (9.8-31.5)	20.9 [#] (10.5-32.0)	19.2 (11.3-61.5)
	Elderly	21.5 [#] (15.0-45.3)	19.2 ^{**} (10.5-28.3)	19.5 ^{###} (14.3-41.2)	18.6 ^{###¶} (11.9-38.3)
(A-a)D _O ₂ (kPa)	Young	2.5 (0.04-12.9)	3.8 (0.2-14.4)	2.8 (0.6-14.4)	2.8 (0.9-19.2)
	Middle	8.1 [#] (0.2-22.1)	7.7 [#] (2.0-25.3)	6.5 ^{###} (1.6-72.9)	8.0 ^{###} (1.4-77.0)
	Elderly	8.6 ^{###} (1.8-29.1)	10.4 ^{###} (1.9-33.9)	8.1 ^{###} (3.4-46.6)	10.4 ^{###} (2.1-50.8)

PPN: pneumoperitoneum, PIP: peak inspiratory pressure

Values are medians (range).

* P < 0.05, ** P < 0.01 vs Preinsufflation of each group.

¶ P < 0.05 vs 15 min after pneumoperitoneum.

P < 0.05, ### P < 0.01 vs Young group at the same time point.

Legend of figures

Figure 1. Box and whisker plot showing Pa_{CO_2} changes caused by pneumoperitoneum in the TLP in a Young Group (□), a Middle Group (▨) and an Elderly Group (▤). The boxes represent interquartile range (25%-75%); the solid horizontal line within the boxes, median; and error bars, 10% to 90%.

** $P < 0.01$ vs Preinsufflation of each group.

++ $P < 0.01$ vs Insufflation of each group.

$P < 0.05$ vs Young group at the same time point.

§§ $P < 0.01$ vs Middle group at the same time point.

Figure 2. Box and whisker plot showing $\text{P(a-ET)}_{\text{CO}_2}$ changes caused by pneumoperitoneum in the TLP in a Young Group (□), a Middle Group (▨) and an Elderly Group (▤). The boxes represent interquartile range (25%-75%); the solid horizontal line within the boxes, median; and error bars, 10% to 90%.

* $P < 0.05$, ** $P < 0.01$ vs Preinsufflation of each group.

++ $P < 0.01$ vs Insufflation of each group.

¶ $P < 0.05$ vs 15 min after pneumoperitoneum.

$P < 0.01$ vs Young group at the same time point.

§ $P < 0.05$ vs Middle group at the same time point.

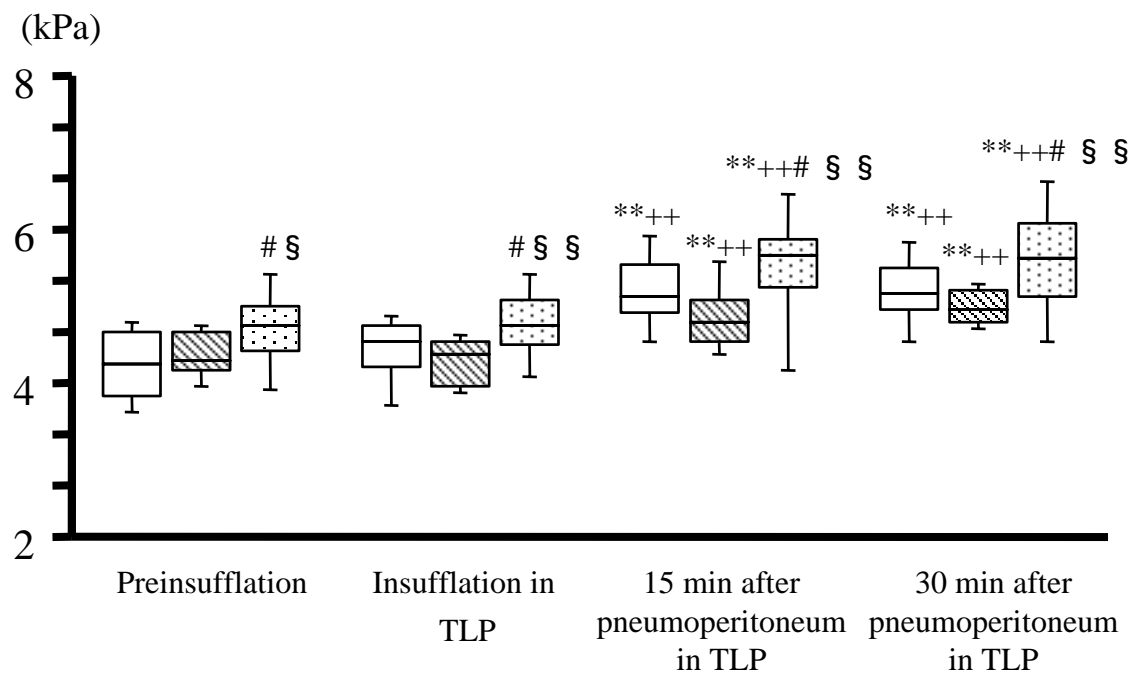


Figure 1

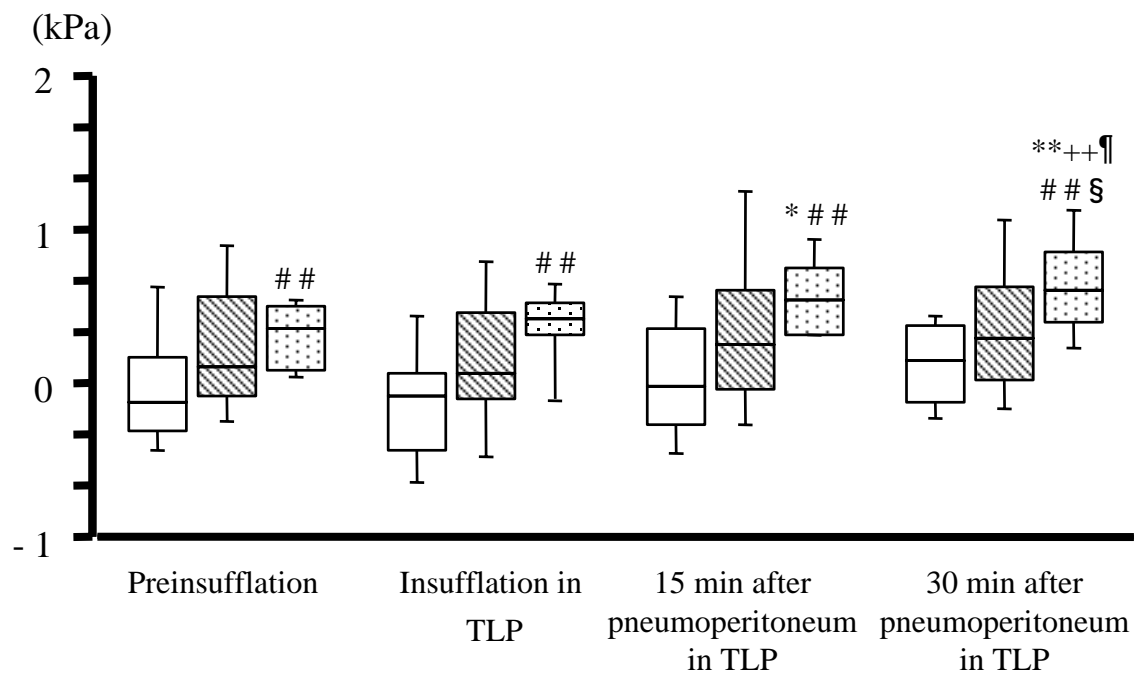


Figure 2