Combination of Tracheal Gas Insufflation and Airway Pressure Release Ventilation*

Kazufumi Okamoto, MD; Hiroshi Kishi, MD; Hyun Choi, MD; and Toshihide Sato, MD

**Study objective:** We hypothesized that the continuous gas flow administration delivered through an insufflation catheter positioned above the carina during airway pressure release ventilation (APRV) would facilitate carbon dioxide (CO₂) elimination, resulting in normocarbia with a substantially reduced peak airway pressure (Paw). To test this hypothesis, we compared intermittent positive pressure ventilation (IPPV), tracheal gas insufflation (TGI), APRV, and combined TGI and APRV (TGI+APRV).

**Design:** Animal study with random application of four ventilatory modes in a canine restrictive-thorax model with and without pulmonary edema.

**Setting:** Research laboratory at Kumamoto (Japan) University School of Medicine.

**Subjects:** Six mongrel dogs.

**Interventions:** Application of four ventilatory modes (IPPV, TGI, APRV, and TGI+APRV).

**Measurements and results:** TGI+APRV facilitated CO₂ elimination. The peak Paw was significantly lower during TGI+APRV than during IPPV (nonpulmonary edema model: 15±4 vs 28±9 cm H₂O, p<0.05; pulmonary edema model: 20±4 vs 34±10 cm H₂O, p<0.05). Normocarbia was observed in both models. Neither TGI nor APRV alone maintained normocarbia.

**Conclusion:** The combined use of TGI and APRV is a more effective method of maintaining normocarbia with reduced peak Paw than either IPPV or APRV alone.

(CHEST 1997; 111:1366-74)

**Key words:** airway pressure release ventilation; barotrauma; mechanical ventilation; respiratory failure; tracheal gas insufflation

**Abbreviations:** APRV=airway pressure release ventilation; CaO₂=arterial oxygen content; CcO₂=pulmonary capillary oxygen content; CO=cardiac output; CO₂=carbon dioxide; DO₂=oxygen delivery; EO₂=oxygen extraction; FIO₂=inspiratory fraction of oxygen; Hb=hemoglobin; HR=heart rate; IPPV=intermittent positive pressure ventilation; MAP=mean arterial pressure; PAP=pulmonary artery pressure; Paw=airway pressure; PAWF=pulmonary artery wedge pressure; PEEP=positive end-expiratory pressure; Pplat=inspiratory plateau pressure; Qo₂=venous admixture; R=respiratory quotient; TGI=tracheal gas insufflation; TGI+APRV=combined use of tracheal gas insufflation and airway pressure release ventilation; VE=minute ventilation; VO₂=oxygen consumption

Intermittent positive pressure ventilation (IPPV) with or without positive end-expiratory pressure (PEEP) is the most frequently used mode of mechanical ventilation in the management of respiratory failure. Although this mode is effective, it results in high peak airway pressures (Paw) in the reduced compliance lung. The resultant high peak Paw can cause alveolar overdistention and produce significant pulmonary complications. As a means of minimizing complications, various new ventilatory strategies have been proposed.

Airway pressure release ventilation (APRV) is a ventilatory alternative that augments carbon dioxide (CO₂) elimination by periodically decreasing the airway pressure from a previously determined continuous positive airway pressure (CPAP). Spontaneous breathing is possible without restriction at both levels. The results of laboratory and human studies have suggested that APRV supports alveolar ventilation and arterial oxygenation with lower peak Paw compared with IPPV. However, to put APRV to use effectively and safely without the development of respiratory acidemia, a method that facilitates CO₂ elimination is required.

*From the Division of Intensive and Critical Care Medicine, Department of Anesthesiology, Kumamoto University School of Medicine, Kumamoto, Japan.


Manuscript received February 6, 1996; revision accepted November 6.

Reprint requests: Dr. Okamoto, Division of Intensive and Critical Care Medicine, Kumamoto University School of Medicine, 1-1-1 Honjo, Kumamoto 860, Japan.
Tracheal gas insufflation (TGI) is a technique in which fresh gas is introduced into the trachea. At a constant flow rate, this has been found to produce alveolar ventilation in apneic dogs when the tip of the insufflation catheter is positioned just above or beyond the carina. In addition, it has been shown that TGI effectively augments alveolar ventilation by reducing anatomic dead space when combined with spontaneous respiration, and chest compression during cardiopulmonary resuscitation.

There are two methods of APRV. The first is a continuous-flow type, and the second is a demand-flow type. In the former, continuous gas flow is required to maintain CPAP. We hypothesized that continuous gas flow maintained through an insufflation catheter positioned above the carina during APRV would facilitate CO₂ elimination, resulting in normocarbia and a substantial reduction in peak Paw. To test this hypothesis, we compared IPPV, TGI, APRV, and combined TGI and APRV (TGI+APRV) in a canine restrictive-thorax model with and without pulmonary edema.

Materials and Methods

Animal Preparation

The protocol for this study was approved by the Animal Research and Use Committee of Kumamoto (Japan) University School of Medicine. Six healthy mongrel dogs weighing 10 to 12 kg (mean ± SD, 11 ± 1 kg) were anesthetized with ketamine (10 mg/kg IM) and diazepam (3 mg/kg IV), and were paralyzed with pancuronium bromide (0.2 mg/kg IV). The dogs were anesthetized and paralyzed to suppress spontaneous respiration so that this variable would not complicate the comparison of the four ventilatory modes. Anesthesia and muscle paralysis were maintained by continuous IV infusions of ketamine (5 mg/kg/h), diazepam (1 mg/kg/h), and pancuronium bromide (0.2 mg/kg/h). The dogs were placed in the supine position and subjected to tracheostomy. A tracheostomy tube (9.0 mm internal diameter; Portex; Kent, England) with an inflatable cuff was then inserted. IPPV was performed with volume-controlled ventilation (Ventilator E100; Newport Medical Instruments; Newport, Calif) under expiratory minute ventilation (Ve) monitoring (Haloscale; Ferraris Development & Engineering; London, UK).

The right femoral artery was catheterized for measurement of the mean arterial pressure (MAP) and arterial blood gases. The right femoral vein was catheterized for volume infusion and administration of drugs. A Swan-Ganz flow-directed thermodilution catheter (93A-131F-7F; American Edwards Lab; Irvine, Calif) was inserted via the left femoral vein into the pulmonary artery under pressure waveform guidance for measurement of pulmonary artery pressure (PAP), central venous pressure (CVP), pulmonary artery wedge pressure (PAWP), mixed venous blood gases, and cardiac output (CO). All vascular pressure monitors were connected to transducers (Statham P23ID; Gould; Cleveland, Ohio), and zeroed at the midthoracic rib cage with the dog in supine position. Monitoring was performed with a polygraph (RM-6200; Nihon Kohden; Tokyo, Japan). CO was measured in triplicate using 10-mL injections of 5% dextrose in water at room temperature and a CO computer (SAT-1; American Edwards Lab). Blood gas samples were studied with a pH/blood gas analyzer (Corning 170; Chiba Corning Diagnostics Co; Medfield, Mass). The blood gas analyzer was calibrated prior to each determination. All blood gas values were corrected for body temperature. Lead II of the ECG was monitored for measurement of heart rate (HR). Hemoglobin (Hb) was measured with an Hb meter (HB-350; Erma; Tokyo, Japan). Oxygen content (O₂) was calculated using the following formula:

\[ O_2 = (0.0031 \times P_O_2) + (Hb \times S_O_2 \times 1.39) \]

where P_O₂ is oxygen tension and S_O₂ is oxygen saturation. Venous admixture was calculated using the following formula:

\[ QV/QT = (C_a O_2 - C_a O_2)/(C_a O_2 - C_v O_2) \]

where C_aO₂ and C_vO₂ were the calculated arterial and mixed venous oxygen contents, respectively, and C_aO₂ was the pulmonary capillary oxygen content, estimated from the alveolar gas equation assuming a respiratory quotient (R) of 0.8. Oxygen delivery (DO₂), oxygen consumption (VO₂), and oxygen extraction (EO₂) were calculated using the following formulas:

\[ DO_2 = CO \times C_a O_2 \times 10 \]

\[ VO_2 = CO \times (C_a O_2 - C_v O_2) \times 10 \]

\[ EO_2 = VO_2/DO_2 \]

Body temperature was monitored with the Swan-Ganz thermodilution catheter and maintained within the normal range using a fluid-filled heating pad.

TGI, APRV, and TGI+APRV Circuits

The three circuits are illustrated in Figure 1. A single-lumen catheter (2.0 mm internal diameter and 2.7 mm outer diameter) was used for TGI. A smaller catheter (1.5 mm internal diameter and 2.0 mm outer diameter) was used to monitor Paw. After the tracheostomy tube was withdrawn, the tip of the TGI catheter was advanced to 1 cm above the carina under bronchoscopic guidance. The tip of the Paw monitoring catheter was placed 2 cm beyond the carina. Each catheter was previously fixed to a metal rod to facilitate insertion and maintain constant orientation. The TGI catheter was connected to a gas delivery system consisting of a flowmeter and an air-oxygen blender attached to the above-mentioned ventilator and a heated humidifier (MR 310: Fisher-Paykel Medical Inc; Auckland, New Zealand). To match for the inspiratory fraction of oxygen (FIO₂), the same air-oxygen blender was used for the comparisons of the four ventilatory modes. The Paw monitoring catheter was connected to a pressure transducer (TP-200T; Nihon Kohden; Tokyo, Japan), and the tracheostomy tube was reinserted.

During TGI, the fresh gas was administered through the catheter above the carina, and the outflow gas was exhaled through the tracheostomy tube into the atmosphere.

The APRV circuit consisted of the aforementioned gas delivery system and an APRV device. The APRV device consisted of a threshold resistor valve regulating the CPAP level and a solenoid release valve controlled by a timer. The solenoid release valve was connected to the expiratory limb in contact with the atmosphere. This APRV circuit was constructed using the basic principles of APRV as described by Stock and Downs and coworkers. The solenoid release valve was closed, Paw was equal to the pressure generated by a threshold resistor valve (Vital Sigus; Totowa, NJ). When the valve was open, gas escaped into the atmosphere at near-ambient pressure. Thus, during APRV, both the gas inflow and outflow were through the tracheostomy tube.
In the TGI+APRV circuit, fresh gas was administered continuously through the TGI catheter above the carina. The outflow gas was exhaled through the tracheostomy tube, which was connected to the expiratory limb. The APRV device regulated the CPAP level and the timing of pressure release into the atmosphere.

**Experimental Protocol**

*Restrictive-Thorax Model Without Pulmonary Edema*: The chest wall compliance in the dog is greater than that in the human. To produce a reduced compliance model, we constricted the thorax and abdomen of the dogs using a band to limit thoracic and diaphragmatic movement. The static compliances of the lungs and thoracic cage were measured by simultaneously clamping both the inflow and outflow lines just after the lungs were inflated using exactly 100 mL. The static compliance (mean ± SD) decreased from 1.6±0.7 to 0.9±0.3 mL/cm H₂O/kg after restriction of the thorax and diaphragm. Prior to data collection, the dogs were initially ventilated with IPPV with an FIO₂ of 0.6, an inspiratory to expiratory time ratio of 1:3 with an inspiratory time of 1 s, and a ventilatory frequency of 15 cycles/min. Under these conditions, the tidal volume to maintain PaCO₂ at 40 mm Hg was predetermined. Subsequently, the dogs were ventilated with TGI+APRV with an FIO₂ of 0.6, a TGI gas flow of 10 L/min, a CPAP to release time ratio of 3:1 with a release time of 1 s, and a release frequency of 15 cycles/min. Under these conditions, the CPAP required to maintain the PaCO₂ at 40 mm Hg was predetermined.

The effects of each of the four ventilatory modes on the respiratory and cardiovascular systems were examined. The order of application of the four different ventilatory modes was randomized. During IPPV, the FIO₂ was set at 0.6, the inspiratory to expiratory time ratio at 1:3 with an inspiratory time of 1 s, and the ventilatory frequency at 15 cycles/min. The tidal volume was set at the predetermined value. During TGI, the FIO₂ was set at 0.6 and the gas flow at 10 L/min. During APRV, the FIO₂ was set at 0.6, the gas flow rate at 10 L/min, the CPAP to release time ratio at 3:1 with a release time of 1 s, and the release frequency at 15 cycles/min. The CPAP was set at the value that was predetermined during TGI+APRV. During TGI+APRV, the FIO₂ was set at 0.6, the gas flow rate at 10 L/min, the CPAP to release time ratio at 3:1 with a release time of 1 s, and the release frequency at 15 cycles/min. The CPAP was set at the predetermined value.

Arterial and pulmonary arterial blood samples were obtained 20 min after the start of each ventilatory mode for blood gas analysis. Hemodynamic parameters were obtained at these time points. Prior to the start of the next ventilatory mode, the dogs were placed on IPPV at an accelerated rate of 30 cycles/min for 5 min, and the ventilatory frequency was decreased to 15 cycles/min. Ventilation at this frequency was maintained for at least 15 min under end-tidal CO₂ monitoring (OIR-7101; Nihon Kohden). Arterial blood gas analysis was repeated until a steady state was noted. This technique was used to ensure that the body stores of CO₂ had returned to approximately baseline values before the next ventilatory mode was tested.

*Restrictive-Thorax Model With Pulmonary Edema*: After the completion of data collection in the canine restrictive-thorax model without pulmonary edema, 0.07 mL/kg of pure oleic acid (Katayama Chemical Co; Osaka, Japan) in 20 mL of 0.9% sodium chloride was vigorously agitated in a vortex for 30 s and then injected into the right atrium to induce acute lung injury. To minimize the variability in pulmonary edema formation, PAWP was maintained at 9 mm Hg by infusing lactated Ringer’s solution. Lung injury was allowed to develop for 90 min under IPPV. The static compliance decreased to 0.8±0.3 mL/cm H₂O/kg. The effects of the four ventilatory modes on the respiratory and cardiovascular systems were examined again in these models with pulmonary edema. The order of application of the four different ventilatory modes was randomized.

**Data Analyses**

The results are expressed as mean±SD. Statistical analysis of differences among the four groups was performed using one-way analysis of variance. Comparisons between the groups were made using the Student’s paired t test with the Bonferroni correction. A p value of <0.05 was considered significant.
RESULTS

Restrictive-Thorax Model Without Pulmonary Edema

An airway pressure recording from one experimental animal during the four ventilatory modes is shown in Figure 2. There were significant differences among the four ventilatory modes in expiratory VE, peak, mean, and end-expiratory Paw, arterial blood gases, Qv/Qt ratio, MAP, HR, mean PAP, CVP, CO, Do2, and Eo2 (Table I and Fig 3). IPPV and TGI+APRV produced normocarbia. Implementation of TGI alone resulted in severe hypercarbia and a significant increase in Qv/Qt ratio even though the gas flow was set at the same value as in TGI+APRV. MAP elevated and HR decreased during TGI. APRV alone did not maintain normocarbia even though the gas flow rate, the release time, the release frequency rate, and the CPAP were set at the same values as used in TGI+APRV. The mean PaCO2 during APRV was significantly higher than that during TGI+APRV. The arterial pH and PaO2 during APRV were significantly lower than those during TGI+APRV. Except for peak and mean Paw along with expiratory VE, the respiratory and cardiovascular parameters during IPPV were not significantly differ-
end-expiratory Paw, arterial blood gases, Qv/Qt ratio, HR, PAWP, and CVP (Table 2 and Fig 4). IPPV and TGI+APRV produced normocarbia. As was found in the model without pulmonary edema, implementation of TGI alone resulted in severe hypercarbia and a significant increase in Qv/Qt ratio. MAP tended to elevate and HR decreased during TGI. The mean PaCO2 was significantly higher during APRV than during TGI+APRV. The mean arterial pH was significantly lower during APRV than during TGI+APRV. Except for expiratory VE and peak Paw, the respiratory and cardiovascular parameters during IPPV did not significantly differ from those during TGI+APRV. The mean peak Paw was significantly lower during TGI+APRV than during IPPV, but the mean value of the mean Paw during TGI+APRV did not differ from that during IPPV.

**DISCUSSION**

In this canine restrictive-thorax model with and without pulmonary edema, TGI combined with APRV facilitated CO2 elimination, resulting in maintenance of normocarbia and oxygenation with a significantly reduced peak Paw compared with IPPV. Peak Paw was significantly lower during TGI+APRV than during IPPV. APRV alone did not maintain normocarbia. This suggests that the combined use of TGI and APRV is a more effective method of maintaining normocarbia and oxygenation with reduced peak Paw than either IPPV or APRV alone.

There is a clear association between high peak Paw and pulmonary barotrauma. Petersen and Baier, in a survey of 171 patients with acute respiratory failure, have reported that peak Paw averaged 81 ± 6 cm H2O in patients with barotrauma and 48 ± 14 cm H2O in those without an air leak. No air leak was observed at a peak Paw of <50 cm H2O. Woodring has reported that barotrauma occurs at or above a Paw of 40 cm H2O in patients with acute respiratory distress syndrome. In experimental studies, it has been shown that ventilation with a high peak Paw can induce alveolar epithelial and capillary injury. In addition, associations have been described between PEEP, mean Paw, inspiratory plateau pressure (Pplat), and underlying disease and development of barotrauma. A study in animal models suggests that alveolar overdistention is the most important determinant of lung injury. Theoretical analyses indicate that mean Paw and Pplat may more closely reflect alveolar pressure. For prevention of these ventilator-induced pulmonary complications, peak Paw, mean Paw, and Pplat should be maintained as low as possible, and alveolar overdistention should be avoided.

**Restrictive-Thorax Model With Pulmonary Edema**

There were significant differences among the four ventilatory modes in expiratory VE, peak, mean, and

![Figure 3](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21747/)

*Figure 3.* Individual values for peak Paw, PaO2, and PaCO2 during IPPV, TGI, TGI+APRV, and APRV in the canine restrictive-thorax model without pulmonary edema.
Table 2—Effects of IPPV, TGI, TGI+APRV, and APRV on the Respiratory and Cardiovascular Parameters in the Canine Restrictive-Thorax Model With Pulmonary Edema

<table>
<thead>
<tr>
<th></th>
<th>IPPV</th>
<th>TGI</th>
<th>TGI+APRV</th>
<th>APRV</th>
<th>ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>$V_t$ or CGF, L/min</td>
<td>3.1±0.9</td>
<td>10.2±0.3</td>
<td>10.3±0.3</td>
<td>1.3±0.3</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Peak Paw, cm H$_2$O</td>
<td>34±10</td>
<td>2±1</td>
<td>20±4</td>
<td>18±4</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Mean Paw, cm H$_2$O</td>
<td>9±3</td>
<td>2±1</td>
<td>14±3</td>
<td>14±4</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>End-expir Paw, cm H$_2$O</td>
<td>0±0</td>
<td>2±1</td>
<td>2±1</td>
<td>0±0</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>Arterial pH</td>
<td>7.25±0.01</td>
<td>6.94±0.1</td>
<td>7.36±0.06</td>
<td>7.11±0.06</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>PaO$_2$, mm Hg</td>
<td>177±77</td>
<td>71±34</td>
<td>157±72</td>
<td>161±73</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>PaCO$_2$, mm Hg</td>
<td>41±3</td>
<td>121±34</td>
<td>40±3</td>
<td>68±9</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Base excess, mEq/L</td>
<td>-8±2</td>
<td>-11±3</td>
<td>-8±3</td>
<td>-10±2</td>
<td>NS</td>
</tr>
<tr>
<td>Qv/Ql, %</td>
<td>18±8</td>
<td>58±18</td>
<td>19±8</td>
<td>25±15</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>MAP, mm Hg</td>
<td>137±23</td>
<td>153±54</td>
<td>138±19</td>
<td>137±26</td>
<td>NS</td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>158±23</td>
<td>95±21</td>
<td>168±22</td>
<td>152±10</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Mean PAF, mm Hg</td>
<td>15±6</td>
<td>18±3</td>
<td>18±8</td>
<td>19±7</td>
<td>NS</td>
</tr>
<tr>
<td>PAWP, mm Hg</td>
<td>8±4</td>
<td>11±2</td>
<td>9±5</td>
<td>10±4</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>GVP, mm Hg</td>
<td>3±1</td>
<td>6±2</td>
<td>5±1</td>
<td>5±1</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>CO, L/min</td>
<td>2.4±0.7</td>
<td>2.4±0.6</td>
<td>2.3±0.6</td>
<td>2.5±0.8</td>
<td>NS</td>
</tr>
<tr>
<td>DO$_2$, mL/min</td>
<td>539±209</td>
<td>421±137</td>
<td>521±181</td>
<td>533±240</td>
<td>NS</td>
</tr>
<tr>
<td>VO$_2$, mL/min</td>
<td>101±40</td>
<td>95±46</td>
<td>113±61</td>
<td>89±40</td>
<td>NS</td>
</tr>
<tr>
<td>Eo$_2$, %</td>
<td>19±2</td>
<td>24±11</td>
<td>22±5</td>
<td>16±3</td>
<td>NS</td>
</tr>
<tr>
<td>Hb, g/dL</td>
<td>14.8±2.5</td>
<td>14.4±3.4</td>
<td>14.4±3.5</td>
<td>14.5±3.4</td>
<td>NS</td>
</tr>
</tbody>
</table>

*See Table 1 for explanation of abbreviations.

1 p<0.01 vs IPPV.
2 p<0.05 vs IPPV.
3 p<0.01 vs TGI.
4 p<0.05 vs TGI.
5 p<0.01 vs TGI+APRV.

APRV is a recently developed mode of ventilation affording lower peak Paw compared with IPPV. In APRV and IPPV, both inspiration and expiration are through an endotracheal tube. Thus, the dead space of the upper airway is preserved. A technique that reduces dead space should decrease the tidal volume required to maintain normocarbia, resulting in a decrease in peak Paw during mechanical ventilation. Tracheostomy may be performed to bypass the anatomic dead space of the upper airway. The other strategy that can be used to decrease the anatomic dead space is TGI. Sznapider and coworkers have shown that continuous positive pressure ventilation combined with TGI facilitates CO$_2$ elimination, resulting in normocarbia and oxygenation with a significantly reduced peak Paw in a canine pulmonary edema model. Nahum and coworkers have also demonstrated the effectiveness of the combined use of TGI and pressure-controlled or volume-controlled ventilation in the augmentation of alveolar ventilation in dogs. In this study, APRV combined with TGI facilitated CO$_2$ elimination more efficiently than did APRV alone in the dog with and without pulmonary edema. Peak Paw during TGI+APRV was maintained at a significantly lower level than during IPPV. These effects of TGI on the augmentation of alveolar ventilation during TGI+APRV are consistent with those reported in previous studies of mechanical ventilation.

The beneficial effects of TGI on the reduction of anatomic dead space have been demonstrated during mechanical ventilation as well as during spontaneous respiration. TGI has been shown to effectively augment alveolar ventilation in hypercapnic patients by reducing the anatomic dead space when combined with spontaneous respiration. The dogs in this study were anesthetized and paralyzed to suppress spontaneous respiration so that comparisons between groups would not be complicated. Thus, APRV in this study essentially becomes pressure control inverse ratio ventilation. However, APRV is fundamentally a ventilatory method in which unrestricted spontaneous breathing is possible at both CPAP and lower levels of support. Suppression of spontaneous respiration represents the worst possible case for CO$_2$ elimination during TGI+APRV. Should TGI+APRV be performed as a partial support of spontaneous respiration, it is possible that CO$_2$ elimination would be further enhanced, resulting in significant decreases in peak and mean Paw.

The mean Paw was maintained at higher levels during TGI+APRV than during IPPV in both models. However, there were no significant differences in CO or DO$_2$ between TGI+APRV and IPPV. Because an elevated mean Paw increases pleural pressure, venous return and CO may be impaired more by TGI+APRV than by IPPV. However, with the spontaneous respiration allowed during
TGI+APRV, pleural pressure may be maintained at a lower level, and the venous thoracic pump mechanism may be less impaired. Thus, it is possible that CO and DO₂ would be less impaired. Further study is needed to determine the effects of spontaneous respiration on Paw and on hemodynamics.

Incidentally, the Pplat has received much attention as a better potential predictor of barotrauma. A recent consensus conference on mechanical ventilation recommended that Pplat should be limited to 35 cm H₂O in acute respiratory distress syndrome. However, Gammon and coworkers have reported that there is no independent relationship between Pplat and barotrauma in patients with acute respiratory distress syndrome. In the present study, IPPV was performed by the ventilator without a function of Pplat. We therefore cannot make reference to barotrauma risk regarding Pplat during IPPV. However, this does not affect our conclusion that APRV combined with TGI facilitated CO₂ elimination more efficiently than APRV alone.

TGI alone caused a significant increase in Qv/Qt ratio that was easily restored to its original condition by applying IPPV. The finding is consistent with that of Vettermann and coworkers. They have shown that TGI causes a significant increase in ventilation perfusion mismatching, which may be due to non-uniform ventilation distribution and a redistribution of pulmonary blood flow. In addition, we calculated Ce’O₂, assuming an R value of 0.8. Due to inadequate CO₂ elimination during the period of TGI, R must have been lower; therefore, Qv/Qt values during TGI were overestimated.

HR decreased despite increased PaCO₂ during TGI. This finding is consistent with that of Kristoffersen and coworkers. They have shown that HR decreases in the levels of about 100 to 200 mm Hg of PaCO₂ during apneic oxygenation in anesthetized dogs. Although the precise mechanism is unclear, anesthesia may modulate the response to increased PaCO₂.

The specific effects of acute hypercarbic acidosis on cardiac function have not been fully explored. Tang and coworkers have shown that increases in PaCO₂ produce corresponding decreases in myocardial contractility. Circulatory collapse occurs when arterial pH reaches 6.5. In the pulmonary edema model, arterial pH reached 6.94 and PaCO₂ reached 121 mm Hg in only 20 min during TGI. This may be why cardiac output in the TGI group with pulmonary edema was similar to that in the other groups despite significantly lower intrathoracic pressures. In addition, we measured PAWP to assess preload. During TGI and TGI+APRV, we observed a small increase in end-expiratory Paw, which might affect PAWP. To determine the precise effects of TGI on hemodynamics, further study is needed under a monitoring of transmural PAWP, which assesses preload more accurately.

Finally, the new ventilator system we have developed that combines TGI with APRV facilitates CO₂ elimination better than APRV alone, resulting in maintenance of normocarbia and oxygenation with a significantly reduced peak Paw compared with IPPV. However, some issues remain to be resolved prior to

![Figure 4. Individual values for peak Paw, PaO₂, and PaCO₂ during IPPV, TGI, TGI+APRV, and APRV in the canine restrictive-thorax model with pulmonary edema.](image-url)
the clinical application of this technique. The tip of the TGI catheter was placed 1 cm above the carina. The effects of changing the TGI catheter position on gas exchange during TGI+APRV are uncertain, although the results of previous studies have suggested that precise catheter placement is not crucial during combined use of TGI and IPPV, provided that the catheter tip lies within a few centimeters of the carina. In humans, the TGI flow rate required for effective elimination of CO₂ and the optimal humidification during TGI+APRV remain to be determined. In addition, we observed the development of intrinsic PEEP during TGI+APRV, probably due to the momentum of TGI and an increase in the expiratory resistance. The risk of pulmonary barotrauma due to an accidental increase of intrinsic PEEP must be taken into account. A reliable pressure relief system to stop catheter flow during endotracheal tube occlusion as well as systems to monitor alveolar pressures and volume are required.

In conclusion, the combined use of TGI and APRV is a more effective method for augmentation of alveolar ventilation with reduced peak Paw than either IPPV or APRV alone. This combined ventilation mode has the potential to decrease the frequency of complications resulting from high peak Paw during IPPV, and to improve the outcome of patients in acute respiratory failure.

References
11 Cane RD, Peruzzi WT, Shapiro BA. Airway pressure release ventilation in severe acute respiratory failure. Chest 1991; 100:460-63
32 Slutsky AS. Mechanical ventilation. Chest 1993; 104:1833-59
33 Dreyfuss D, Saumon G. Role of tidal volume, FRC, and end-inspiratory volume in the development of pulmonary edema following mechanical ventilation. Am Rev Respir Dis 1993; 148:1194-1203