Combined Effects of Inversed Ratio Ventilation (IRV) with Positive End-expiratory Pressure Ventilation (PEEP) on Cardiorespiratory Function in Acute Respiratory Failure

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Combined effects of inversed ratio ventilation (IRV) with positive end-expiratory pressure (PEEP) on cardiorespiratory function were examined in 24 patients with acute respiratory failure. Patients were divided into two groups: the IRV group (n=12) who showed no significant increase in Pa_{O_2} with a 6 cmH_2O of PEEP and PEEP group (n=12) who were ventilated mechanically with PEEP only at maximum level of 10 cmH_2O. In IRV group step-wise prolongation of the I:E ratio from 1:1.9 to 2.6:1 or 4:1 was applied as a Pa_{O_2} was improved and in PEEP group also level of PEEP was increased from 0, 5 to 10 cmH_2O after one hour period irrespective of Pa_{O_2}. Inversed ratio ventilation and PEEP increased significantly Pa_{O_2}/FI_{O_2}, the increase being observed 6 hrs (I:E = 2:1) and 2 hrs (10 cmH_2O) after starting IRV or PEEP. Further improvement of oxygenation was not observed in IRV even if I:E ratio was prolonged up to 2.6:1 or 4:1. These results suggested that combinations of IRV with PEEP were effective and an I:E ratio of 2:1 may be optimal, and IRV is advantageous compared to PEEP, but will take more long time to improve oxygenation than PEEP. (Key words: mechanical ventilation, IRV, I:E ratio, PEEP, cardiac output, oxygen delivery)

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The most commonly used method of improving oxygenation in a ventilated patient with acute respiratory failure (ARF) is the application of positive end-expiratory pressure (PEEP). However, application of PEEP is not necessarily without complication of reduction of cardiac output (CO)[1], redistribution of blood flow from well-ventilated to poorly ventilated regions of the lung[2], and pulmonary barotrauma (PBT) due to high peak airway pressure[3]. Therefore, various efforts had been exercised to find more effective ventilatory pattern with less adverse effects. It has been reported by Reynolds et al.[4] and Reynolds[5] first that a similar improvement occurs at significantly lower peak inspiratory pressure than PEEP when the inspiratory: expiratory time ratio is inverted to 2:1 or even 3:1 or 4:1. Since it has been suggested that the use of inversed ratio ventilation (IRV) may be preferable to the

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Table 1. Patient's characteristics

Mode of ventilation	IRV	PEEP
No. of patients	12	12
Age (yr)	66 ± 17	58 ± 18
Sex		
female	7	7
male	5	5
Causes of ARF		
pulmonary infection	5	4
sepsis	3	4
cardiogenic ARF	3	3
aspiration	1	1
Days of mechanical ventilation	17 ± 19	13 ± 12
Complications	2	0
Outcome		
survived	5	4
died	7	8

Abbreviation; see text, Mean ± SD

use of PEEP because peak pressure is less thus diminishing the risk of BTR. Inversed ratio ventilation has been applied experimentally and clinically to ARF to improve arterial oxygenation. However, improvement in arterial oxygenation by IRV is controversial, some investigators reported beneficial effects of IRV[6–8], but others showed no advantage[9–12]. This discrepancy might be due to different periods of IRV or difference in subjects, experimental animals or human diseases. We, therefore, examined the effects of IRV in combination with PEEP on Pa_{O_2} with time in 12 patients with ARF of diverse causes when PEEP failed to increase Pa_{O_2} and compared them with those of PEEP in other patients.

Methods

Twenty-four patients (table 1) were studied who had ARF from diverse causes which necessitated mechanical ventilation. All patients were mechanically ventilated by a Servo 900 C ventilator (Siemens-Elema, Sweden). They were sedated with intravenous injection of diazepam or buprenorphine and were paralyzed with pancuronium bromide for facilitating mechanical ventilation. The IRV group consisted of twelve patients in whom Pa_{O_2} could not be maintained above 80 mmHg while breathing 100 per cent of oxygen or the peak inspiratory pressure (PIP) exceeded 40 cmH_2O at 6 cmH_2O of PEEP. For comparison of respiratory and hemodynamic effects of IRV with PEEP, patients who were able to expect improvement of oxygenation by PEEP were considered candidates for PEEP. The PEEP group consisted of twelve patients in whom Pa_{O_2} could not be maintained above 100 mmHg while breathing 100 per cent of oxygen. Both groups were otherwise treated similarly.

All patients continuously received intravenous infusion of dopamine at a rate of 5–10 $\mu g \cdot kg^{-1} \cdot min^{-1}$. Patients with cardiogenic ARF received sodium nitroprusside at a rate of 3–5 $\mu g \cdot kg^{-1} \cdot min^{-1}$, or dobutamine at a rate of 5–10 $\mu g \cdot kg^{-1} \cdot min^{-1}$ in combination with dopamine for maintain adequate arterial blood pressure or filling pressure.

Study Protocol

In the IRV group, the I:E ratio was increased stepwise from 1:2 to 2:1 and to 2.6:1 or 4:1. Prolonged inspiratory time was superimposed with 6 cmH_2O of PEEP, because reduction in PEEP level might lead patients to hypoxemia. In the PEEP group, when Pa_{O_2} was not maintained above 100 mmHg on FI_{O_2} of 1.0, PEEP was increased stepwise from 0 to 5, and to 10 cmH_2O ev-

Table 2. Effects of IRV on pulmonary functions in patients with ARF

Variables/I:E ratio		1:2	2:1	2.6–4:1
FI_{O_2}		1.0	1.0	1.0
Pa_{O_2}	mmHg	65 ± 15	115 ± 42*	136 ± 45*
Pa_{CO_2}	mmHg	51 ± 15	52 ± 13	51 ± 15
pH		7.41 ± 0.13	7.41 ± 0.12	7.38 ± 0.04
Base Excess	$mEq \cdot l^{-1}$	8 ± 8	7 ± 4	5 ± 7
A-aDO_2	mmHg	581 ± 65	452 ± 130	461 ± 143
$\dot{Q}s/\dot{Q}t$	%	42 ± 11	30 ± 10*	27 ± 5*
Pa_{O_2}/FI_{O_2}		65 ± 15	115 ± 42*	136 ± 46*
PIP	cmH_2O	25 ± 5	26 ± 7	33 ± 9
MAWP	cmH_2O	10 ± 4	13 ± 5	17 ± 7

*Significantly different from values of an I:E ratio of 1:2 ($P < 0.05$)

ery one hour after application of each value of PEEP. Systemic and pulmonary hemodynamics, blood gas, oxygen consumption ($\dot{V}O_2$), oxygen delivery ($\dot{D}O_2$), and oxygen content in arterial and mixed venous blood (Ca_{O_2} and $C\bar{v}_{O_2}$) were measured in both IRV and PEEP groups at each step.

Measurements

Radial artery was cannulated for the measurement of arterial pressure and blood sampling. Flow-directed pulmonary artery catheter (Edward Laboratories, MA, U.S.A.) was percutaneously placed in the pulmonary artery through the right internal jugular vein to measure the right atrial pressure (RAP), mean pulmonary arterial pressure (MPAP), pulmonary capillary wedge pressure (PCWP), and CO. The catheter's position was confirmed by a portable chest radiographic and visualization of the appropriate pressure wave forms in the pulmonary artery. Cardiac output was determined by thermodilution technique using 10 ml of 5% dextrose and water cooled to 0°C. Pulmonary vascular resistance (PVR) was calculated from the ratio of the difference between MPAP and PCWP, and CO. All measurements of pressure, including PIP, mean airway pressure (MAWP) and of CO were taken on the day of admission to the ICU and then at 2 to 6 hrs after changing I:E ratio in IRV group and at 1 hr after changing PEEP level. Values were the means of triplicated measurements. Arterial and mixed venous P_{O_2}, P_{CO_2}, and pH were measured with a blood gas analyzer (178 pH/Blood Gas Analyzer, Corning Medical and Scientific, MA, USA). Oxygen saturation (Sa_{O_2}, $S\bar{v}_{O_2}$) and concentration of hemoglobin in blood (Hb) were measured with a Hemoximeter (OSM2, Radiometer, Copenhagen, Denmark). Oxygen content was calculated from hemoglobin oxygen-carrying capacity and the amount of dissolved oxygen, as estimated from Pa_{O_2} and oxygen solubility. The intrapulmonary shunt was calculated using the standard equation[13]; $\dot{Q}s/\dot{Q}t = Cc'_{O_2} - Ca_{O_2}/Cc'_{O_2} - C\bar{v}_{O_2}$, where Cc'_{O_2} is pulmonary capillary oxygen content. To calculate $\dot{Q}s/\dot{Q}t$ we assumed that pulmonary capillary oxygen tension was the same as alveolar oxygen tension. A ratio of Pa_{O_2}/FI_{O_2} was calculated as an index of arterial oxygenation. The oxygen delivery was calculated as the product of Ca_{O_2} and CO. Using the Fick principle $\dot{V}O_2$ was calculated as follows; $\dot{V}O_2 = CO \times (Ca_{O_2} - C\bar{v}_{O_2})$.

Data analysis

All variables were calculated with a programable calculator (HC-20, Epson, Shinshu Seiki, Tokyo, Japan). All values are expressed as mean + standard deviation (SD). The data were analyzed statistically using analysis of variance. P value of < 0.05 was considered statistically significant.

Results

Patient's characteristics are shown in table 1.

Table 3. Effects of IRV on pulmonary hemodynamics and oxygen delivery in patients with ARF

Variables/I:E ratio		1:2	2:1	2.6–4:1
CI	$ml \cdot min^{-1} \cdot m^{-2}$	3.7 ± 1.7	4.2 ± 1.7	3.0 ± 0.7
SVI	$ml \cdot b^{-1} \cdot m^{-2}$	32 ± 14	32 ± 13	30 ± 11
MAP	mmHg	78 ± 15	84 ± 17	67 ± 16
HR	$b \cdot min^{-1}$	116 ± 29	113 ± 20	107 ± 18
CVP	mmHg	8 ± 4	8 ± 3	11 ± 3
SVR	dyn $sec \cdot cm^{-5}$	1163 ± 553	1227 ± 497	995 ± 243
PCWP	mmHg	11 ± 6	10 ± 4	11 ± 3
LVSWI	$gm\text{-}m \cdot m^{-2} \cdot b^{-1}$	30 ± 16	31 ± 18	32 ± 12
RVSWI	$gm\text{-}m \cdot m^{-2} \cdot b^{-1}$	9 ± 8	10 ± 7	9 ± 6
MPA	mmHg	23 ± 8	24 ± 8	24 ± 9
PVR	dyn $sec \cdot cm^{-5}$	195 ± 121	223 ± 113	225 ± 84
$P\bar{v}_{O_2}$	mmHg	35 ± 6	38 ± 5	39 ± 7
Ca_{O_2}	vol%	12 ± 3	13 ± 4	12 ± 1
$C\bar{v}_{O_2}$	vol%	8 ± 3	9 ± 3	7 ± 2
$\dot{V}O_2$	$ml \cdot min^{-1} \cdot m^{-2}$	164 ± 79	175 ± 81	146 ± 25
$\dot{D}O_2$	$ml \cdot min^{-1} \cdot m^{-2}$	507 ± 253	591 ± 273	378 ± 164

Abbreviation; see text, mean ± SD

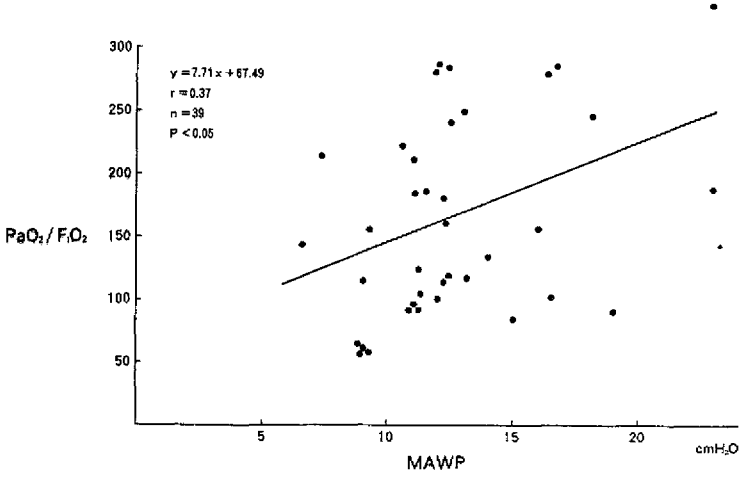

Fig. 1. Correlation between Pa_{O_2}/FI_{O_2} (y) and mean airway pressure (MAWP) (x) during inversed ratio ventilation (IRV). Regression equation is y = 7.71x + 67.49 (r = 0.37, n = 39, $P < 0.05$).

IRV group

Table 2 shows the changes of respiratory variables and table 3 shows systemic and pulmonary hemodynamics, and $\dot{D}O_2$ and $\dot{V}O_2$, respectively. Significant improvements in Pa_{O_2}, $\dot{Q}s/\dot{Q}t$, and Pa_{O_2}/FI_{O_2} were observed by increasing I:E ratio from 1:2 to 2:1, but not from 2:1 to 2.6:1 or 4:1. Positive linear relationship was observed between Pa_{O_2}/FI_{O_2} (y) and MAWP (x) (y = 7.71x + 67.49, r = 0.37, n = 39, $P < 0.05$, fig 1). Arterial P_{O_2} and Pa_{O_2}/FI_{O_2} did not improve significantly until 3 hrs after initiation of IRV. A linear correlation existed between Pa_{O_2}/FI_{O_2} (y) and time course (x) including various I:E ratio, the regression equation being y = 11.29x + 76.17 (r = 0.75, n = 33, $P < 0.01$). There were no significant changes in parameters of pulmonary and systemic hemodynamics, tissue oxygenation or $\dot{D}O_2$.

Table 4. Effects of PEEP on pulmonary function in patients with ARF

Variables/PEEP		0	5	10
$F_{I_{O_2}}$		0.9 ± 0.1	0.8 ± 0.2	0.9 ± 0.1
Pa_{O_2}	mmHg	80 ± 27	102 ± 49	110 ± 25*
Pa_{CO_2}	mmHg	44 ± 9	49 ± 13	51 ± 11
pH		7.36 ± 0.10	7.36 ± 0.06	7.35 ± 0.05
Base Excess	$mEq \cdot l^{-1}$	5 ± 4	7 ± 4	7 ± 7
A-aD_{O_2}	mmHg	542 ± 76	440 ± 140	432 ± 117
$\dot{Q}s/\dot{Q}t$	%	43 ± 15	38 ± 16	36 ± 11
$Pa_{O_2}/F_{I_{O_2}}$		87 ± 32	127 ± 59	132 ± 30*
PIP	mmHg	23 ± 5	27 ± 9	28 ± 5
MAWP	mmHg	7 ± 2	9 ± 3*	15 ± 4**

Mean ± SD
*Significantly different from values of 0 cmH_2O of PEEP ($P < 0.05$)
**Significantly different between 5 and 10 cmH_2O of PEEP ($P < 0.01$)

Table 5. Effects of PEEP on hemodynamics in patients with ARF

Variables/PEEP		0	5	10
CI	$ml \cdot min^{-1} \cdot m^{-2}$	4.3 ± 0.4	4.6 ± 0.5	4.9 ± 1.7
SVI	$ml \cdot b^{-1} \cdot m^{-2}$	40 ± 13	40 ± 15	47 ± 13
MAP	mmHg	74 ± 11	79 ± 13	80 ± 16
HR	$b \cdot min^{-1}$	111 ± 28	117 ± 21	106 ± 23
CVP	mmHg	10 ± 5	10 ± 4	11 ± 5
SVR	dyn $sec \cdot cm^{-5}$	916 ± 489	931 ± 465	788 ± 348
PCWP	mmHg	13 ± 8	12 ± 5	13 ± 7
LVSWI	$gm \cdot m \cdot m^{-2} \cdot b^{-1}$	32 ± 12	36 ± 17	43 ± 17
RVSWI	$gm \cdot m \cdot m^{-2} \cdot b^{-1}$	14 ± 6	15 ± 8	18 ± 10
MPA	mmHg	28 ± 8	32 ± 20	26 ± 9
PVR	dyn $sec \cdot cm^{-5}$	240 ± 242	303 ± 358	146 ± 81
$P\bar{v}_{O_2}$	mmHg	39 ± 6	41 ± 5	43 ± 8
Ca_{O_2}	vol%	13 ± 5	13 ± 4	14 ± 5
$C\bar{v}_{O_2}$	vol%	10 ± 4	10 ± 4	11 ± 4
$\dot{V}_{O_2}$	$ml \cdot min^{-1} \cdot m^{-2}$	118 ± 40	124 ± 35	130 ± 60
$\dot{D}_{O_2}$	$ml \cdot min^{-1} \cdot m^{-2}$	492 ± 117	560 ± 220	654 ± 315

Abbreviation; see text, mean ± SD

No significant changes in Pa_{CO_2} and PIP were observed at any I:E ratio.

Patients had no complications related to IRV except for two cases with interstitial pneumonia, who developed a pneumothorax on the 2nd and 3rd day of following IRV with an I:E ratio of 2:1. A chest tube was effectively placed immediately after the episode. Seven patients died from multiple organ failure while on the ventilator in the ICU.

PEEP group

Table 4 shows the effects of PEEP on the respiratory parameters, and table 5 shows systemic and pulmonary hemodynamics, and $\dot{D}_{O_2}$ and $\dot{V}_{O_2}$. Significant increase in MAWP was observed when PEEP was elevated to 5 cmH_2O but not in Pa_{O_2} and $Pa_{O_2}/F_{I_{O_2}}$. When PEEP was elevated to 10 cmH_2O, both Pa_{O_2} and $Pa_{O_2}/F_{I_{O_2}}$ significantly increased in association with a significant increase in MAWP. The ratio of $Pa_{O_2}/F_{I_{O_2}}$

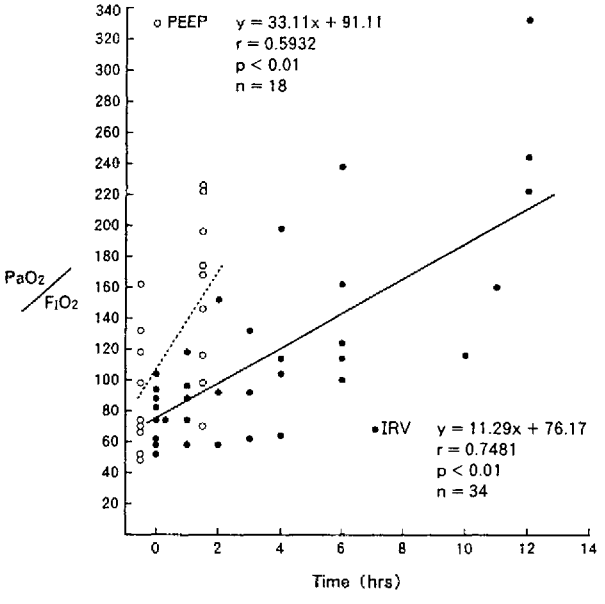

Fig. 2. Time course of changes in Pa_{O_2}/FI_{O_2} in the IRV (closed circles) and PEEP (open circles) at various levels. In both groups a linear correlation existed between Pa_{O_2}/FI_{O_2} (y) and time (x), and those equations were $y = 11.29x + 76.16$ ($r = 0.75$, $n = 33$, $P < 0.01$) and $y = 33.11x + 91.11$ ($r = 0.59$, $n = 18$, $P < 0.01$), respectively. There was a significant difference between the two equations ($P < 0.01$).

had increased significantly two hours after initiation of PEEP of 5 cmH_2O (fig. 2). There was linear relationship between Pa_{O_2}/FI_{O_2} and time course (x), the regression equation being $y = 33.11x + 91.11$ ($r = 0.59$, $n = 18$, $P < 0.01$). There were no correlation between Pa_{O_2} and MAWP. No significant changes in hemodynamics, or $\dot{D}O_2$ and $\dot{V}O_2$ were observed. Elevation of PEEP values increased MWAP significantly but it did not increase PIP.

There was no complication related to PEEP in this group. Eight patients died from multiple organ failure.

Discussion

The major findings of this study were that superimposition of IRV on PEEP was effective on arterial oxygenation when PEEP failed to raise Pa_{O_2} in patients with ARF of diverse causes but IRV produced pneumothorax in 2 patients, and there was difference in time in the manifestation of Pa_{O_2} improvement, i.e.; 6 hrs and 2 hrs after initiation of IRV and PEEP, respectively.

It is widely accepted that the improvement of arterial oxygenation by PEEP is caused by maintaining alveolar patency and by increasing the functional residual capacity (FRC). This mechanism may also explain the direct correlation between the change in FRC and Pa_{O_2} that follows a change in level of PEEP[14].

Why oxygenation improves during IRV is uncertain. One mechanism by which IRV is thought to exert its beneficial effects on Pa_{O_2}/FI_{O_2} is through increase in FRC. Increased FRC has also been postulated as mechanism for the effects attributed to PEEP[15].

Theoretically, mechanism for improvement of arterial oxygenation by IRV is explained by the following equation[16]: $FRC = Vt/e^{(t/Tc)} - 1$.

It can be shown that an increase in FRC will occur if the tidal volume (Vt) or the time constant (Tc) is increased or the expiratory time (t) is decreased, that is, inspiratory time is increased. Baum et al.[6] have suggested that prolonged inspiration may produce a "individual PEEP" which mainly affects the alveolar units with longer Tc. Clinically, Cole et al.[16] compared the effects of IRV and PEEP on external end-expiratory volume (EEEV) as approximated by changes measured by respiratory inductance plethysmography. The external end-expiratory volume was increased by IRV

an average of 1,200 ml. Similar changes in EEEV could be produced by an average of 12.8 cmH_2O of PEEP. However, improvement in oxygenation and ventilation could also be demonstrated by ratios of 1.1:1 and 1.7:1 that did not significantly change the EEEV. This may suggest that FRC change is not the sole determinant of the change of arterial oxygenation by IRV. In pediatric patients with severe lung disease, Boros[17] showed that increase in oxygenation by IRV was directly related to increase in MAWP and suggested that MAWP may play a role in improving arterial oxygenation by IRV as another mechanism. The role of MAWP has been debated[11,18,19], however, our data suggested that Pa_{O_2} in the IRV group was a function of MAWP (fig. 1) and supported the observations by Boros[17] and Stewart et al[18].

In the PEEP group, an improvement of arterial oxygention did not paralled to an increase in MAWP. With a PEEP of 5 cmH_2O, $Pa_{O_2}/F_{I_{O_2}}$ did not increase significantly, but when PEEP was raised to 10 cmH_2O the $Pa_{O_2}/F_{I_{O_2}}$ increased significantly as MAWP increased significantly. Mean airway pressure change by 5 cmH_2O may be too low to increase FRC in severe ARF in our patients.

Since there was no significant difference in MAWP between IRV and PEEP at any level, the factor to improve arterial oxygenation may not be the sole determinants.

Duncan et al.[20] concluded that the beneficial effects on pulmonary gas exchange attributed to IRV could be entirely due to the presence of additional PEEP. Duma and co-workers[7] had reported that improvement of arterial oxygenation with IRV were not observed immediately after applying IRV but observed when IRV was maintained for prolonged period of time. In the present study we observed that it took more than 3 hrs to provide a significant increase in Pa_{O_2} (fig. 2). The reports that failed to demonstrate an improvement of Pa_{O_2} with IRV might, therefore, be due to the fact that the measurements were only performed 15 to 60 min after initiation of IRV[9–12].

Even if I:E ratio was prolonged above 2:1, further improvement of oxygenation was not observed in our patients. These evidences indicate that it may be necessary for improving oxygenation by IRV to take time rather than further prolongation of inspiratory time. On the other hand, PEEP was much faster in improving arterial oxygenation within 2 hrs than IRV. Difference in time to improve oxygenation between IRV and PEEP may be due to the difference in mechanism.

Although, PEEP improves gas exchange by preventing collapse of terminal airway and increasing the FRC, it increase PIP[21].

Accordingly, such high level of PEEP as producing PIP above 50 cmH_2O are reported to increase the incidence of PBT and a safe upper limit of PEEP has not been established yet[23]. An additional advantage of IRV is the lower inspiratory flow which produces a lower PIP than does conventional mechanical ventilation and may reduce the risk of PBT[24]. However, two patients out of 12 (17%) developed pneumothorax during IRV in the present study. Petersen and Baier[22] reported that the incidence of PBT was 8 per cent (14 of 171 patients) and no PBT occured with a PIP of less than 50 cmH_2O. The peak inspiratory pressure of our patients with pneumothorax was less than 40 cmH_2O, so that higher level of PIP may not be the sole cause. Primary diseases of these two patients were chronic myeloblastic leukemia and systemic lupus erythematosus, respectively, complicated with interstitial pneumonia, which may have made lungs vulnerable to PBT. Inversed ratio ventilation and PEEP may reduce CO by decreasing venous return because of an increase in FRC and impair $\dot{D}_{O_2}$ to the tissue, despite an increase in Pa_{O_2}[25].

In the present study we observed that IRV or PEEP provided better gas exchange without its adverse effect on systemic hemodynamics, $\dot{D}_{O_2}$, and tissue oxygenation. Mixed venous P_{O_2} was maintained above 31 mmHg both applying IRV and PEEP at any level. It was reported that no evidence of tissue hypoxemia was observed when $P\bar{v}_{O_2}$ was above 31 mmHg[26].

In conclusion, IRV in patients with ARF

improved arterial oxygenation without increase in PIP but further improvement of oxygenation was not observed even if I:E ratio was prolonged above 2:1. Positive end-expiratory pressure also improved arterial oxygenation in those patients. Although previous reports[3,13,16] indicated that IRV was analogous to the use of PEEP, the present study suggestes that there is some difference in mechanism for improvement of arterial oxygenation between IRV and PEEP because of difference in time to raise Pa_{O_2}.

Inversed ratio ventilation offers an alternative method of ventilatory support to be considered when PEEP faile to raise Pa_{O_2} inspite of high PIP.

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References

1. Kumar RW, Falke KJ, Geffin B, Aldredge CF, Laver MB, Lowenstein E, Pontoppidan H: Continuous positive pressure ventilation in acute respiratory failure. Effects on hemodynamics and lung function. N Engl J Med 283:1430–1436, 1970
2. Mink SN, Light RB, Cooligan T, Hood LDH: Effects of PEEP on gas exchange and pulmonary perfusion in canine lobar pneumonia. J Appl Phsiol 50:517–523, 1981
3. Kirby RR, Downs JB, Civetta JM, Modell JH, Dannemiller FJ, Klein EF, Hodges M: High level positive end expiratory pressure (PEEP) in acute respiratory insufficiency. Chest 67:156–163, 1975
4. Reynolds EOR: Effect of alternations in mechanical ventilator settings on pulmonary gas exchanges in hyaline membrane disease. Arch Dis Child 46:152–159, 1971
5. Reynolds EOR, Taghizadeh A: Improved prognosis of infants mechanically ventilated for hyaline membrane disease. Arch Dis Child 49:505–515, 1974
6. Baum M, Benzer H, Mutz N, Pauser G, Tonczar L: Inversed ratio ventilation (IRV). Die Rolle des Atemzeitverhaltniss in der Beatmung beim ARDS. Anaesthetist 29:592–596, 1980
7. Duma S, Baum H, Koller W, Mutz N, Pauser G: Inversed ratio ventilation (IRV) nach kardiochirurgishen Eingriffen. Anaesthesist 31:549–556, 1982
8. Gurevitch MJ, Van Dyke J, Young ES, Jackson K: Improved oxygenation and low peak airway pressure in severe adult respiratory distress syndrome. Treatment with inverse ratio ventilation. Chest 89:211–213, 1986
9. Fuleihan SF, Wilson RS, Pontoppidan H: Effect of mechanical ventilation with end-inspiratory pause on blood-gas exchange. Anesth Analg 58:122–130, 1976
10. Tyler DC, Cheney FW: Comparison of positive end-expiratory pressure and inspiratory plateau in ventilation of rabbits with experimental pulmonary edema. Anesth Analg 58:288–292, 1979
11. Berman LS, Downs JB, Van Eden A, Delhagen D: Inspiratory: expiratory ratio. Is mean airway the difference? Crit Care Med 9:775–777, 1981
12. Perz-Chada RD, Gardaz RG, Madgwick RG, Sykes MK: Cardiorespiratory effcts of an inspiratory hold and continuous positive pressure ventilation in goats. Intensive Care Med 9:263–269, 1983
13. Comroe HJ, Forester RE, Dubois AB, Briscoe WA, Carlsen E: The lung, Year Book Medical Publisher, Chicago, 1962, pp. 343–345
14. McIntyre RW, Laws AK, Ramachandran PR: Positive expiratory pressure plateau: Improved gas exchange during mechanical ventilation. Can Anaesth Soc J 16:477–486, 1969
15. Tharratt RS, Allen RP, Albertson TE: Pressure controlled inversed ratio ventilation in severe adult respiratory failure. Chest 94:755–762, 1988
16. Cole AGH, Well SF, Sykes MK: Inversed ratio ventilation. Compared with PEEP in adult respiratory failure. Intensive Care Med 10:227–232, 1984
17. Boros SJ: Variation in inspiratory: expiratory ratio and airway pressure wave form during mechanical ventilation: The significance of mean airway pressure. J Pediatr 94:114–117, 1979
18. Stewart AR, Fine NN, Peters KL: Effects of alterations of inspiratory/expiratory ratios on mean airway pressure, blood gas, and intracranial pressure. Pediatrics 67:474–481, 1981
19. Gurevitch MJ, Van Dyke J, Young ES, Jackson K: Improved oxygenation and lower peak airway pressure in severe adult res-

piratory distress syndrome. Treatment with inverse ratio ventilation. Chest 89:211–213, 1986
20. Duncan SR, Rizk NW, Raffin TA: Inverse ratio ventilation, PEEP in disguise? Chest 92:390–392, 1987
21. Morgan BC, Martin WE, Horbein TH, Crawford EW, Guntheroth WG: Hemodynamic effects of intermittent positive pressure respiration. Anesthesiology 27:584–590, 1966
22. Petersen BG, Baier H: Incidence of pulmonary barotrauma in a medical ICU. Crit Care Med 11:67–69, 1983
23. Ravizza AG, Carugo D, Cerchari EL, Ferrante M, Della Puppa T, Villa L: Inversed ratio and conventional ventilation: Comparison of the respiratory effects. Anesthesiology 59:A523, 1983
24. Hubmayr RD, Abel MD, Rehder K: Physiologic approach to mechanical ventilation. Crit Care Med 18:10–113, 1990
25. Lutch JS, Murray JF: Continuous positive-pressure ventilation: Effects on systemic oxygen transport and tissue oxygenation. Ann Intern Med 76:193–202, 1972
26. Shibutani K, Komatsu T, Kubal K, Sanchala V, Kumar V, Bizzarri D: Critical level of oxygen delivery in anesthetized man. Crit Care Med 11:640–643, 1983