A Study about the Efficacy of CO₂ Elimination in the Postoperative Management of Cardiac Child-patients; As a Guide for the Weaning from the Mechanical Ventilation

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Introduction

Children have some anatomic and physiological handicaps in the respiratory system compared to adults. Small size of the respiratory tract, abundant airway secretion, increased oxygen requirements due to high metabolic rate, etc. make postoperative respiratory care difficult. Postoperative heart and lung lesions and intraoperative impairments of respiratory and circulatory function added more difficulties in undergoing cardiac operation. Accordingly, the respiratory assistance with a respirator is usually necessary for a certain period of time. If the use of a respirator is prolonged, impairment of ciliary activity[23,24], mucosal ulceration and granuloma formation of the airway[3], infection of the airway[15] and the lung, barotrauma of the lung[16] and so on may occur. Weaning from a respirator and extubation of the endotracheal tube at an early and appropriate time are essential for postoperative respiratory care especially in infants and small children who are predisposed to obstruction of the respiratory tract and are likely to become dependent on a respirator.

Vital capacity and maximum inspiratory force have been reported as the most reliable indexes for weaning from a respirator[12]. However, these can not be measured in children because they are not cooperative in the tests. Measurements of intrapulmonary shunt, A-aDo₂ and Pao₂ have also been used commonly as indexes of the efficacy of oxygenation.

However, the efficacy of carbon dioxide elimination has been paid little attention. I investigated the usefulness of the Elimination Index of CO₂ (E.I.CO₂) which was related to the alveolar dead space per the tidal volume from BOHR's equation, that is, wasted ventilation.

Patients and Methods

One hundred and thirty-nine postoperative patients, including 78 boys and 61 girls ranging in ages from 6 days to 12 years (mean ± S.D.: 30 ± 26 months) were subjected to this study.

Table 1. Clinical materials

Group	No. of cases	Ages at operations		Anomalies
		Range	Mean±S.D. (mo)	
Operation with CP-bypass				
Group I: Left-to-right shunt (Pp/Ps≧0.75)	32	3 mo~ 7 yr, 5 mo	23.1±19.9	VSD 29, DORV 2, ECD (type I) 1.
Group II: Left-to-right shunt (Pp/Ps>0.75)	47	7 mo~ 12 yr	48.9±35.4	VSD 28, ASD 14, ECD (type I) 4, LV-RA 1.
Group III: Complex anomalies	12	6 days~ 2 yr, 9 mo	10.8± 8.5	TGA 4, ECD (type III) 3, IAA·VSD·PDA 1, Truncus 1, CoA complex 1, TAPVC 1. APW·AORPA 1.
Group IV: TOF	22	13 mo~ 7 yr, 9 mo	36.1±28.7	
Operation without CP-bypass				
Group V: PDA	16	6 mo~ 4 yr, 11 mo	17.9±13.4	
Group VI: Complex anomalies	10	28 days~ 3 yr	8.7±11.8	CoA complex 9, IAA·VSD 1.

Legend: S.D., Standard deviation. CP-bypass, Cardiopulmonary bypass. Pp/Ps, Pulmonary-to-systemic systolic arterial pressure ratio. TOF, Tetralogy of Fallot. VSD, Ventricular septal defect. DORV, Double-outlet right ventricle. ASD, Atrial septal defect. LV-RA, Left ventricular right atrial communication. TGA, Complete transposition of the great arteries. ECD, Endocardial cushion defect. TAPVC, Total anomalous pulmonary venous connection. IAA, Interrupted aortic arch. Truncus, Truncus arteriosus. CoA complex, Coarctation of the aorta with intracardiac anomalies. APW, Aortico-pulmonary window. AORPA, Anomalous origin of the right pulmonary artery.

They were operated upon for congenital heart diseases at Shizuoka Children's Hospital from July, 1977 to March, 1981. The patients undergoing a shunt operation were excluded because their arterial CO_2 contents were affected by venous admixture.

The patients were categorized into six groups (Table I). Operations were performed with the cardio-pulmonary bypass (CPB) in groups of I, II, III and IV, and without CPB in groups of V and VI. Group I included 32 patients with the left-to-right shunt and systolic pulmonary arterial pressure more than 75% of the systemic level: 29 patients with ventricular septal defect (VSD), 2 with double outlet right ventricle (DORV), and one with endocardial cushion defect (ECD) type I. Their ages ranged from 3 months to 7 years and 5 months (mean ± S.D.: 23 ± 20 months). Group II included 47 patients with the left-to-right shunt with the systolic pulmonary arterial pressure less than 75% of systemic level; 28 with VSD, 14 with atrial septal defect (ASD), 4 with ECD type I and one with left ventricular right atrial communication (LV-RA). Their ages ranged from 7 months to 12 years (mean ± S.D.: 49 ± 35 months). Group III included 12 patients with complex anomalies; 4 with complete transposition of the great arteries (TGA), 3 with ECD type III, one with interrupted aortic arch (IAA), VSD and patent ductus arteriosus (PDA), one with persistent truncus arteriosus (Truncus), one with total anomalous pulmonary venous connection (TAPVC), one with residual ASD after the correction for coarctation of the aorta and PDA, one with aortico-pulmonary window (APW) and anomalous origin of the right pulmonary artery (AORPA). Their ages ranged from 6 days to 2 years and 9 months (mean ± S.D.: 11±9 months). Group IV included 22 patients with tetralogy of Fallot (TOF),

ranging in ages from 13 months to 7 years and 9 months (mean $\pm$ S.D.: 36 ± 29 months). Group V included 16 patients with patent ductus arteriosus, ranging in ages from 6 months to 4 years and 11 months (mean$\pm$S.D.: 18 ± 13 months). Group VI included 10 patients; 9 with coarctation of the aorta with intracardiac anomalies (CoA complex) and one with IAA c VSD, ranging in ages from 28 days to 3 years (mean $\pm$ S.D.: 9 ± 12 months).

After returning to the intensive care unit (ICU), patients were connected to a volume-limited ventilator Servo 900B (Siemens-Elema AB, Solona Sweden). Inspiratory time and pause time were set at 25% and 10% of a respiratory cycle respectively, in order to attain even distribution of the inspired gases[29] and to decrease the slope of the alveolar plateau. Minute volume was adjusted to keep tidal volume at approximate 10 ml. per Kg., fractional concentration of oxygen in the inspired gas (F_{IO_2}) was set as low as possible according to the patient's condition. Positive end-expiratory pressure (PEEP) under 6 cmH₂O was applied to prevent alveolar collapse and to increase Pa_{O_2} when necessary.

In simultaneous measurements of Pa_{O_2}, Pa_{CO_2} and endtidal carbon dioxide concentration were performed at resting and steady state at least 20 minutes later when setting of the respirator was changed.

The measurements were done immediately after returning to ICU, and immediately prior to weaning trials. The value of each measurement was expressed as early postoperative value and preweaning value respectively.

Blood gases were measured with blood gas analyzer IL 813 (Instrumentation Laboratory Inc., Mass., USA). Endtidal CO₂ concentration was measured with infrared Servo 930 CO₂ analyzer (Siemens-Elema AB, Solona Sweden), which was calibrated with the standard gas of IL 813. The CO₂ content was converted to the partial pressure, estimating the barometric pressure being 760 mmHg and the vapor pressure (PH₂O) being equal to that at the alveolar level, i.e. $PET_{CO_2}=760\times FET_{CO_2}$ (mmHg.) (PET_{CO_2}. endtidal P_{CO_2}, FET_{CO_2}: fractional concentration of endtidal CO₂).

The other calculations were made as follows;

$Pa_{O_2}=(P_B-PH_2O)\times F_{IO_2}-Pa_{CO_2}=(760-47)\times F_{IO_2}-Pa_{CO_2}$ (mmHg), Respiratory Index (RI)$=$A-aD_{O_2}/Pa_{O_2}, and Elimination Index of CO₂ (E.I. CO₂)$=$a-ETD_{CO_2}/Pa_{CO_2},

where PA_{O_2} is alveolar oxygen pressure, P_B is barometric pressure, A-aD_{O_2} is alveolar to arterial O₂ pressure difference and a-ETD_{CO_2} is arterial to endtidal CO₂ pressure difference.

The RI which was suggested by SIEGEL and FARREL is the ratio between A-aD_{O_2} and Pa_{O_2} which is expressed by the ratio, PA_{O_2}/Pa_{CO_2}. And so it is feasible to compare oxygenation-efficacy under different alveolar oxygen tension. GOLDFALB and his associates reported that a value of RI of 0.1 to 0.37 is normal, and patients with the RI of 2 or greater were necessitated intubations and respiratory supports with the respirators.

In 29 patients Swan-Ganz catheters were inserted into the main pulmonary artery during operations, 14 patients in group I, 11 patients in group II and 4 patients in group IV. Determinations of the cardiac index (CI) were obtained 31 times in group I, 17 times in group II and

7 times in group IV

Results

As demonstrated in Table II, endotracheal intubation periods of each group ranged from 8 to 320 hours (mean $\pm$ S.D.: 38 ± 54 hrs) in group I, 3 to 47 hours (mean $\pm$ S.D.: 10 ± 10 hrs) in group II, 16 to 180 hours (mean $\pm$ S.D.: 67 ± 50 hrs) in group III, 14 to 68 hours (mean $\pm$ S.D.. $26 \pm$ hrs) in group IV one to 20 hours (mean $\pm$ S.D.: 6 ± 6 hrs) in group V. and 3 to 30 hours (mean $\pm$ S.D.: 18 ± 7 hrs) in group VI.

Concerning E.I.CO_2 in the patients operated upon with CPB, the values obtained early postoperatively in the groups I and III (mean $\pm$ S.D.. 0.12 ± 0.08 and 0.22 ± 0.17) were significantly higher than those in groups II and IV (mean $\pm$ S.D.: 0.01 ± 0.05 and 0.04 ± 0.08) ($p < 0.01$). E.I.CO_2 values at the preweaning period in the group I and III (mean$\pm$S.D.: 0.04 ± 0.07 and 0.06 ± 0.04) improved significantly ($p < 0.001$ and $p < 0.02$). E.I.CO_2 values

Table 2. Duration of Endotracheal Intubation

Group	Range (hrs.)	Mean$\pm$S.D. (hrs.)
with CP-bypass		
I	$8 \sim 320$	38 ± 54
II	$3 \sim 47$	10 ± 10
III	$16 \sim 180$	67 ± 50
IV	$14 \sim 68$	26 ± 16
without CP-bypass		
V	$1 \sim 20$	6 ± 6
VI	$3 \sim 30$	18 ± 7

Legend: S.D., Standard deviation. CP-bypass. Cardio-pulmonary bypass.

Table 3. E.I. CO_2 and RI of each group at early postoperative and preweaning period.

Group	No. of cases	E.I. CO_2 (Meam$\pm$S.D.) Early postop.	Preweaning	p value	Respiratory Index (Mean$\pm$S.D.) Early postop.	Preweaning	p value
Operation with CP-bypass							
Group I: Left-to-right shunt (Pp/Ps$\geqq$0.75)	32	$0.12 \pm 0.08^{1)}$	$0.04 + 0.07$	$p < 0.001$	1.4 ± 1.3	1.1 ± 0.7	N.S.
Group II: Left-to-right shunt (Pp/Ps$>$0.75)	47	$0.01 \pm 0.05^{2)}$	$-0.01 + 0.06$	N.S.	0.7 ± 0.8	0.6 ± 0.4	N.S.
Group III: Complex anomalies	12	$0.22 \pm 0.17^{3)}$	0.06 ± 0.04	$p < 0.02$	3.3 ± 3.3	1.4 ± 0.9	$p < 0.05$
Group IV: TOF	22	$0.04 \pm 0.08^{4)}$	0.01 ± 0.08	N.S.	0.9 ± 1.1	0.9 ± 0.7	N.S
Operation without CP-bypass							
Group V: PDA	16	0.06 ± 0.09	——		0.9 ± 0.7	0.6 ± 0.3	N.S.
Group VI: Complex anomalies	10	0.13 ± 0.07	0.07 ± 0.04	$p < 0.05$	1.4 ± 1.7	0.9 ± 0.5	N.S.

Legend: E.I. CO_2, Elimination index of carbon dioxide. RI, Respiratory index. S.D. Standard deviation. Pp/Ps. Pulmonary-to-systemic systolic arterial pressure ratio. CP-bypass, Cardio-pulmonary bypass. TOF, Tetralogy of Fallot. PDA, Patent ductus arteriosus. N.S., Not significant.
p$<$0.01: 1) and/or 3) versus 2) and/or 4).

at the preweaning period in the groups II and IV (mean $\pm$ S.D.: -0.01 ± 0.06 and 0.01 ± 0.08) did not change significantly.   In the patients operated upon without CPB, $E.I.CO_2$ values obtained at early postoperative period in the group V and VI were 0.06 ± 0.09 and 0.13 ± 0.07 (mean $\pm$ S.D.).   In most patients of group V, measurements were not performed at the preweaning period, because the periods of mechanical ventilation were too short.   In group VI, $E.I.CO_2$ values improved considerably at preweaning period (mean $\pm$ S.D.: 0.07 ± 0.04, $p < 0.05$) (Table III).

RI tended to improved during the period of mechanical ventilation.   However, as to RI, there was no significant difference between the early postoperative values and the preweaning values of each group except group III; 1.4 ± 1.3 and 1.1 ± 0.7 in group I, 0.7 ± 0.8 and 0.6 ± 0.4 in group II, 3.3 ± 3.3 and 1.4 ± 0.9 in group III ($p < 0.05$), 0.9 ± 1.1 and 0.9 ± 0.7 in group IV, 0.9 ± 0.7 and 0.6 ± 0.3 in group V and 1.4 ± 1.7 and 0.9 ± 0.5 in group VI (Table III).

As shown in Figure 1, $E.I.CO_2$ at the early postoperative period was correlated fairly well the preoperative pulmonary-to-systemic systolic arterial pressure ratio (Pp/Ps) in the group I and II with the left-to-right shunt ($r = 0.62$, $p < 0.001$).   At preweaning period there was a slight correlation between them ($r = 0.50$, $p < 0.001$).   The higher $E.I.CO_2$ at the early postoperative
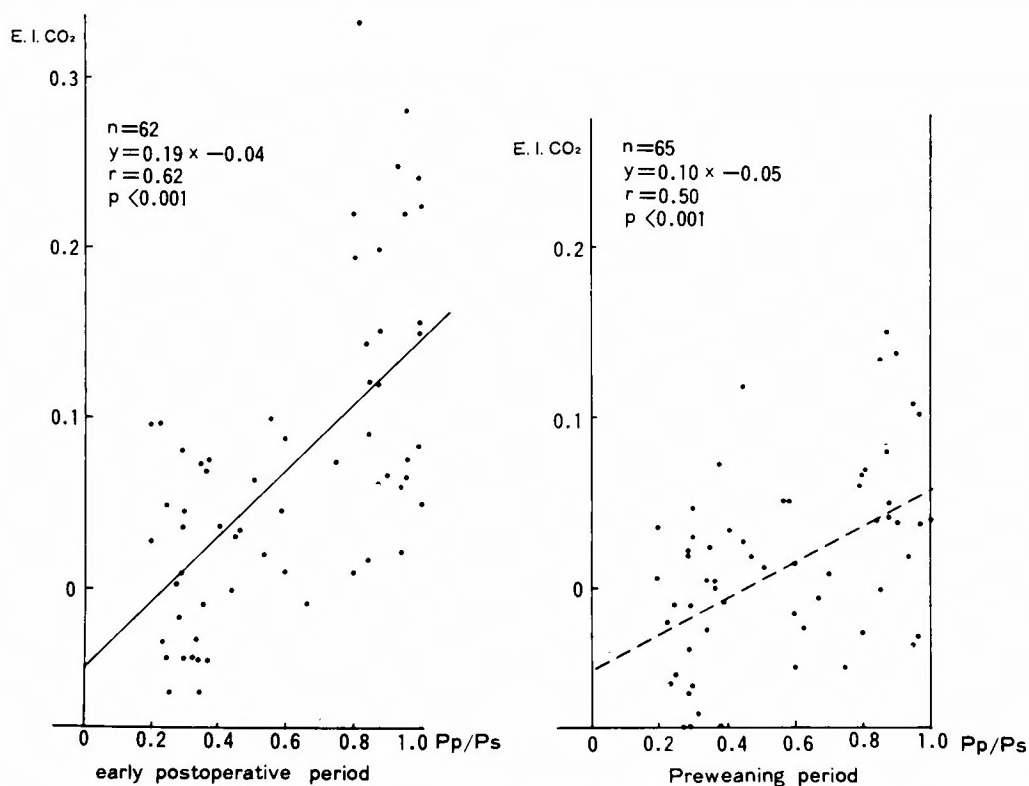

Fig. 1.   Correlation between E.I. CO₂ and preoperative Pp/Ps in the left-to-right shunt group at early postoperative period (left) and at preweaning period (right).
Legend: E.I. CO₂, Elimination index of carbon dioxide. Pp/Ps, pulmonary-to-systemic systolic arterial pressure ratio.

period showed the more improvement at the preweaning period.

The cardiac indexes of group I (mean $\pm$ S.D.: 4.0 ± 0.9 L/min/m²) were significantly higher than those in group II (mean $\pm$ S.D.: 3.0 ± 0.9 L/min/m²) ($p < 0.005$). E.I.CO_2 and CI were inversely correlated in group I ($r = -0.68$, $p < 0.001$) and II ($r = -0.61$, $p < 0.01$) when analyzed separately (Figure 2). Those measured with PEEP were excluded, because E.I.CO_2 higher due to local alveolar overinflation. In group IV, no correlation was obtained. The regression line of group I was deviated upward from that of group II. In the other word, with the same CI the patients with pulmonary hypertension showed higher E.I.CO_2 than those without pulmonary hypertension.

E.I.CO_2 and RI were correlated slightly in the early postoperative period ($r = 0.49$, $p < 0.001$), but were not correlated at the preweaning period ($r = 0.35$) (Figure 3).

In the patients with TOF, E.I.CO_2 stayed low during the mechanical ventilation. Eight of 10 patients with E.I.CO_2 over 0.05 at the early post operative period required mechanical ventilation more than 24 hours, whereas 8 of 10 patients with E.I.CO_2 below 0.05 at the early postoperative period could be weaned from a respirator within 24 hours, excluding 2 patients whose E.I.CO_2 were not measured at early postoperative period (Figure 4).

Nine patients failed to wean from a respirator and reintubated 11 times in total; once in group I (one patient), 8 times in group III (6 patients) and twice in group IV (2 patients) (Table IV). In these patients, E.I.CO_2 at unsuccessful weaning ranged from 0.03 to 0.25 with mean $\pm$ S.D. of 0.14 ± 0.07, excluding one patient with TGA in whom E.I.CO_2 was not obtained at the
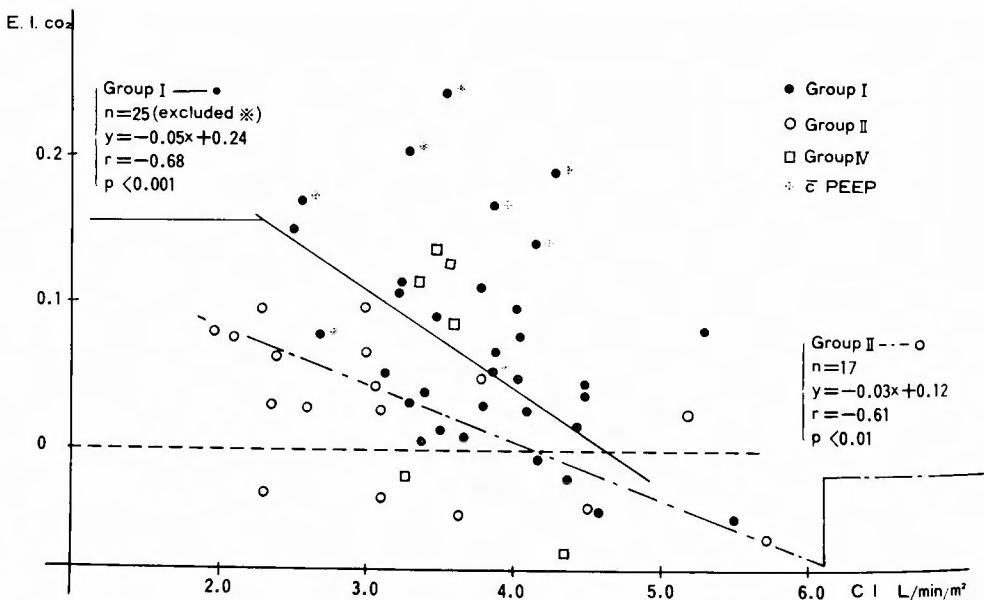

Fig. 2. Correlation between E.I. CO_2 and cardiac index after cardiac operations. E.I. CO_2 and cardiac index were inversely correlated in group I and II when analyzed separately and excluded the values when EEPP were used.
Legend: E.I. CO_2, Elimination index of carbon dioxide. CI, Cardiac index. PEEP, Positive end-expiratory pressure.
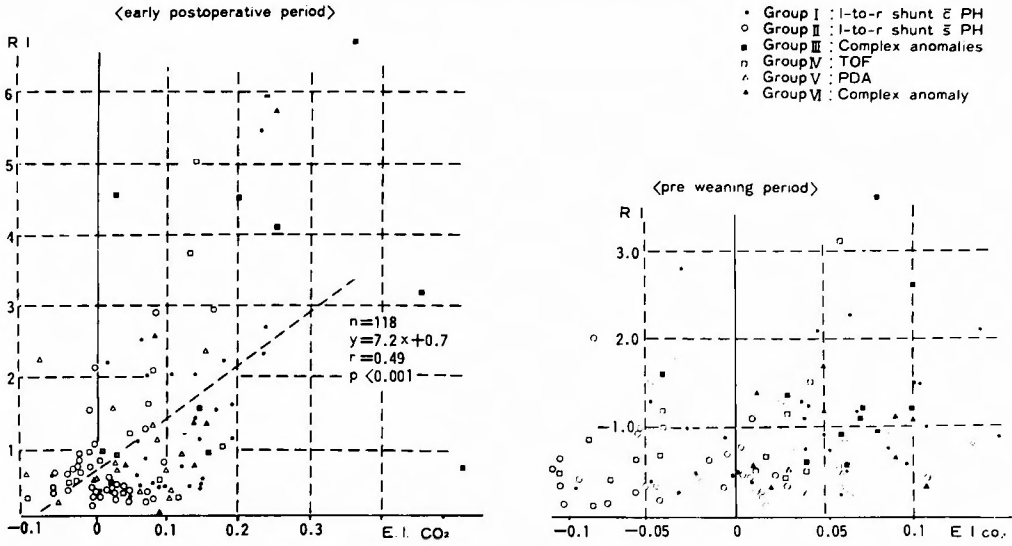
Fig. 3. Correlation between E.I. CO_2 and RI at early postoperative period (left) and preweaning period (right). E.I. CO_2 correlated slightly with RI at early postoperative period ($r=0.49$), but did not correlated at preweaning period ($r=0.35$). Ledend: E.I. CO_2, Elimination index of carbon dioxide. RI, Respiratory index. 1-to-right, left-to-right. PH, Pulmonary hypertension. TOF, Tetralogy of Fallot. PDA, Patent ductus arteriosus.
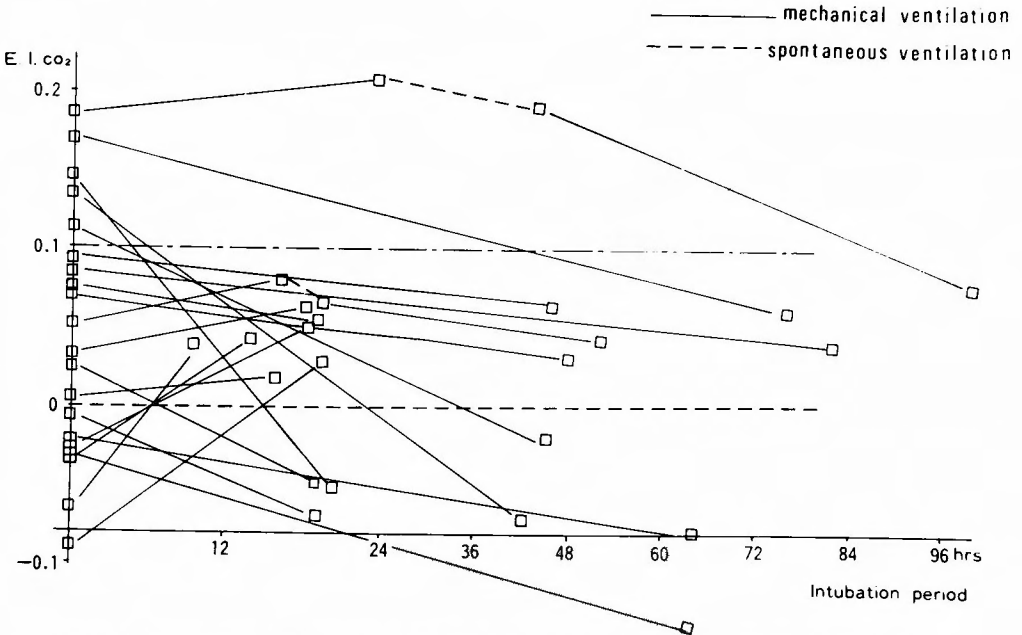

Fig. 4. Changes in E.I.CO_2 of the patients with TOF from early postoperative period to successful preweaning period.
Legend: E.I. CO_2. Elimination index of carbon dioxide. TOF, Tetralogy of Fallot.

Table 4. Comparison of E.I. CO_2 with RI at unsuccessful weaning and final successful weaning of the reintubated patients.

Group	Diagnosis	Unsuccessful weaning		Time to reintubation from extubation (hrs.)	Finally weaned	
		E.I. CO_2	RI		E.I. CO_2	RI
I	VSD c PH, Down	0.06	1.3	20	0.09	0.6
	IAA·VSD·PDA	0.18	0.5	3	} 0.06	0.5
		0.11	0.6	28		
	ECD (type III)	0.03	1.0	30	0.03	1.4
III	TGA	0.30	2.8	1	} —	—
		0.20	1.4	30		
	TGA	0.25	3.1	12	0.08	3.0
	Truncus	0.12	3.0	15	0.10	2.6
	APW	0.22	1.0	7	0.1	1.2
IV	TOF	0.08	0.7	3	0.04	2.0
	TOF	0.21	2.0	27	0.08	1.1
	mean ± S.D.	0.14*† ±0.07	1.5* ±0.9	16 ±11	0.07† ±0.02	1.6 ±0.8

Legend: E.I. CO_2. Elimination index of carbon dioxide. RI, Respiratory index. VSD. Ventricular septal defect. PH, Pulmonary hypertension. Down, Down syndrome. ECD, Endocardial cushion defect. TGA, Complete transposition of the great arteries. Truncus, Truncus arteriosus. APW. Aorticopulmonary window. S.D., Standard deviation.
*; excluding one patient with TGA in whom E.I. CO_2 was not obtained at the final successful weaning period.
†; $p > 0.05$—Each E.I. CO_2 was compared.

final successful weaning period. However, E.I.CO_2 decreased in all of these patients at the final successful weaning, ranging from 0.03 to 0.1 (mean ± S.D.: 0.07 ± 0.02). There was a significant difference between E.I.CO_2 at the time of unsuccessful and those at successful weaning ($p < 0.05$). On the other hand, RI at unsuccessful weaning (mean ± S.D.: 1.5 ± 0.9) was not significantly different from those at successful weaning (mean ± S.D.: 1.6 ± 0.8), rather exacerbated. Three patients failed to be weaned from respirators in spite of E.I.CO_2 under 0.1. One patient with VSD, pulmonary hypertension and Down syndrome whose E.I.CO_2 was 0.06 at the time of unsuccessful weaning proved to have paralysed left hemidiaphragm. A second patient was ECD (type III) who was obligated to be reintubated by abruptly occurred hemolysis and simultaneous circulatory deterioration after 30 hours from initial extubation (E.I.CO_2: 0.03). The third patient was one of TOF who was reintubated due to pulmonary edema caused by left ventricular failure. Similar course was observed in the other patient with TOF who was also reintubated. The durations between the extubation and the reintubation of these patients ranged from one to 30 hours (mean: 16 hrs).

In retrospect, 128 out of 131 patients (98%) were successfully extubated with this E.I.CO_2 0.1 or below, included 19 patients whose E.I.CO_2 were already below 0.1 at early postoperative period, and were not measured immediately before weaning because of short intubation's period. This index improved during assisted ventilation, but stayed low when it was far below 0.1 im-
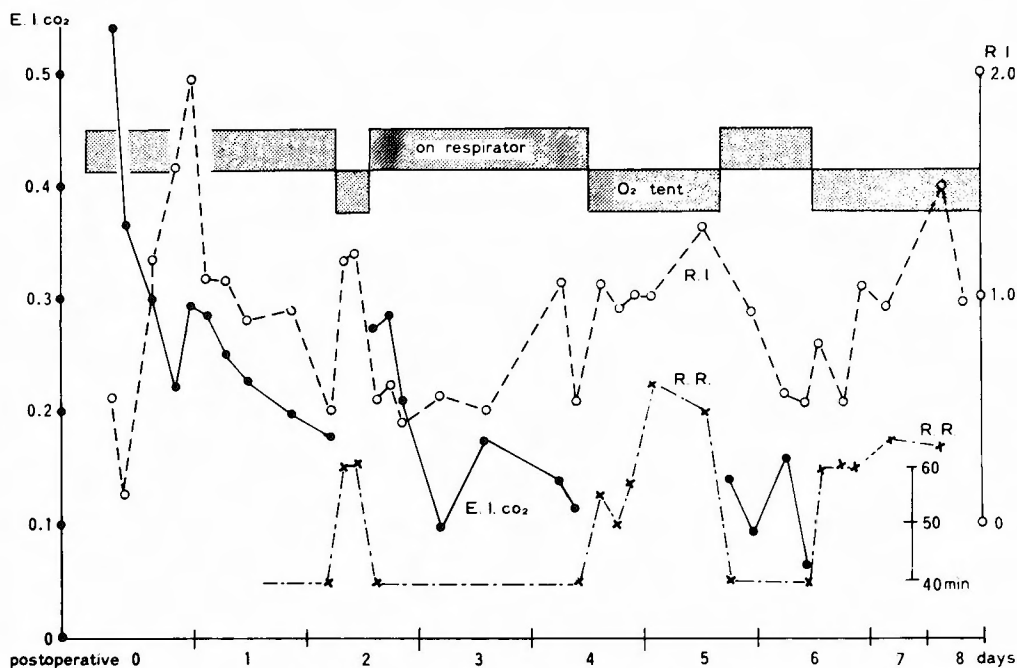
Fig. 5. Graphic presentation of postoperative changes in E.I. CO₂, RI and respiratory rates in a 3-month-old infant with IAA, VSD and PDA. Note higher E.I.CO₂ (0.54) when returning to ICU, which gradually improved. Two-times of extubation with E.I. CO₂ over 0.1 were followed by increased respiratory rates and dyspnea, necessitating reintubations. Final success was obtained with E.I.CO₂ of 0.06 on the sixth day. RI did not change significantly through the intubation period.

Legend: E.I.CO₂, Elimination index of carbon dioxide. RI, Respiratory index. R.R., Respiratory rate. IAA, Interrupted aortic arch. VSD, Ventricular septal defect. PDA, Patent ductus arteriosus. ICU, Intensive care unit.

mediately after surgery. On the other hand, 8 of 15 extubations (53%) with this E.I.CO₂ over 0.1 resulted in failure and reintubations..

An illustrative case is presented to reveal E.I.CO₂ as a useful index for weaning from a respirator (Figure 5). Case T.T., a 3-month-old infant following simultaneous correction for IAA, VSD and PDA showed high E.I.CO₂ (0.54) and low RI (0.6) when returning to ICU. The patient was extubated on the second day with E.I.CO₂ 0.18 and RI 0.5. However, 3 hours later she was intubated again due to dyspnea and deteriorated blood gases (PH 7.261, Pa_{CO_2} 55 mmHg, Pa_{O_2} 72 mmHg with F_{IO_2} 0.4). On the fourth postoperative day, she was extubated again with E.I.CO₂ 0.11 and RI 0.6. However, 28 hours later, she deteriorated again (respiratory rate over 70 per minutes, Pa_{CO_2} 53 mmHg, RI 1.6) and reintubated. On the sixth day E.I.CO₂ improved (0.06) and finally she could be extubated successfully. In this case weaning from the respirator was attempted in vain in the presence of high E.I.CO₂ (over 0.1). RI stayed low all the time far below the usual criteria of weaning, namely 2.0.

Discussion

On the development of the respiratory physiology, the knowledge of the gas exchange in the lung, especially ventilation-perfusion relationship appeared in 1917 when KROGH and LINDHARD[20] wrote about inspiratory gas inequality distribution. HALDANE in 1922[11] discussed about arterial hypoxemia from the ventilation-perfusion ($\dot{V}_A/\dot{Q}$) inequality. In the late 1940s, RILEY and his colleagues[32] clarified the quantitative relationships between ventilation, blood flow and gas exchange by means of the introduction of the oxygen-carbon dioxide diagram. Since the first report using the isotope material appeared in 1955,[17] $\dot{V}_A/\dot{Q}$ inequality has been demonstrated more clearly.

In spite of the knowledge of $\dot{V}_A/\dot{Q}$ inequality as above mentioned, it was believed that uneven ventilation-perfusion interfered with oxygen transfer by the lung but carbon dioxide was unaffected. It was taught that because of linear dissociation curve of CO_2, the overventilation in some parts of the lungs will wash out CO_2 from the blood in the same proportion as the underventilation fails to wash it out, and the mixed arterial blood CO_2 will be normal if the total alveolar ventilation is normal.

In 1971, JOHN B WEST[53] pointed out that ventilation-perfusion inequality can interfere dramatically with carbon dioxide output as with oxygen uptake by means of digital computer technic using series lung models. Furthermore he demonstrated that the shape of the blood-gas dissociation curve made remarkably little difference to the effect of uneven distribution on gas transfer[52], and that the greater vulnerability of O_2 uptake and CO_2 elimination is the slope, not the shape of the two gas dissociation curve, i.e. solubility of the two gases in the clinically controlled range. And later WAGNER[50,51] and WEST[54,55] clarified the relationship between the type and extent of $\dot{V}_A/\dot{Q}$ inequality and the differential susceptibility of different gases to uptake and elimination, and demonstrated that vulnerability of a gas in the presence of a particular $\dot{V}_A/\dot{Q}$ distribution depends on the quantitative distribution of ventilation and blood flow. They clarified that the higher $\dot{V}_A/\dot{Q}$ distribution, the more likely CO_2 elimination is disturbed, and the lower $\dot{V}_A/\dot{Q}$ distribution, even if serially ventilated, affects O_2 more than CO_2.

In the presence of a large alveolar dead space ($V_T(alv)$), it is possible to maintain CO_2 output without increasing minutes ventilation simply by increasing the mixed venous P_{CO_2} as O_2 uptake improvement by increased F_{IO_2}. Such adaptation can be easily observed in elderly emphysematous patients, and it may be advantageous and necessary for decreasing energy loss. Such adaptation would require simultaneous adjustment of respiratory center sensitivity and metabolic compensatory mechanism to prevent the increased ventilation and not to change acid-base balance. It is occasionally advantageous for respiratory center to respond hypercapnia dull. It is also of interest that trained athletes at rest exhibit diminished ventilatory drives to both hypercapnia and hypoxia[30]. I experienced that a patient with VSD and Down syndrome reintubated for the paralysis of left phrenic nerve in spite of a low CO_2 climination index and was successfully weaned from the respirator 13 days later, when she adapted to relatively high range of Pa_{CO_2} between 50 and 60 mmHg.

Determination of the physiological dead space per tidal volume has been the sole means of evaluating CO_2 elimination, although this has not commonly used due to its technical tediousness. At spontaneous breathing, the normal value of the physiological dead space per tidal volume (V_D/V_T) is below 0.3 independent of the size of the tidal volume and weaning from the respiratory was recommended with V_D/V_T below 0.6. A small rise in V_D/V_T above 0.6 requires an inordinately large rise in minute ventilation to maintain arterial P_{CO_2} constant[28]. However, with the mechanical ventilation the value of V_D/V_T can be changed by the setting of the respirator[2] V_D/V_T increases inevitably with decreased V_T, since V_D contains the constant mechanical as well as anatomical dead space.

Measurement of expired alveolar carbon dioxide tension has been used as an estimate of arterial carbon dioxide tension since the time of HALDANE and PRIESTLY[14]. In real lungs, positive a-AD_{CO_2} is expected to arise from ventilation-perfusion inequalities, in particular when these are due to the presence of unperfused (or little perfused) alveoli whose ventilation constitutes alveolar dead space ventilation ($\dot{V}_D(alv)$). In fact, it is customary to estimate $V_D(alv)$ assuming P_{CO_2} equibrium between alveolar gas and end-capillary blood of perfused alveoli[39]. However, recent experimental evidence suggest that under special condition, negative arterial to endtidal P_{CO_2} difference is observed not only rebreathing equibrium with zero net CO_2 exchange but also in steady state gas exchange[39], for example in exercise[14], hypercapnea[9,13,38] and septic state[19]. ROBERTSON and his associates[33] proposed the probability of additional extra CO_2 release from the normal lungs. About this paradoxical negative a–AD_{CO_2}, two hypotheses have been proposed to explain; the charged membrane hypothesis[9] and delayed equilibration hypothesis[5]. The HALDANE's effect also produce rapid increase of P_{CO_2} in alveoli[21]. On the other hand, SCHEID and his associates[39] pointed out that this phenomenon was caused simply by directional technical error to measure blood and gas P_{CO_2}. Hence, the classical assumption of "PA ideal CO_2 equal to Pa ideal CO_2" would underestimate alveolar dead space. And further, expiratory gases contain both fast and slow space which expire asynchronously, and so there may be slope in a much steeper alveolar plateau for O_2 and CO_2 in the latter part of expiration[27]. Tidal volume (V_T) will also influenced indirectly the amplitude of $P_{ET_{CO_2}}$ fluctuation by modifying the time of expiration; at high V_T the longer expiration allow $P_{ET_{CO_2}}$ to climb closer to mixed venous CO_2 pressure[14,16]. However, the endtidal measurement was reported to be most reliable approximation of mean alveolar gas in clinical practice of pulmonary patients[22]. In this study negative a–$ET_{D_{CO_2}}$ observed in some patients who could be easily weaned from a respirator. Negative a–$ET_{D_{CO_2}}$ is considered rather to mean that alveolar dead space and high $\dot{V}_A/Q$ inequility are minimized. This is an advantageous condition to eliminate CO_2.

The equation of a-$ET_{D_{CO_2}}/Pa_{CO_2}$ (: E.I.CO_2) derived from HOHR's equation, is related to alveolar dead space/(tidal volume minus anatomic dead space), assuming that $P_{ET_{CO_2}}$ is equal to mean alveolar CO_2 tension (PA_{CO_2}) and P_{CO_2} of the gas in the correctly perfused alveoli is equal to Pa_{CO_2}, neither of which assumption is strictly correct as above mentioned.

From the partial pressure-solubility diagram[54], it is easily clarified that the magnitude of arterial-alveolar difference depends on the partial pressure of the gas delivered to the lung from the

mixed venous blood. On the other hand, the ratio of arterial to alveolar partial pressure is independent of the mixed venous blood concentration[34] and therefore is reliable under more different mixed venous CO_2 concentration levels, usually ranging between 30 and 50 mmHg. It is also advantageous that this ratio is independent of air leak, anatomical dead space and compressive air volume.

After cardiopulmonary bypass, most patients manifest some degree of pulmonary dysfunction. This is usually characterized by increased work of breathing[6], arterial hypoxemia and increased fluid in the tracheobronchial tree[18]. Hypoxia which is caused by diffusion disturbance, shunt and $\dot{V}_A/\dot{Q}$ inequality can be improved by increasing F_{IO_2} to some extent. On the other hand, disturbance of CO_2 elimination, i.e. increased wasted ventilation must be compensated by the patient's own energy loss: hyperventilation and increased perfusion. This wasted ventilation is increased by anesthesia[26,31,36], microembolization[10,37,44,48] due to extracorporeal circulation[4,43] and blood transfusion[1], pulmonary hypotension[8], low lung-compliance[28], and so forth.

Although the patients operated upon with extracorporeal circulation for complex anomalies showed increased $E.I.CO_2$ (Table III), the patients with TOF showed considerably lower $E.I.CO_2$ in spite of a long bypass time. In Group I (left-to-right shunt with pulmonary hypertension) $E.I.CO_2$; was higher than in Group II (left-to-right shunt without pulmonary hypertension) with the perfusion time being equal in both groups. My study also revealed a significant correlation between $E.I.CO_2$ and preoperative degree of pulmonary hypertension at the early postoperative periods. This may suggest that the increased $E.I.CO_2$ following surgery is mainly caused by the severity of the preoperative lung lesions, and is probably less influenced by the duration of the extracorporeal circulation. In the discussion on the pathogenesis of postperfusion lung, NORMAN[25] pointed out the abnormality of the preoperative lung as one of the factors causing respiratory insufficiency following extracorporeal circulation along with the length of perfusion, and sequestration of polymorphonuclear leucocytosis in the vessels of the alveoli. WAGENVOORT and his associates[49] reported that an increase in the thickness of both media and intima of pulmonary vessels and also an increase in hemosiderosis correlated with increased pulmonary hypertension. SANG and his associates[35] observed hyperinflation in the cases with high pulmonary artery pressure and high pulmonary artery flow. Those changes bring about increment of alveolar dead space.

The increased wasted ventilation following open heart surgery showed a tendency to improve within a rather short period of time, suggested by the gradually decreasing $E.I.CO_2$. In the case of IAA, VSD and PDA, increased early postoperative $E.I.CO_2$ (0.54, highest value in the series) decreased down to 0.06 on the sixth postoperative day at the final successful extubation. In most patients $E.I.CO_2$ were as low as 0.1 at the time of extubation. This wasted ventilation can improved with time possibly by pathophysiological changes in the alveoli and/or adaptation of ventilation and purfusion in the lung. Therefore, assisted ventilation is recommended until the wasted ventilation improves.

Alveolar dead space was reported to be inversely correlated with CI[45]. In the present study $E.I.CO_2$ was more increased in the group of left-to-right shunt with pulmonary hypertension than

in the group of left-to-right shunt without hypertension for the comparable CI (Figure 2). There-fore, it is suggested that disturbance of CO_2 elimination is correlated not only with pulmonary perfusion but also with preoperative lung lesion, that is, pulmonary hypertension. Increased cardiac output observed postoperatively in the group with pulmonary hypertension for uncertain cause, may suggest that more lung blood flow is necessitated in the presence of the inequality of $\dot{V}_A/\dot{Q}$, particularly of lung perfusion.

Although the most patients with TOF showed decreased $E.I.CO_2$ (<0.1) in spite of consider-ably longer duration of extracorporeal circulation, those with $I.E.CO_2$ more than 0.05 required mechanical ventilation of longer durations than those less than 0.05 (Figure 4). However, a few patients with TOF required reintubation in a few days following the initial extubation with $E.I.CO_2$ below 0.1 for the lung congestion, probably because of poor development of left ventricle. On the other hand, three patients with VSD and pulmonary hypertension were able to wean from the respirators barely in spite of $E.I.CO_2$ more than 0.13. Similarly, TERES and his associates[47] reported successful weaning in two patients with V_D/V_T above 0.65. Possibly these patients could tolerate the increased energy loss following extubation by the compensatory mechanism provided by the sufficient cardiac reserve. However, the assisted ventilations were necessary for minimiz-minimizing the energy loss in such patients with limited cardiac reserve or residual uneffective cardiac function as those with TOF or complex anomalies, and those with postoperative com-plication which increased the cardiac work-load. SKILLMAN and his associates[42] reported that the cardiac index rose significantly after a few ten minutes of attempted weaning in the patients in whom the weaning failed.

Analysis of the cases with reintubation revealed that the R1 representing the efficacy of oxygenation was not a good indicator for weaning (Table 4). On the other hand, $E.I.CO_2$ representing the efficacy of CO_2 elimination was a reliable index for weaning in these cases, because energy loss following extubation can be assumed by $E.I.CO_2$ (Table 4). Since there was a time lag of some hours between the initial extubation and the reintubation and since signs of cardiac failure such as restlessness and so forth were observed prior to hypoxemia, it was con-sidered that the failure of the compensatory mechanism occurred in this situation. Namely, decreased efficacy of CO_2 elimination was initially compensated by increased respiratory work (such as increased respiratory rate), which caused the increase in the cardiac work load and ultimately deteriorated circulatory state.

In this study, 128 out of 131 patients (98%) were successfully extubated with this $E.I.CO_2$ 0.1 or below. On the other hand, only 7 out of 15 trials of extubation (47%) with this $E.I.CO_2$ more than 0.1 could be successful but the remaining 8 (53%) failed to be weaned and necessitat-ed reintubations. Since most of the patients required reintubations when $E.I.CO_2$ were over 0.1, $E.I.CO_2$ more than 0.1 was regarded as the critical level above which cardiac exhaustion was accelerated, necessitating reintubation. Therefore, it is advisable to start weaning after $E.I.CO_2$ improved and lowered 0.1 or below in the usual cardiac postoperative state of limited cardiac reserve, particularly in the state of increased cardiac work load for residual handicapped anomalies or additional complication.

Summary

Usefulness of the Elimination Index of CO_2 (E.I.CO_2), a-$ET D_{CO_2}$/Pa_{CO_2} was investigated in 139 child-patients after cardiac operations. E.I.CO_2 is related to alveolar dead space per tidal volume, i.e. wasted ventilation. E.I.CO_2 was slightly correlated with respiratory index (RI), representing the oxygenation's efficacy, only at the early postoperative period, although each index expresses the impairment of gas transfer in the lung. E.I.CO_2 improved sufficiently from the early postoperative period to the preweaning period, but RI remained less improved. E.I.CO_2 correlated significantly with preoperative pulmonary-to-systemic systolic arterial pressure ratio at the early postoperative period in left-to-right shunt group. E.I.CO_2 and CI were inversely correlated significantly in the groups with left-to-right shunt with or without pulmonary hypertension when analyzed separately. And with the comparable CI the patients with pulmonary hypertension showed higher E.I.CO_2 than those without pulmonary hypertension. In severely ill patients who failed to wean from the respirators, E.I.CO_2 served as an useful guide for the weaning, but RI was not helpful. E.I.CO_2 improved significantly at final successful weaning period, whereas RI did not change. All of them had weaned successfully from respirators with this E.I.CO_2 under 0.1. Retrospective analysis revealed successful extubations in 128 of 131 (98%) with E.I.CO_2 0.1 or below. On the other hand, 8 of 15 extubations (53%) with E.I.CO_2 over 0.1 resulted in failure and reintubations. Assuming from this study, energy-loss from respiratory work was considered to be more dependent on the efficacy of CO_2 elimination than that of O_2 uptake. Therefore, it is advisable to start the weaning after E.I.CO_2 improved 0.1 or below in the cardiac postoperative state of limited cardiac reserve, particularly in the states of increased cardiac work-load for residual handicapped anomalies and/or additional complication.

Acknowledgement

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和文抄録

小児心臓手術後管理に於ける炭酸ガス排泄効率に関する研究；
特に人工呼吸器からの離脱の指標として

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小児心臓手術後，とくに乳児あるいは重症例では，肺機能状態の把握が困難であり，従来より酸素化効率の指標が重視されて来た．今回著者は炭酸ガス排泄効率に注目し，肺胞死腔換気率に関係する $a\text{-}ETD_{CO_2}/Pa_{CO_2}$ を Elimination Index of CO₂ (E. I. CO₂) と命名し，その臨床的有効性について，従来の酸素化能の指標として用いられている Respiratory Index (RI) と比較検討した．

対象は静岡県立こども病院での心臓手術例139例であり，病態的に6群に分類した．Ⅰ群よりⅣ群は開心術例で，Ⅰ群は左右短絡群で肺体動脈収縮期圧比75％あるいはそれ以上の32例，Ⅱ群は左右短絡群で肺体動脈収縮期圧比75％以下の47例，Ⅲ群は複雑心奇形の12例，Ⅳ群はファロー四徴症の22例である．Ⅴ，Ⅵ群は非開心術例で，Ⅴ群は動脈管開存症の16例，Ⅵ群は心内奇形を伴う大動脈縮窄症および大動脈弓離断症の10例である．各群の術後気管内挿管時間はⅠ，Ⅲ及びⅣ群で平均24時間を超える比較的長期の挿管を要した．それ以外の群では平均20時間以下であった．

各群のE. I. CO₂の平均はⅠ，Ⅲ及びⅥ群で術直後に0.10を超えⅢ群では最も高く平均0.21を示した．しかし人工呼吸器からの離脱前には3群とも有意に低下し，平均0.10以下を示した．一方RIは術直後と離脱前でⅢ群以外では有意の低下を示されなかった．E. I. CO₂とRIはともに肺のガス交換障害の指標であるが，E. I. CO₂が換気に比して相対的に血流の少ない肺胞部分の影響を受け易く，RIはその逆に血流に比して相対的に換気の少ない肺胞部分の影響を受け易い為に病的肺では両者は必ずしも平行して変化しない．

本研究に於ても両者は術直後に軽度の相関を示したのみで，その後は相関を示さなかった．

Ⅰ，Ⅱ群の左右短絡疾患では術後のE. I. CO₂は術前の肺体動脈収縮期圧比と有意の相関を示し，術後の炭酸ガス排泄率低下に術前の肺の状態が大きく影響することが考えられる．さらに術後のE. I. CO₂と心係数との関係をみると，Ⅰ及びⅡ群ともそれぞれ有意の逆相関を示し，Ⅰ群の方がⅡ群よりもE. I. CO₂及び心係数のいづれも有意に高い値を示した．つまり心拍出量が少ない程血流分布異常を示し易いが，逆に肺血流分布異常を来す病的肺では心拍出量を増大させる可能性が示唆された．

E. I. CO₂が0.10あるいはそれ以下で人工呼吸器からの離脱を試みた131例中128例（98％）で離脱が可能であった．一方E. I. CO₂が0.10以上では15回中8回（53％）が不成功に終り，再挿管・呼吸補助を必要とした．これらの人工呼吸器からの離脱不成功例では，RIは不成功時と最終的な離脱成功時で変化が見られなかったが，E. I. CO₂は不成功時の平均：0.14から最終離脱時にはすべて0.10以下に改善した．

炭酸ガス排泄効率の低下は酸素化能の低下に比して換気量の増大による呼吸仕事量を著しく増加させる為，心予備力の低下している心臓手術後とくに重症例の術後では従来用いられて来た酸素化効率の指標よりも炭酸ガス排泄障害の指標であるE. I. CO₂がより有用と考えられ，本指標が0.10あるいはそれ以下になるまで待って人工呼吸器からの離を開始すべきであると考える．