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Respiratory system compliance and postoperative ventilator dependence in neonates with left-sided congenital diaphragmatic hernia

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Abstract

Purpose. The purpose of this prospective consecutive patient study was to test if perioperative respiratory system compliance of patients undergoing surgical repair of congenital diaphragmatic hernia (CDH) can predict the need for prolonged postoperative mechanical ventilation.

Methods. All neonates over 35 weeks of gestation who had surgical repair of left-sided CDH between July 1994 and December 1996 ($n = 10$) were included in this study. Static respiratory system compliance (C_{rs}) was measured by the passive occlusion method with muscle relaxation before (C_{pre}) and after (C_{post}) surgical repair of left-sided CDH. We examined the relationship between respiratory system compliance and postoperative ventilator-dependent duration.

Results. The mean birthweight-corrected C_{post} was lower than that of birthweight-corrected C_{pre} (0.41 ± 0.18 *vs* $0.54 \pm 0.18\,ml \cdot cmH_2O^{-1} \cdot kg^{-1}$, $P = 0.04$). One neonate died on postoperative day 31 from intraventricular hemorrhage, and the other nine neonates survived. The patient who died was excluded from the rest of our calculations. The ventilator-dependent duration was 16.7 ± 12.3 days. The postoperative ventilator-dependent duration was longer when the birthweight-corrected C_{post} was smaller, with a significant correlation between these parameters ($P = 0.006$).

Conclusion. C_{post}, but not C_{pre}, may be useful to predict the need for prolonged postoperative mechanical ventilation in neonates with left-sided CDH.

Key words Diaphragmatic hernia-congenital · Respiratory function tests · Respiratory system compliance · Mechanical ventilation

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Introduction

Congenital diaphragmatic hernia (CDH) is still associated with severe mortality and morbidity [1,2], despite recent advances in respiratory therapy, including high-frequency oscillatory ventilation (HFO) and extracorporeal membrane oxygenation (ECMO) [3–5]. The cause of death of CDH patients is mainly related to respiratory failure, pulmonary hypertension, or both [6–9]. Respiratory failure is caused by hypoplasia and biochemical abnormalities of the lungs and by mechanical compression by hernia contents [7–11].

The outcome for CDH patients is reported to correlate well with respiratory parameters, such as arterial blood gas value, respiratory system compliance (C_{rs}) before surgery, physiologic dead space/tidal volume ratio, and functional residual capacity [11–16]. Of these parameters, physiologic dead space/tidal volume ratio and functional residual capacity cannot be easily measured. Arterial blood gas values and respiratory system compliance (C_{rs}) before surgery can be measured at the bedside. These parameters, however, might not be reliable indexes in cases in which surfactant or nitric oxide (NO) is used [17,18], since surfactant and NO inhalation can affect arterial blood gas value and C_{rs}.

Therefore, there seems to be a need for an easier method to predict mortality and morbidity, even when NO inhalation, surfactant replacement therapy (SRT), or both are utilized. In this study we focused on C_{rs} during the perioperative period, because there are no reports concerning how the postoperative respiratory course may be related to C_{rs} during the perioperative period. We hypothesized that C_{rs} during the perioperative period has some relationship to postoperative pulmonary outcome. To assess this hypothesis, we measured static C_{rs} just before and after the repair, and searched for the relationship between C_{rs} and postoperative ventilator-dependent duration.

Methods

Subjects

All neonates over 35 weeks of gestation who received surgical repair for left-sided CDH at Osaka Medical Center and Research Institute for Maternal and Child Health between July 1994 and December 1996 were enrolled in this study ($n = 10$). CDH was diagnosed in utero in four neonates, all of whom were delivered by cesarean section; all of the others who were not diagnosed with CDH in utero were delivered vaginally. None had any intracardiac anomaly. One patient (no. 2) had Pallister-Killian syndrome (mosaic tetrasomy 12p) characterized by slightly decreased muscle tonus. This study was approved by the Institutional Ethics Committee. Informed consent was obtained from the parents of all subjects.

Clinical management

All four neonates who were diagnosed with left-sided CDH in utero were intubated at birth. The others were intubated when they needed mechanical ventilation or when the diagnosis was made. Then, in order to prevent ventilator-induced lung injury [3,19] and pulmonary hypertension, HFO (Humming II, Senko Medical Instrument Manufacturing, Tokyo, Japan) was started with 100% oxygen and continuous intravenous injection of morphine (1–2 $\mu g \cdot kg^{-1} \cdot min^{-1}$), midazolam (1–2 $\mu g \cdot kg^{-1} \cdot min^{-1}$), and pancuronium (2–3 $\mu g \cdot kg^{-1} \cdot min^{-1}$), and was continued until pulmonary hypertension was controlled. On starting HFO ventilation, we set the mean airway pressure at 15 cmH_2O, ventilatory frequency at 15 Hz, and stroke volume at 5 $ml \cdot kg^{-1}$, and the ventilation settings were adjusted to keep $PaCO_2$ below 35 mmHg. When surfactant deficiency was suspected because of frequent atelectasis, poor lung expansion, or poor results on the stable microbubble test, modified natural surfactant (Surfacten, Tokyo-Tanabe, Tokyo, Japan) was administered. When suprasystemic pulmonary hypertension was demonstrated as the right-to-left shunt through patent ductus arteriosus or when the oxygenation index ($100 \cdot F_IO_2 \cdot$mean airway pressure$\cdot PaO_2^{-1}$) was >25, NO inhalation was started by addition of NO to the constant oxygen flow at the inspiratory limb of the HFO ventilator. If the postductal oxygenation index was >30 for more than 2 h after NO was started, ECMO was initiated.

Surgical repair was performed when pulmonary hypertension was controlled and the patient was stabilized. The same surgeons were involved in all cases. Anesthesia was induced and maintained with intravenous injection of fentanyl and midazolam, and muscle relaxation was obtained with pancuronium.

After surgery, weaning from mechanical ventilation was managed by the same members of the intensive care unit (ICU) staff and pediatric surgeons who were blinded to perioperative C_{rs} data in all cases. Our weaning strategy was as follows. First, the ventilation mode was changed from HFO to intermittent mandatory ventilation with peak inspiratory pressure less than 25 cmH_2O. Second, sedatives and muscle relaxants were discontinued when postductal PaO_2 was equal to preductal PaO_2. Then the inspiratory oxygen concentration, concentration of NO (if used), inspiratory pressure, and synchronized intermittent mandatory ventilation rate were reduced while PaO_2 was maintained above 70 mmHg, $PaCO_2$ below 50 mmHg, and spontaneous respiratory rate below 60/min. The timing of extubation was determined by the same ICU staff member according to clinical status. Postoperative ventilator-dependent duration is calculated as the days on mechanical ventilator from the day of surgery to the final extubation in the ICU.

Respiratory system compliance measurements

We measured static C_{rs} just before and after surgery in the operating room with muscle relaxation. A passive expiratory flow-volume technique was used [20]. During pulmonary function tests, the ventilatory mode was changed from HFO to pressure-limited, constant-flow-type intermittent mandatory ventilation. After a manual large inflation (inspiratory pressure up to 30 cmH_2O) was applied, static C_{rs} was measured. The peak inspiratory pressure was set at 25 cmH_2O with zero end-expiratory pressure. Other ventilatory settings were determined by the anesthetist. The respiratory rate was set low enough to avoid auto-positive end-expiratory pressure (PEEP) (there should be no flow at end-expiration). Airway pressure and flow were measured at the proximal end of the endotracheal tube by a computerized pulmonary function device (CP100 Neonatal, Bicore, Irvine, CA, USA). Volume was automatically calculated by integration of flow. We applied cricoid pressure, if needed, to keep the air leak less than 10% of inspiratory volume during the measurement. At one of the end-inspirations of the ventilator, we occluded the airway with a balloon (filling time, 12 ms; duration of occlusion, 0.3 to 1.0 s), allowing the airway pressure to equilibrate and to give the occlusion pressure (P_{occl}, cmH_2O). After a short period of occlusion, the airway was unoccluded and the occlusion volume (V_{occl}, ml) was measured. The C_{rs} ($ml \cdot cmH_2O^{-1}$) was calculated by the following equation:

$$C_{rs} = V_{occl}/P_{occl}$$

We repeated the measurements until three consecutive close (less than 10% variance) values were obtained.

Table 1. Clinical characteristics of patients

Patient no.	Sex	GA (weeks.days)	Birthweight (g)	AP	Delivery	Onset (h)	Age (days)	Organ	preD P/F	postD P/F	SRT	NO	ECMO	Outcome	Associated problem
1	F	36.3	1920	9	V	18	4	S	445	382	Y	Y	N	S	—
2	M	35.5	4340	5	C	0	7	S	315	302	N	Y	N	S	Tetrasomy 12p
3	M	38.1	2714	6	C	0	5	S	—	339	Y	Y	N	S	—
4	M	37.1	3096	6	C	0	7	S	258	195	Y	Y	Y	D	—
5	F	39.5	3278	7	V	1	2	S	553	423	N	N	N	S	—
6	M	37.5	3060	3	C	0	0	S&L	165	60	Y	Y	N	S	Absent pericardium
7	M	39.6	3420	7	V	0	0	S	379	309	N	Y	N	S	—
8	M	39.3	2628	8	V	0	1	n	491	376	N	N	N	S	—
9	F	39.1	2980	8	V	0	2	S	435	357	Y	Y	N	S	—
10	M	38.3	2732	9	V	8	1	n	—	351	Y	N	N	S	—
Mean ± SD		38.1 ± 1.3	3017 ± 625	7 ± 2		3 ± 6	3 ± 3		380 ± 128	309 ± 107					

M/F, Male/female; GA, gestational age at birth; AP, Apgar score at 1 min; C/V, cesarean section/vaginal delivery; onset, onset time of respiratory distress after birth; age, age at surgery; organ(L/S/n), left lobe of liver or stomach in hernia or not; preD P/F, preoperative best preductal PaO_2/F_IO_2; postD P/F, preoperative best postductal PaO_2/F_IO_2; SRT, surfactant replacement therapy; NO, nitric oxide inhalation; ECMO, extracorporeal membrane oxygenation; S/D, survived/died; Y/N, yes/no

The measurements of C_{rs} were averaged and were standardized by dividing by birthweight. Accuracy of the device (less than 5% deviation) was confirmed for volume with a 50-ml syringe and for pressure with a water manometer.

Data from all patients who could be extubated were pooled to analyze the correlation between ventilator-dependent duration and birthweight-corrected preoperative C_{rs} (C_{pre}), birthweight-corrected postoperative C_{rs} (C_{post}), or the ratio of C_{post} to C_{pre} (C_{post}/C_{pre}).

Data analysis

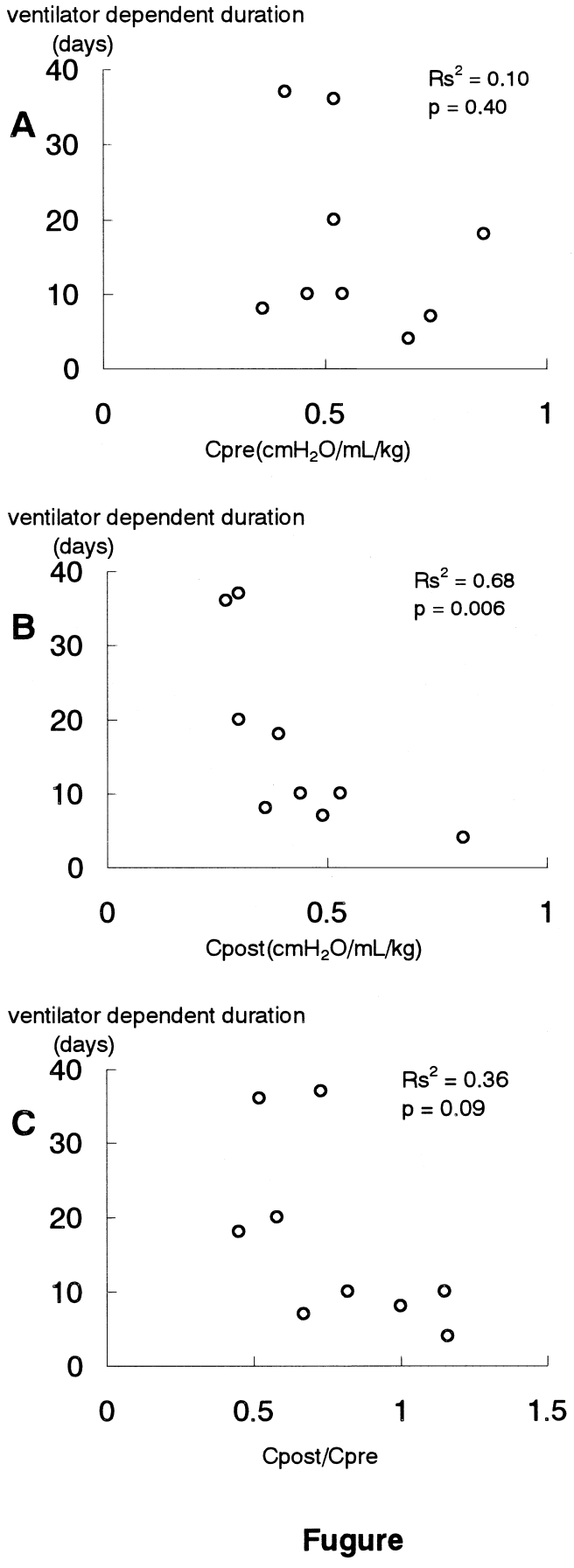
Birthweight-corrected C_{pre} and C_{post} were compared by the paired *t*-test. The correlation between postoperative ventilator-dependent duration and birthweight-corrected C_{pre}, birthweight-corrected C_{post}, and C_{post}/C_{pre} was assessed with Spearman's correlation coefficient by ranks. Statistical significance was accepted at $P < 0.05$.

Results

Ten patients were enrolled in our study. Their clinical characteristics are shown in Table 1. Seven patients presented with respiratory distress within an hour after birth. Six neonates received SRT and seven had NO inhalation preoperatively. One patient (no. 4) was treated with ECMO prior to the operation but died on postoperative day 31 from hypoxia and intraventricular hemorrhage. This patient was excluded from the analysis of postoperative ventilator-dependent duration. The other nine neonates were extubated successfully at the first trial and survived to be discharged from the ICU. The highest values of preoperative preductal and postductal PaO_2/F_IO_2 taken from the medical charts are shown in Table 1. We could not measure the highest preductal PaO_2 of patients 3 and 10 because of failure to place a catheter.

Individual compliance data and ventilator-dependent duration are shown in Table 2. In seven patients, C_{rs} decreased after surgery. The overall mean C_{rs} ($n = 10$) value decreased after surgery compared with C_{pre} (0.41 ± 0.18 *vs* $0.54 \pm 0.18\,ml \cdot cmH_2O^{-1} \cdot kg^{-1}$, $P = 0.04$).

In the nine neonates who survived, the mean ventilator-dependent duration was 16.7 ± 12.3 days. Ventilator-dependent duration was significantly correlated with birthweight-corrected C_{post} ($P = 0.006$), whereas no significant correlation was observed between ventilator-dependent duration and C_{post}/C_{pre} ($P = 0.09$) or birthweight-corrected C_{pre} ($P = 0.40$) (Fig. 1).



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Discussion

In this study, we showed that C_{rs} decreased after surgical repair in many neonates with CDH (Table 2), and birthweight-corrected C_{post} was significantly correlated with their postoperative ventilator-dependent duration (Fig. 1A). As far as we know, there have been no studies in which the relationship between C_{rs} and postoperative ventilator dependency was investigated. Low C_{post} may predict prolonged ventilator-dependent duration of neonates with CDH.

The degree of impairment of lung function after surgery depends on the maturity of the lung [10], inherent lung volume [8,9], and the effects of surgery [11]. When the hernia contents are repositioned into the abdomen and the diaphragm on the hernia side is plicated by surgery, the chest wall will be distorted, the intra-abdominal pressure and diaphragmatic tension toward the pleural space will rise if the abdominal wall is not compliant enough to hold the hernia contents, and as a result, chest wall compliance will be reduced [11]. Furthermore, overinflation of the lung on the non-herniated side will be caused by central shift of the mediastinum by surgery and postoperative mechanical ventilation with a high airway pressure [11]. We think that all three of these factors affected C_{post} in combination.

The reason why C_{post} and ventilator-dependent duration are correlated is unclear, but the following may be assumed. Although we did not measure C_{rs} before extubation in this study, C_{rs} just before extubation has been shown to be one of the decisive factors in successful extubation [21,22]. Therefore, some time may be needed to improve C_{rs} to the extent that the infants can be weaned from mechanical ventilation. Thus, C_{post} may predict the length of the period between surgery and extubation.

In this study, C_{pre} was not correlated with postoperative ventilator-dependent duration (Fig. 1B). This might suggest that physiologic changes after the surgical repair of hernia or the effects of surgery itself are more decisive factors in the postoperative respiratory course than lung volume or lung maturity at birth, because lung volume or lung maturity should be related to C_{pre}. Although the reason for the difference between the results of previous studies that showed a significant correlation between C_{pre} and mortality and morbidity [12,15] and the results of our study is not clear, the usage of surfac-

Fig. 1. Postoperative ventilator-dependent duration plotted against birthweight-corrected C_{pre} (**A**), birthweight-corrected C_{post} (**B**), and C_{post}/C_{pre} (**C**). Only birthweight-corrected C_{post} had a significant relationship with ventilator-dependent duration ($P = 0.006$)

Table 2. Compliance and postoperative ventilator-dependent duration

Patient no.	Corrected C_{pre} ($ml \cdot cm\ H_2O^{-1} \cdot kg^{-1}$)	Corrected C_{post} ($ml \cdot cm\ H_2O^{-1} \cdot kg^{-1}$)	C_{post}/C_{pre}	Ventilation (days)
1	0.86	0.39	0.45	18
2	0.52	0.27	0.52	36
3	0.52	0.3	0.58	20
4	0.28	0.17	0.62	31[a]
5	0.74	0.49	0.67	7
6	0.41	0.3	0.73	37
7	0.54	0.44	0.82	10
8	0.36	0.36	1	8
9	0.46	0.53	1.15	10
10	0.69	0.81	1.16	4
Mean ± SD	0.54 ± 0.18	0.41 ± 0.18[b]	0.77 ± 0.26	16.7 ± 12.3

Corrected C_{pre}, Preoperative birthweight-corrected C_{rs}; corrected C_{post}, postoperative birthweight-corrected C_{rs}; C_{post}/C_{pre}, ratio of C_{post} to C_{pre}; ventilation, postoperative ventilator-dependent duration

[a] Died on postoperative day 31 and excluded from calculations of ventilation period

[b] $P < 0.05$ *vs* corrected C_{pre}

tant might have affected C_{pre} and had an influence on the relationship between C_{pre} and outcome. On the other hand, C_{post}/C_{pre} also was not significantly correlated with the number of ventilator-dependent days. Change in C_{rs} during surgery (i.e., C_{post}/C_{pre}) must be an effect of surgery, including the influence of several physiologic changes. Therefore, although the effect of surgery is a major reason for prolonged postoperative mechanical ventilation, change in C_{rs} by itself cannot be the only reason.

Additional retrospective analysis revealed that there was a significant relationship between NO usage and postoperative ventilator dependence. In six patients who survived with preoperative NO inhalation, postoperative ventilator-dependent duration was significantly longer than in three patients who did not receive NO (21.8 ± 12.1 vs 6.3 ± 2.1 days, $P = 0.02$ by Mann-Whitney U test). We assume that the patients who did not require NO support had milder lung disease and better pulmonary outcome than those who required NO. On the other hand, there was no relationship between SRT and postoperative ventilator duration.

We excluded patients with right-sided CDH because there was a report that patients with right-sided CDH and those with left-sided CDH have different prognosis [1], and because we had the impression that the prognosis of right-sided CDH may depend not only on pulmonary hypoplasia but also on other problems, such as circulatory disturbance or hepatic dysfunction [23]. We also limited subjects to those with a gestational age of 35 weeks, because even in normal neonates, pulmonary surfactant is not sufficient until 34 weeks of gestation [24].

The present study has some limitations. First, we used ventilator-dependent duration as an index of respiratory insufficiency. However, ventilator-dependent duration is affected by many factors besides respiratory ability, including gestational age, central nervous system disorders, muscle tone, intestinal abnormalities, infections, and postoperative iatrogenic problems. Among our subjects, patient no. 2 had a weak muscle tone. This might have affected our results. Second, we could not prove our speculation that C_{post} was affected by inherent lung volume or change in chest wall compliance, because we did not measure functional residual capacity, esophageal pressure, or intra-abdominal pressure. Evaluation of these factors is required to assess mechanisms of deterioration of postoperative respiratory function.

In summary, respiratory system compliance decreased after surgical repair in neonates with CDH, and neonates with low postoperative respiratory system compliance needed longer ventilator dependency. Postoperative respiratory system compliance may predict the postoperative respiratory outcome of neonates with CDH.

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