Treatment and Outcome of Congenital Diaphragmatic Hernia

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Background and purpose: Congenital diaphragmatic hernia (CDH) is a challenging condition and is associated with a high mortality rate; optimal therapy remains unclear. This retrospective study describes the clinical characteristics of treatment and outcome in 48 infants with CDH.

Methods: Twenty-eight male (58%) and 20 female (42%) infants with CDH were treated from 1987 through 1998. The goals of the ventilator strategy were permissive hypercapnea ($PaCO_2 \leq 55$ mm Hg) and avoidance of hyperventilation. Infants were initially ventilated with an intermittent mandatory rate of 40 to 60 per minute, peak inspiratory pressure of 20 to 25 cm H_2O, and positive end-expiratory pressure of 5 cm H_2O. High-frequency positive pressure ventilation was used if hypoxemia or severe hypercapnea ($PaCO_2 > 60$ mm Hg) occurred. Most infants underwent repair after 3 days of age and only four infants underwent early repair within 24 hours of birth. A prophylactic chest tube was placed in the ipsilateral hemithorax postoperatively in all patients treated before 1996. The severity of respiratory distress was estimated by alveolar-arterial oxygen difference, oxygenation index, and alveolar-arterial ratio.

Results: Forty-six patients presented with Bochdalek CDH, and two with Morgangni CDH. Antenatal diagnosis was made in 10 cases. Respiratory distress was the major manifestation and usually occurred immediately after birth. Six cases were diagnosed several months after birth and presented mainly with gastrointestinal symptoms. Eleven patients died before surgery and 37 patients underwent surgical repair. Two infants died postoperatively because of congestive heart failure and tension pneumothorax, respectively. The overall mortality rate was 27%. The major causes of mortality were severe respiratory failure, persistent pulmonary hypertension, pneumothorax, and associated anomalies.

Conclusion: Nearly 75% of patients in this series survived. This suggests that non-invasive respiratory care combined with delayed surgery may be an acceptable strategy for the treatment of CDH, and can be used in most medical institutions without equipment for extracorporeal membrane oxygenation therapy.

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Key words:
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permissive hypercapnea
delayed surgery

The diaphragm develops anteriorly as a septum between the thoracic and abdominal cavities and progresses backward to close at around 8 to 10 weeks' gestation. The bowel migrates from the yolk sac at about the 10th week of gestation. Herniation of the bowel can occur if it arrives before the diaphragm has closed. Congenital diaphragmatic hernia (CDH) has an incidence of one in 2,000–5,000 live births [1]. Despite advances in neonatal intensive care during the past decade, the mortality rate of CDH remains relatively unchanged, at 40% to 50% [2]. The optimal preoperative management, timing of surgery, need for prophylactic chest tube insertion after repair, optimal ventilator therapy, and optimal vasodilator therapy remain controversial [2–4]. Recent evidence suggests that emergency surgery may cause a decrease in respiratory compliance and subsequently hinder lung function [4]. Hence, initial stabilization of cardiopulmonary status is crucial before surgery.

Most patients undergo primary closure, and a prosthetic patch may be necessary for a large defect.

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Avoiding the use of a chest tube after repair may prevent excessive mediastinal shift and reduce the risk of wide swings of intrathoracic pressure [4]. Respiratory therapy with gentle ventilation is used to minimize the risk of barotrauma.

Several studies have reported that survival has improved since the introduction of extracorporeal membrane oxygenation (ECMO) therapy [5, 6]. However, Azarow et al showed that conventional ventilation with high-frequency oscillatory ventilation (HFOV) produces a survival rate equal to that achieved with conventional ventilation with ECMO [7]. Inhaled nitric oxide (iNO) may selectively dilate pulmonary vessels and improve persistent pulmonary hypertension in neonates (PPHN). However, the response and benefit may be temporary in infants with CDH [8]. ECMO and iNO were not readily available at our hospital during the study period. The purpose of this study was to review the records of infants with CDH treated at our institution from January 1987 through December 1998.

Patients and Methods

The medical records of 48 patients with CDH treated at Chang Gung Children's Hospital from 1987 through 1998 were reviewed. Preoperative, operative, and postoperative data from each patient were collected for analysis. Preoperative data included documentation of a prenatal diagnosis, gestational age at birth, sex, birth body weight, initial presenting symptoms and signs, initial arterial blood gas analysis, associated anomalies, and time from birth to operative repair. Operative data included the side of the hernia, the presence of abdominal organs in the hemithorax, and the presence or absence of a hernia sac. Postoperative data included whether or not a chest tube was inserted, parameters of postoperative ventilator settings, and prognosis.

If CDH had been diagnosed by prenatal ultrasound examination, notification was given before delivery and the neonatal resuscitation team was present at the delivery room with a detailed evaluation of the prenatal history. Gentle baby care was given immediately after birth with avoidance of mask ventilation, and endotracheal intubation was performed. A large-bore Fr 10 nasogastric tube was inserted for decompression of the intrathoracic gastrointestinal loops.

Infants were ventilated initially using the conventional mode with a time-cycled, pressure-limited, and continuous-flow ventilator. The initial ventilator setting was at an intermittent mandatory (IMV) rate of 40 to 60 breaths per minute, peak inspiratory pressure (PIP) of 20 to 25 cm H_2O, and positive end-expiratory pressure (PEEP) of 4 to 6 cm H_2O. The aim of ventilator therapy was to maintain the preductal PaO_2 between 60 and 90 mm Hg and the $PaCO_2$ between 40 and 55 mm Hg. If oxygenation was not adequate or the $PaCO_2$ was greater than 60 mm Hg, high-frequency positive pressure ventilation (HIPPV) with the same ventilator was used, with the IMV rate increased to 100 breaths per minute, with a PIP of 20 cm H_2O and a PEEP of 0 cm H_2O.

After 1993, HFOV was used as a rescue ventilator regimen, with a Sensormedics 3100 ventilator (ETL Testing Laboratories Inc., Cortland, NY, USA) at a frequency of 10 to 15 Hz and a mean airway pressure of 2 cm higher than the previous conventional ventilatory therapy. If the ventilator settings were adequate for chest wall excursion but hypoxemia persisted because of PPHN, vasodilator therapy with tolazoline or magnesium sulfate and a cardiotonic drug such as dopamine was added, without increasing the PIP or the IMV rate to avoid hyperventilation. A diagnosis of PPHN was made if the preductal and postductal oxygen tension difference was greater than 20 mm Hg, or by color Doppler echocardiographic evidence of atrial and/or ductal right-to-left shunt.

Most surgical repair was undertaken if gas exchange improved and the cardiopulmonary status stabilized. All operative repairs were accomplished through an abdominal approach via a subcostal incision on the side of the defect. The diaphragm was primarily closed, and a prosthetic patch was used if there was insufficient muscle for primary closure. A prophylactic chest tube was placed in the ipsilateral hemithorax postoperatively in infants treated during or before 1996. However, this practice was discontinued thereafter. The severity of respiratory distress was estimated by alveolar-arterial oxygen difference ($AaDO_2$), oxygenation index (OI), and alveolar-arterial (a/A) ratio.

The prognostic factors possibly associated with mortality were compared between survivors and nonsurvivors using Student's *t* test or the chi-square test. A *p* value of less than 0.05 was considered statistically significant.

Results

The series of infants treated for CDH comprised 28 male and 20 female patients. Of these 48 patients, 26 were referred from outside institutions. Thirty-nine patients presented with left-sided defects and seven with right-sided defects. Only two cases were Morgagni type. The majority of our patients were full-term neonates and most had a birth body weight greater than 2,500 g. Table 1

Table 1. Characteristics, time to surgery, and outcome in infants with congenital diaphragmatic hernia

Item	No.	(%)
Sex		
Male	28	(58)
Female	20	(42)
Type		
Bochdalek		
Left-sided	39	(81)
Right-sided	7	(15)
Morgagni	2	(4)
Diagnosis		
Prenatal	10	(21)
Postnatal	38	(79)
Birth body weight		
≥ 2,500 g	44	(92)
< 2,500 g	4	(8)
Age of symptom onset		
< 24 hours	25	(52)
24–72 hours	11	(23)
> 72 hours	12	(25)
Surgical repair	37	(77)
Time to surgery		
< 24 hours	4	(8)
24–72 hours	9	(19)
> 72 hours	24	(73)
Outcome		
Survival	35	(73)
Death	13	(27)
Preoperative	11	(23)
Postoperative	2	(4)

shows the preoperative and operative characteristics of patients and outcome. The diagnosis was made with prenatal sonography in 10 patients, and eight of these patients died. The earliest prenatal diagnosis of CDH was made at a gestational age of 26 weeks.

In most cases, the diagnosis was made postnatally; 52% of patients (25/48) presented with early-onset symptoms of respiratory distress, mostly within 6 hours after birth. Eleven patients had symptoms during the second and third days of life. CDH was diagnosed several months after birth in six patients, who mainly presented with gastrointestinal symptoms. All six of these patients had Bochdalek CDH, and three of them also had gastric volvulus.

Most patients tolerated the ventilatory strategy of permissive hypercapnea and avoidance of hyperventilation well. HIPPV was used in cases of persistent hypoxemia and/or severe hypercapnea, and the blood gas levels usually improved thereafter. Only seven infants received HFOV as a rescue therapy and none of them survived. Eleven patients died before surgical intervention; 37 were able to undergo surgical repair. Only four infants underwent emergency surgical repair, and 24 patients received surgical intervention after 72 hours of age. Overall, 35 patients (95%) survived after the operation. Only two patients (5%) died in the postoperative period—because of congestive heart failure and tension pneumothorax, respectively (Table 1).

During the period from 1997 through 1998, the policy of inserting a prophylactic chest tube during the operation was abandoned. Although all patients developed transient pneumothorax and pleural effusion, these complications resolved spontaneously within 1 week.

The overall mortality rate was 27% (13/48). The presence of associated major anomalies, such as chromosomal anomalies (trisomy 13 and trisomy 21) and congenital heart disease (transposition of the great artery and truncus arteriosus), was associated with a higher mortality. Other major prognostic factors associated with poor outcome were severe respiratory failure with a high $AaDO_2$, a low a/A ratio, a high oxygenation index (OI), pneumothorax, PPHN, and prenatal diagnosis of CDH (Table 2).

Discussion

Despite various therapeutic strategies for treating congenital diaphragmatic hernia, the survival rate is still around 50% to 60% [2]. During the past decade, many reports have described that the survival rate improved after the introduction of newer therapeutic regimens including ECMO therapy [5, 6], HFOV [7], and iNO therapy [8]. However, interpretation of these reports can be difficult because of the small number of patients and the difference in the severity of CDH among patients. The survival rate of 73% in our series is comparable with that of two recent reported series [3, 7].

Table 2. Comparison of prognostic factors between non-survivors and survivors

Items	Non-survivors	Survivors	*p* value
$AaDO_2$ (mm Hg)	625 ± 87	385 ± 48	< 0.001*
a/A ratio	0.28 ± 0.16	0.69 ± 0.28	< 0.001*
Oxygenation index	52.1 ± 16.5	26.5 ± 14.8	< 0.001*
Pneumothorax	6 / 13	3 / 35	0.011†
PPHN	12 / 13	4 / 35	< 0.001†
Congenital anomalies	4 / 13	0 / 35	0.005†
Prenatal diagnosis	8 / 13	2 / 35	< 0.001†

Data are mean ± standard deviation where indicated. $AaDO_2$ = alveolar-arterial oxygen difference; a/A = alveolar-arterial ratio; PPHN = persistent pulmonary hypertension in neonates.*p value by Student's t-test; †p value by chi-square test.

Immediate surgical repair of CDH might be followed by a decrease in respiratory compliance [4]. Wung et al reported that delay of surgery in patients with CDH encouraged spontaneous respiration without overzealous respiratory therapy, and that not using a prophylactic chest tube resulted in improved survival and decreased the need for rescue ECMO [4]. However, Azarow et al reported that the overall outcome in their patients treated with delayed surgical repair was not improved [7]. In our institution, ECMO and iNO were not available during the study period. Ventilator therapy for permissive hypercapnea and avoidance of hyperventilation was used in all cases. In cases of severe hypoxemia or hypercapnea, the ventilator setting was changed to a high IMV rate of 100 breaths per minute, the PIP was decreased to 5 cm H_2O below the previous setting, and zero PEEP was applied. Most patients tolerated these new settings well and the blood gas levels improved thereafter. Barotrauma was a relatively rare (18%) complication of this strategy. In 1997, we discarded the policy of routine insertion of a chest tube at the time of repair. Thereafter, secondary PPHN never occurred. Postoperative pneumothorax and pleural effusion were not problematic and usually resolved spontaneously.

HFOV has been reported to be a useful alternative option when conventional ventilation is ineffective [7]. The rationale is that small tidal volume and gas transport by augmented diffusion result in lower shear stresses and less barotrauma [7]. Most authors advocate that the timing of introduction of the HFOV is the most important determinant of outcome [1, 2]. Seven of our patients received HFOV as a rescue regimen and all of them died. Intractable respiratory failure was the main cause of death in these patients.

The use of partial cardiopulmonary bypass via ECMO allows for lung rest and decreases pulmonary vascular resistance. Ryan et al [5] and Connors et al [6] reported that ECMO therapy was more effective than conventional management. However, the complications of ECMO may increase morbidities such as embolic and thrombotic events, systemic and intracranial bleeding, and cerebral infarction. ECMO is also expensive and sophisticated and not always available in many hospitals. iNO therapy may selectively dilate pulmonary vasculature and improve hypoxemia caused by PPHN. However, the responses may not always be reliable and may even be temporary, especially in cases of CDH with severe pulmonary hypoplasia [8].

Sweed and Puri found that the presence of associated major anomalies such as cardiac and chromosome anomalies is often associated with a poor prognosis [9]. In this series, all of our four patients with major congenital anomalies died. Attempts have also been made to determine other prognostic factors in infants with CDH [10–12]. In our series, we found that severe respiratory failure and a high $AaDO_2$ ($p < 0.001$), a low a/A ratio ($p = 0.001$), and a high OI ($p = 0.001$) were associated with increased mortality. Pneumothorax, PPHN, and prenatal diagnosis of CDH were also associated with a decreased survival rate.

In conclusion, the survival rate of patients with CDH treated with non-invasive ventilator therapy and delayed surgery was nearly 75%. Permissive hypercapnea and avoidance of hyperventilation will reduce ventilation-induced lung damage. Delayed surgical repair may be necessary for stabilization of cardiopulmonary status in these patients. This strategy can be used in most medical institutions where ECMO therapy is not available.

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