World J Surg (2019) 43:282–290
https://doi.org/10.1007/s00268-018-4780-x

ORIGINAL SCIENTIFIC REPORT

Predicting Survival of Congenital Diaphragmatic Hernia on the First Day of Life

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Published online: 30 August 2018
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Abstract

Background This study aimed to determine perinatal risk factors for 30-day mortality of congenital diaphragmatic hernia (CDH) patients and develop a prognostic index to predict 30-day mortality of CDH patients. Identifying risk factors that can prognosticate outcome is critical to obtain the best management practices for patients.

Methods A retrospective study was performed for patients who were diagnosed with CDH from November 2000 to August 2016. A total of 10 prenatal risk factors and 14 postnatal risk factors were analyzed. All postnatal variables were measured within 24 h after birth.

Results A total of 95 CDH patients were enrolled in this study, including 61 males and 34 females with mean gestational age of 38.86 ± 1.51 weeks. The overall 30-day survival rate was 63.2%. Multivariate analysis revealed that five factors (polyhydramnios, gestational age at diagnosis <25 weeks, observed-to-expected lung-to-head ratio ≤45, best oxygenation index in 24 h >11, and severity of tricuspid regurgitation ≥ mild) were independent predictors of 30-day mortality of CDH. Using these five factors, a perinatal prognostic index for 30-day mortality was developed. Four predictive models (poor, bad, good, and excellent) of the perinatal prognostic index were constructed, and external validation was performed.

Conclusions Awareness of risk factors is very important for predicting prognosis and managing patients. Five independent perinatal risk factors were identified in this study. A perinatal prognostic index was developed for 30-day mortality for patients with CDH. This index may be used to help manage CDH patients.

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Introduction

Congenital diaphragmatic hernia (CDH) is an uncommon congenital anomaly that affects about 1 in 2000–5000 births [1–3]. With improvement in antenatal imaging techniques, accurate and faster diagnosis has improved maternal care so that appropriate treatment is available. Neonatal care such as gentle ventilation, delayed surgery, and extracorporeal membrane oxygenation (ECMO) has also been improved. Nevertheless, the overall mortality rate of CDH patients remains 20–50% [2–7].

The outcome of patients with CDH is very difficult to predict. Knowing the risk factors for predicting their outcome is vital for establishing patient management and the best clinical practices, as well as for clinician and parent counseling. Despite the controversies regarding risk factors for CDH, accepted risk factors for mortality of CDH patients include prenatal factors such as gestation age (GA) at prenatal diagnosis, chromosomal anomaly, major heart anomaly, maternal polyhydramnios, right-side CDH, lung-to-head ratio (LHR), observed-to-expected LHR (O/E LHR), fetal lung volume on magnetic resonance imaging, quantitative lung index (QLI), and liver herniation [8–14] and postnatal factors such as oxygenation index (OI), birth weight, defect size, Apgar scores (at 1 and 5 min), McGoon index and pulmonary artery index, ECMO, high-frequency oscillation (HFO), nitric oxide (NO), echocardiographic findings able to measure the severity of pulmonary hypertension include severity of tricuspid regurgitation (TR), flattening or left deviation of the interventricular septum, and patent ductus arteriosus (PDA) shunt direction [15–24].

The ability to accurately and easily predict the postnatal outcome of CDH patients can be a valuable management tool. Many studies have attempted to predict the clinical course of CDH patients by analyzing prenatal or postnatal factors [11, 25–30]. However, few studies have analyzed the patient's clinical course by simultaneously analyzing the prenatal and postnatal factors. In this study, prenatal and postnatal factors obtainable within 24 h after birth were analyzed to identify independent risk factors for 30-day mortality. These factors were then used to develop a perinatal prognostic index for 30-day mortality of CDH patients. The aim of this study was to develop and validate a simplified clinical method for predicting survival outcomes within 30-day of patients with CDH.

Methods

We retrospectively reviewed 95 patients diagnosed with inborn Bochdalek hernia from November 2000 to August 2016 at the Seoul National University Children's Hospital. Eighty-three (87.4%) patients had Bochdalek hernia diagnosed prenatally, while the diagnosis of the remaining 12 patients (12.6%) was achieved postnatally despite regular prenatal workup. These patients showed respiratory distress. Bochdalek hernia was confirmed after radiologic studies, including plain chest X-ray.

Inclusion criteria were inborn Bochdalek hernia and prenatal diagnosis of CDH or postnatal diagnosis within 12 h after birth. Exclusion criteria were outborn patients and hiatal hernia.

The following were investigated as possible risk factors for 30-day mortality in CDH patients: prenatal factors (maternal polyhydramnios, GA at CDH diagnosis, LHR, O/E LHR, QLI, right-side CDH, liver herniation, and gastrointestinal (GI), major heart, and chromosomal anomalies) and postnatal factors (birth weight, pneumothorax, HFO, NO, 1- and 5-minute Apgar scores, OI, alveolar arterial oxygen gradient [A-a gradient], and echocardiographic findings). In echocardiography, severity of TR and PDA shunt direction were investigated as factors for severe pulmonary hypertension. Arterial blood gas measurements, OI, and A-a gradients were analyzed based on initial values after birth and worst and best values within 24 h. Overall, 10 prenatal and 14 postnatal factors were analyzed.

All postnatal factors were analyzed at birth up to 24 h after birth. The primary study endpoint was mortality within 30 days after birth. Four patients underwent CDH repair (range 12–22 h) on the day of birth. These patients were analyzed for arterial blood gas measurement, HFO, and NO before surgery. Two patients underwent ECMO after 20 and 23 h after birth, respectively. These patients were also assessed for arterial blood gas measurement, HFO, and NO before procedures. CDH repair and ECMO application were excluded from postnatal factor in this study because they were rarely performed within 24 h after birth.

LHR is a calculated by measuring the longest axis of the contralateral lung and the perpendicular diameter thereof [31]. All prenatal images were measured at 22–38 weeks GA. O/E LHR was calculated using the standardized calculation reported previously [32]. QLI was calculated using a previously published formula [14]. A major heart anomaly was defined as the presence of a heart anomaly except PDA, patent foramen ovale, and atrial septal defect. GI or major heart anomalies included those diagnosed prenatally or those found on ultrasonography performed within 24 h postnatally. Pneumothorax included both the affected lung and contralateral lung. OI was calculated using the fraction of inspired oxygen (FiO_2), mean airway pressure (MAP), and arterial PO_2 (PaO_2) after arterial catheterization ($OI = FiO_2 \times MAP \times 100/PaO_2$). A-a gradient was calculated using FiO_2, arterial PCO_2 ($PaCO_2$), and PaO_2 (A-a gradient = [FiO2 × (760 − 47)]–($PaCO_2$/

0.8) − PaO_2). TR severity was graded by transthoracic echocardiography as no gurgitation, trivial, mild, moderate, and severe [33]. The PDA shunt direction was classified as left-to-right, bidirectional, and right-to-left.

All continuous variables were converted to categorical variables. Variables with previously established cutoff values were also used in our study. For the following variables, the median values obtained in this study were used as cutoff values: birth weight, Apgar scores, initial and worst OI, A-a gradient, severity of TR, and PDS shunt direction. Correlations between variables were evaluated by the Chi-square test. Logistic regression analysis was used to identify independent risk factors for 30-day mortality. Statistical differences were considered significant at $p < 0.05$. The final model was constructed using the forward selection method and was ultimately determined considering clinically significant and predictive factors among similar c-index models.

There were no missing data for all factors except for GA at diagnosis as a CDH, LHR, O/E LHR, and QLI of 12 postnatally diagnosed patients. These patients were diagnosed as CDH at GA > 25 weeks. In addition, LHR, O/E LHR, and QLI of these patients were classified as >1.35, >45, and >0.6, respectively.

Herein, a perinatal prognostic index for 30-day mortality was developed. The score was adjusted to a total sum of 100 using values of parameter estimates of prenatal and postnatal independent risk factors for 30-day mortality identified in multivariate logistic regression analysis. The sum of the parameter estimates of the five independent factors in Table 1 was 11.4219. Multiplying this value by 8.7551 equaled 100. Then, 8.7551 multiplied by 2.4084, the parameter estimate of polyhydramnios, was 21.08, and so for all other variables, 15.64, 25.63, 24.38, and 13.26, respectively. Rounding all of these values to the first decimal place was the adjusted score indicated in Table 2. Perinatal prognostic index for each patient was calculated as follows: Total score = Polyhydramnios + GA at prenatal diagnosis + O/E LHR + Best oxygenation index + Tricuspid regurgitation. Polyhydramnios was given a value of 21 if polyhydramnios was absent, and a value of zero if present. GA at prenatal diagnosis was given a value of 16 if the gestational age at prenatal diagnosis was ≥25 weeks or undiagnosed in the prenatal period, 0 otherwise. O/E LHR was given a value of 26 if O/E LHR was >45 or undiagnosed in the prenatal period, 0 otherwise. Best oxygenation index was given a value of 24 if the best oxygenation index was ≤11 mmHg, and a value of 0 otherwise. Tricuspid regurgitation was given a value of 13 if the patient had no or trivial tricuspid regurgitation, and a value of 0 if significant regurgitation was present.

The perinatal prognostic index was categorized into four groups based on the best predictability of survival through tree regression. The internal validity of the perinatal prognostic index was confirmed by c-index and calibration. An external validation evaluated the predictive power of the perinatal prognostic index for 30-day mortality using data from other tertiary hospitals. These data were collected from Samsung Medical Center (57 patients), Severance Children's Hospital (35 patients), and Pusan National University Children's Hospital (27 patients). Overall, 119 patients, between April 2001 and March 2016, were investigated for external validation. Inclusion and exclusion criteria were the same as those used for this study.

This study was approved by the Institutional Review Board (IRB File No. 1702-061-831).

Results

Ninety-five patients were enrolled; 61 (64.2%) were male. A total of 83 patients (87.4%) had prenatal diagnosis. The mean GA of prenatal diagnosis was 26.18 ± 6.32 weeks. Mean GA was 38.86 ± 1.51 weeks. The mean birth weight was 3085.5 ± 533.8 g. Eighty-four cases (88.4%) presented left-side CDH; none were bilateral. Seventy-eight patients (82.1%) received CDH repair with mean age at operation of 2.87 ± 1.39 days. Twenty-five patients (32%) had large defect size, which was closed using a patch. Thirty-four patients (35.8%) had liver herniation, and eight patients developed pneumothorax within 24 h after birth.

Table 1 Multivariate logistic regression analysis of perinatal risk factors of 30-day mortality

Variable	Parameter estimate	*P* value	Odds ratio	95% CI
Polyhydramnios	2.4084	0.0206	11.116	1.72–71.851
GA at diagnosis <25 weeks	1.7863	0.0114	5.967	1.315–27.083
O/E LHR ≤45	2.9277	0.0007	18.684	3.458–100.958
Best oxygenation index >11	2.7848	0.0011	16.196	3.025–86.715
Severity of TR ≥ mild	1.5147	0.0453	4.548	1.032–20.048

CI Confidence interval, *GA* gestational age, *O/E LHR* observed-to-expected lung-to-head ratio, *TR* tricuspid regurgitation

Table 2 Perinatal prognostic index for 30-day mortality

Variable	Contents	Score
Polyhydramnios	No	21
GA at prenatal diagnosis	≥25 weeks or undiagnosed at prenatal period	16
O/E LHR	>45 or undiagnosed at prenatal period	26
Best oxygenation index	≤11 mmHg	24
Tricuspid regurgitation	No or trivial	13
Total score		100

GA Gestational age, *O/E LHR* observed-to-expected lung-to-head ratio

Mortality before 30 days was 35 (36.8%), and the mean time to death was 8.29 ± 8.18 days (median 5 days; range 1–28 days) (Table 3).

In Table 4, continuous variables were converted to categorical variables. Of the prenatal factors, polyhydramnios was higher in non-survivors (57.1% vs. 15%, $p < 0.001$). Patients with CDH diagnosis at GA of 25 weeks had a significantly higher survival rate than those <25 weeks. A LHR >1.35 had a better survival rate (80.8%). Those with O/E LHR >45 had a survival rate of 88.9%, which was significantly higher than patients with O/E LHR ≤45. QLI >0.6 had a significantly higher survival rate than patients with QLI ≤0.6 (86.2% vs. 27%, $p < 0.001$). Liver herniation was significantly higher in the non-survivors (62.8% vs. 20%, $p < 0.001$). Right-side CDH, GI anomaly, and major heart anomaly were similar between the two groups. Of postnatal factors, birth weight ≥3090 g had a higher, albeit nonsignificant, survival rate than birth weight <3090 g ($p = 0.087$). Pneumothorax was lower in the survivor group. HFO and NO were also significantly less applied in the survivor group (HFO: 40% vs. 91.4%, $p < 0.001$, NO: 26.7% vs. 88.6%, $p < 0.001$). When analyzing four and seven points as the cutoff point for 1- and 5-minute Apgar scores, respectively, there was a significant difference in survival rate. For OI and A-a gradients, the cutoff points for initial value, worst value in 24 h, and best value in 24 h were analyzed. All showed significant differences in survival, with rates significantly higher in patients with no or trivial TR than in those with TR ≥ mild (76.3% vs. 41.7%, $p = 0.001$). Bidirectional or left-to-right PDA shunt direction also showed a significantly higher rate of survival than right-to-left direction (80% vs. 26.7%, $p < 0.001$).

Table 3 Characteristics of CDH patients

Variables	Numbers
Male	61 (64.2%)
Gestational age (weeks)	38.86 ± 1.51
Birth weight (g)	3085.5 ± 533.8
Side of lesion	
Left	84 (88.4%)
Right	11 (11.6%)
CDH repair	78 (82.1%)
Age at operation (days)	2.87 ± 1.39
Body weight at operation (g)	3160.5 ± 567.2
Patch closure	25 (32%)
Survivor	60 (76.9%)
Liver herniation	34 (35.8%)
Pneumothorax in first day	8 (14.7%)
Survivors after 30 days	60 (63.2%)
Median follow-up (days)	257 (1–4017)

Multivariate logistic regression analysis was performed to identify independent risk factors based on statistically significant predictors emerging from the univariate logistic regression analysis. Prenatal independent risk factors were polyhydramnios, GA at diagnosis <25 weeks, and O/E LHR ≤45. Postnatal independent risk factors were best OI in 24 h > 11 and TR ≥ mild (Table 1).

With the five independent perinatal risk factors, a perinatal prognostic index for 30-day mortality was developed. Each variable described a good prognosis. The higher the score sum, the better the prognosis (Table 2). When the perinatal prognostic index was applied to the study patients, those with a sum score between 0 and 39 points had a survival rate of 0% (poor prognosis). The survival rate was 37.5% for those with a sum score of 40–60 points (bad prognosis); for 61–75 points, survival was 82.3% (good prognosis); for a score of ≥76 points, the 100% survival was associated with excellent prognosis (Fig. 1). The observed survival probabilities and the predicted mortality consistency in the four groups were confirmed by calibration plots. The c-index was calculated for discrimination (c-index of internal validation = 0.967).

External validation of the perinatal prognostic index for 30-day mortality was performed using data of 119 CDH patients from other tertiary hospitals. There was a significant ($p < 0.0001$) difference in the probability of survival stratifying patients by the four groups depending on the

Table 4 Comparison of perinatal risk factors for 30-day mortality between survivors and non-survivors

Variable	Cutoff	Survivor (n =60)	Non-survivor (n =35)	Survival (%)	P-value	Odds ratio	95% CI
Polyhydramnios		9	20	31	<0.001	7.556	2.850–20.028
GA at diagnosis (weeks)	≥25	41	10	80.4	<0.001	5.395	2.165–13.443
	<25	19	25	43.9			
LHR	>1.35	59	14	80.8	<0.001	88.5	10.957–714.794
	≤1.35	1	21	4.5			
O/E LHR	>45	48	6	88.9	<0.001	19.333	6.546–57.101
	≤45	12	29	29.3			
QLI	>0.6	50	8	86.2	<0.001	16.875	5.959–47.785
	≤0.6	10	27	27			
Right-side CDH		5	6	45.4	0.204	2.276	0.64–8.097
Liver herniation		12	22	35.3	<0.001	6.769	2.663–17.206
Associated anomaly		33	20	62.3	0.839	1.091	0.471–2.529
Gastrointestinal		20	8	71.4	0.282	0.593	0.228–1.539
Heart		8	4	66.7	0.788	0.839	0.233–3.016
Chromosome		1	5	16.7	0.041	9.833	1.099–88
Birth weight (g)	≥3090	35	14	71.4	0.087	2.1	0.899–4.908
	<3090	25	21	54.3			
Pneumothorax		2	7	22.2	0.018	7.25	1.414–37.185
HFO		24	32	42.8	<0.001	16	4.399–58.197
NO apply		16	31	34	<0.001	21.312	6.496–69.926
Apgar score, 1 min	≥4	48	13	78.7	<0.001	6.769	2.663–17.206
	<4	12	22	35.3			
Apgar score, 5 min	≥7	47	10	82.4	<0.001	9.038	3.473–23.525
	<7	13	25	34.2			
Oxygenation index							
Initial	≤15.91	44	4	91.7	<0.001	21.312	6.496–69.926
	>15.91	16	31	34			
Worst in 24 h	≤21.67	43	4	91.5	<0.001	19.603	6.005–63.99
	>21.67	17	31	35.4			
Best in 24 h	≤11	56	13	81.2	<0.001	23.692	6.964–80.601
	>11	4	22	15.4			
A-a gradient (mm Hg)							
Initial	≤241.4	43	5	89.6	<0.001	15.176	5.048–45.627
	>241.4	17	30	36.2			
Worst in 24 h	≤293.9	44	4	91.7	<0.001	21.312	6.496–69.926
	>293.9	16	31	34			
Best in 24 h	≤101.2	44	5	89.8	<0.001	16.5	5.458–49.878
	>101.2	16	30	34.8			
Severity of TR	≤trivial	45	14	76.3	0.001	4.5	1.841–10.999
	≥mild	15	21	41.7			
PDA shunt direction	Bi or L to R	52	13	80	<0.001	11	3.998–30.262
	R to L	8	22	26.7			

CI confidence interval, *GA* gestational age, *LHE* lung-to-head ration, *O/E LHR* observed to expected lung-to-head ratio, *QLI* quantitative lung index, *CDH* congenital diaphragmatic hernia, *HFO* high frequency oscillation, *NO* nitric oxide, *A-a gradient* alveolar-arterial oxygen gradient, *TR* tricuspid regurgitation, *PDA* patent ductus arteriosus, *Bi* bidirectional, *L to R* left to right, *R to L* right to left

sum scores (group 1: score 0–39, group 2: score 40–60, group 3: score 61–75, and group 4: score 76–100). To evaluate the validity of the prediction model, receiver operating characteristic area curves (area under the curve = 0.9628, 95% confidence interval: 0.9296–0.9959) for survival prediction were calculated (Fig. 2).

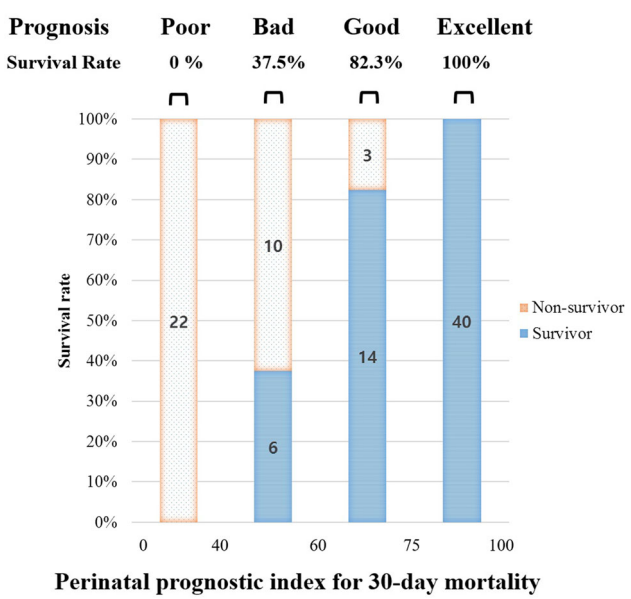

Fig. 1 Perinatal prognostic index for 30-day mortality

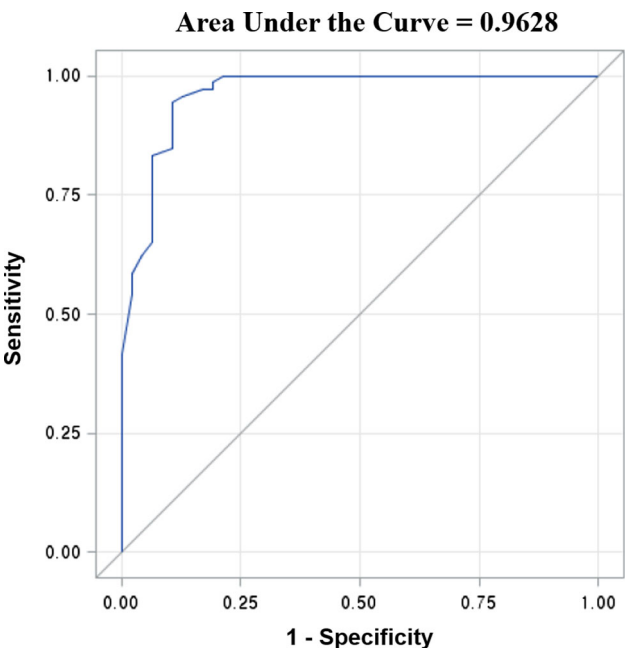

Fig. 2 Receiver operating characteristic curve of external validation for survival prediction

Discussion

CDH has produced improved outcomes recently given the development of gentle ventilation strategies and neonatal management protocols. Nevertheless, CDH patients still have a high mortality rate. CDH prognosis depends on the severity of pulmonary hypertension, which is determined by the degree of pulmonary hypoplasia [34]. Many studies have predicted the degree of pulmonary hypoplasia by determining predictors or risk factors for mortality in CDH patients. Awareness of the risk factor is crucial for predicting prognosis and patient management.

Of the 95 patients in this study, 36 died during the follow-up period, of which 35 died within 30 days of birth. One patient died at the age of 23 months due to heart failure caused by transposition of the great arteries. There have not been many concurrent studies evaluating prenatal and postnatal risk factors for mortality of CDH patients. Of these, few postnatal factors evaluable within 24 h after birth have been analyzed. Herein, a perinatal prognostic index of mortality within 30 days of birth was developed by analyzing five independent perinatal risk factors. External validation of our perinatal prognostic index was performed using data from CDH patients from three external tertiary Korean hospitals. This index includes prenatal as well as five easily obtainable independent postnatal risk factors. The purpose of this index was to predict the mortality of CDH patients within 30 days using data available during the prenatal period and within 24 h after birth. This index may represent an excellent tool to predict patient prognosis.

Regarding prenatal risk factors identified in this study, maternal polyhydramnios has been associated with poor survival [9]. However, subsequent studies have suggested that maternal polyhydramnios has no predictive value [35, 36]. Timing of prenatal diagnosis of CDH may not be related to outcome [37, 38]. However, babies who are diagnosed with CDH at GA 25 weeks have lower mortality than those who are diagnosed at GA <24 weeks [17, 31, 39, 40]. In addition, mortality rates at 28 days were shown to be significantly increased compared to those with GA at diagnosis (61.1, 39.2, and 10.4% for a diagnosis at the first, second, and third trimesters, respectively) [41]. LHR, first reported in 1996, is the best validated prenatal predictor of mortality in CDH worldwide [31]. However, LHR increases with increasing GA; thus, the O/E LHR has been as a proposed adjustment [12] and has been considered an applicable index regardless of GA. However, O/E LHR is also dependent on GA [42]. As an alternative, a QLI independent of the GA has been proposed with QLI ≤0.6 indicating poor prognosis [14]. Herein, polyhydramnios, GA <25 weeks at diagnosis and O/E LHR ≤45 were identified as independent prenatal risk factors for 30-day mortality.

In a study of 2202 CDH infants, birth weight <1500 g, absent or 5-minute Apgar score <7, chromosomal or major cardiac anomaly, and suprasystemic pulmonary hypertension have been analyzed as predictors of CDH severity [18]. This study has great value because of the vast number of CDH infants enrolled. Of the postnatal risk factors analyzed, low birth weight, and chromosomal or major

cardiac anomalies might have been excluded as independent risk factors due to the small number of subjects present in our study.

Recently, the search for predictors using blood gas analysis has been actively conducted. OI has been used as an important indicator of ECMO and has been reported as a predictor of outcome in respiratory failure patients [43]. Furthermore, OI has been reported as a predictor of mortality. The best OI in 24 h >11 was a risk factor for mortality [44], and a cutoff point of 12 has been suggested [45]. Herein, the initial and worst values were added in addition to the best 24-hour value.

Several echocardiography measurements can indicate pulmonary hypertension, including direction and velocity of the ductus arteriosus, interventricular septum position, and severity of TR [46–48]. Herein, the degree of TR was analyzed as an independent factor for mortality by analyzing PDA direction and the degree of TR, of which there were no missing data in echocardiographies performed <24 h.

The ECMO procedure was not actively applied to CDH patients at our center. In some recently reported studies, about 30% of CDH patients treated with ECMO showed a 51% survival [49], while 27% of CDH patients were treated with ECMO, of which 59% survived [29]. There would be an indication for each institution for the ECMO application, but most researchers will agree to apply it when the OI >40 [50]. At our institution, ECMO was applied to 10 of 95 CDH patients (10.5%), all of which died. The ECMO indication and contraindication in our institution follows the extracorporeal life support organization guidelines for neonatal respiratory failure [51]. However, even if the oxygenation index was greater than 40, the ECMO was not applied if the caregiver rejected the ECMO apply or if there was a clear brain injury in our institution.

Detailed analysis of the difference between the predicted probability and the actual survival probability for the four groups in the calibration plot of the external validation groups showed that the predicted and actual survival probabilities of groups 1, 3, and 4 were very similar (actual survival probability: group 1 2.5%, group 3 88.9%, and group 4 94%). However, the predicted probability of group 2 was 37.5% and the actual survival probability was 66.7%. We have no explanation for these differences. Because the external hospital validation study only investigated five factors (polyhydramnios, GA at diagnosis, O/E LHR, best OI in 24 h, and severity of TR), it was not possible to analyze all other data in detail (for example, incidence of ECMO application). Nonetheless, point estimation showed that the prediction model tended to be underestimated except for group 4. The difference between the predicted probability and the actual survival probability was >10% in group 2, albeit the difference between the predicted probability and the actual survival probability in the other group was minimal. Because of the insufficient number of enrolled patients, the confidence interval for the actual survival probabilities for each group was wide; thus, an adequate number of patients for external validation are needed to test this prediction model.

Our report consisted of a study of 24 variables in a single center. It was meaningful given the vast number of variables analyzed. More importantly, an external validation of the perinatal prognostic index developed in this study was performed. However, our study is limited due to the small number of patients analyzed and its retrospective nature; thus, many variables could not be examined over the same study period. OI should also be measured as preductal arterial blood; however, we did not perform this measurement for all cases (preductal 55.8%, postductal 27.4%, and left radial artery 16.8%). The number of patients included in the external validation was also small. We had also been concerned about how to classify prenatal risk factors, especially LHR, O/E LHR, and QLI of 12 postnatally diagnosed patients in this study. The 12 postnatally diagnosed patients were patients whose CDH had not been detected by routine prenatal examination. We emphasized in the text that these patients received a regular prenatal assessment. Prenatal examinations closely monitor the lungs, and none of these patients showed any abnormalities other than normal development of the lungs at the antenatal visit until the third trimester of pregnancy. Indeed, the mean initial oxygenation index of these patients was 9.3 and the mean worst oxygenation index was 13.3 within 24 h after birth. Therefore, we classified the values of LHR, O/E LHR, and QLI in 12 postnatally diagnosed patients into better ones. Another limitation of our study was that 18 patients died after CDH repair. Nine of these patients underwent ECMO. Among the 9 patients on ECMO, there were 3 patients in which ECMO was applied after CDH repair and six patients underwent procedures while on ECMO. As mentioned earlier, our study's mean age at operation was 2.87 days. In our institution, we think that the CDH repair was performed when the patient was hemodynamically stable. However, our institution performed relatively earlier CDH repair compared to other institutions, and it was true that many patients had died after surgery. These results suggest that we need to more consideration for our strategy of the true hemodynamically stable for CDH repair timing in our institution. To develop a better 30-day perinatal prognostic index of mortality, additional patients are needed for external validation. Furthermore, long-term morbidity and mortality studies assessing the perinatal prognostic index classification are needed.

Conclusion

Accurate predictors of postnatal outcome in patients with CDH can be useful to clinicians and for consultations with a child's parents. Independent 30-day perinatal risk factors for mortality included three prenatal factors (maternal polyhydramnios, GA <25 weeks at diagnosis, and O/E LHR ≤45) and two postnatal factors (best OI in 24 h >11 and TR ≥ mild). Based on these perinatal risk factors, a 30-day perinatal prognostic index of mortality for CDH patients was developed. External validation revealed that this index could be used to predict 30-day mortality of CDH patients using results obtained within 24 h after birth and might assist in management of CDH patients.

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