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A novel congenital diaphragmatic hernia prediction model for Chinese subjects: A multicenter cohort investigation

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ABSTRACT

Purpose of the study: Brindle et al. (2014) and the Congenital Diaphragmatic Hernia Study Group constructed a simplified clinical prediction rule (Brindle score) to stratify infants with congenital diaphragmatic hernia based on disease severity. We aimed to develop a predictive model applicable to Chinese patients with congenital diaphragmatic hernia and externally validate whether the Brindle score is applicable to the Chinese population.

Patients and the methods: Multiple imputations supplemented the missing data. A least absolute shrinkage and selection operator regression was used to screen the factors influencing adverse outcomes. Internal validation was performed by bootstrap resampling. The C-index, area under the receiver operating characteristic curve, and the Hosmer-Lemeshow test evaluated the predictive power.

Results: A nomogram named "CCDH score" (Chinese Congenital Diaphragmatic Hernia score), including pulmonary hypertension, low 5-min Apgar score (<7), chromosomal anomaly, major cardiac anomalies (MCAs), observed-to-expected lung-to-head ratio, and the percentage of liver herniation, was constructed. The CCDH score revealed good calibration and discriminative abilities, with a C-index of 0.941. In the training and external validation cohorts, the area under the receiver operating characteristic curve of the Brindle score were 0.820 and 0.881, respectively. The Brindle score has fair predictive power in the Chinese population, but the newly established CCDH score seems more suitable for Chinese patients with congenital diaphragmatic hernia.

Conclusion: The CCDH score is the first predictive model constructed based on the characteristics of the Chinese population and can accurately predict the survival outcomes of patients with congenital diaphragmatic hernia.

1. Introduction

Congenital diaphragmatic hernia (CDH) is characterized by developmental defects in the diaphragm. The accurate prenatal judgement of patient prognosis is crucial for family counseling, formulating appropriate clinical treatment plans, and the rational use of clinical resources.

Popular predictive parameters in clinical practice are the observed-to-expected lung-to-head ratio (O/E LHR) and observed-to-

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expected total fetal lung volume (TFLV) [1,2]. The univariable prediction of outcomes in patients with CDH is flawed; moreover, the outcomes of patients with CDH are often influenced by multiple factors, including genetics and the environment [1,3,4]. Therefore, predictive models constructed by comprehensively considering multiple factors that can affect CDH outcomes should be more reliable than those based on single factors.

Although several CDH risk prediction models have been reported, few are developed based on Asian populations, with the Score for Neonatal Acute Physiology-Perinatal Extension II score (SNAP-II) [5], Congenital Diaphragmatic Hernia Study Group (CDHSG) rule based on birth weight and Apgar score at 5 min [6], Brindle score [7]. The Brindle score is a simple predictive model developed by collecting data from many patients with CDH from 59 medical centers in 10 countries. The model included low birth weight (<1500 g), low 5-min Apgar score (<7), missing 5-min Apgar score, severe PH, and the presence of major cardiac and chromosomal anomalies. This model stratified patients into low-, intermediate-, and high-risk death groups. The Brindle score has been shown to differentiate risk groups well in cohorts from multiple institutions [8–10].

Compared to other predictive models, the Brindle score can easily be applied within the first few hours of life. However, whether this score applies to the Chinese population has not been elucidated yet, and there are few studies in China on models for predicting outcomes in patients with CDH. Our study used multicenter patient data to validate the Brindle score in the Chinese population and combined it with other relevant variables to develop a CDH outcome prediction model suitable for Chinese people.

2. Results

2.1. Characteristics of patients with CDH

The process of inclusion and grouping in this study is illustrated in Fig. 1. To avoid bias, our study included patients with missing information. Fig. 2A shows variables with missing conditions and the proportion of missing data, and the type of missing data is missing at random. The data distribution after interpolation was regular, and the interpolation effect was good (Fig. 2B).

The survival rates of the training and external validation cohorts were 86.2% and 89.2%, respectively ($p = 0.533$). The minimum gestational age for patients with CDH in the total cohort was 31 weeks, with a median age of 38 weeks. The median birth weight was 2960 g, whereas the minimum birth weight was 1790 g. Moreover, 17.6% of patients had a low Apgar score at 5 min. Low birth weight (<1500 g) and a missing 5-min Apgar score, as defined by the Brindle score, were absent. Left CDH was present in 82% of patients, and gastric herniation into the thoracic cavity was present in 56.7% of patients. Except for the major cardiac anomalies (MCAs), the

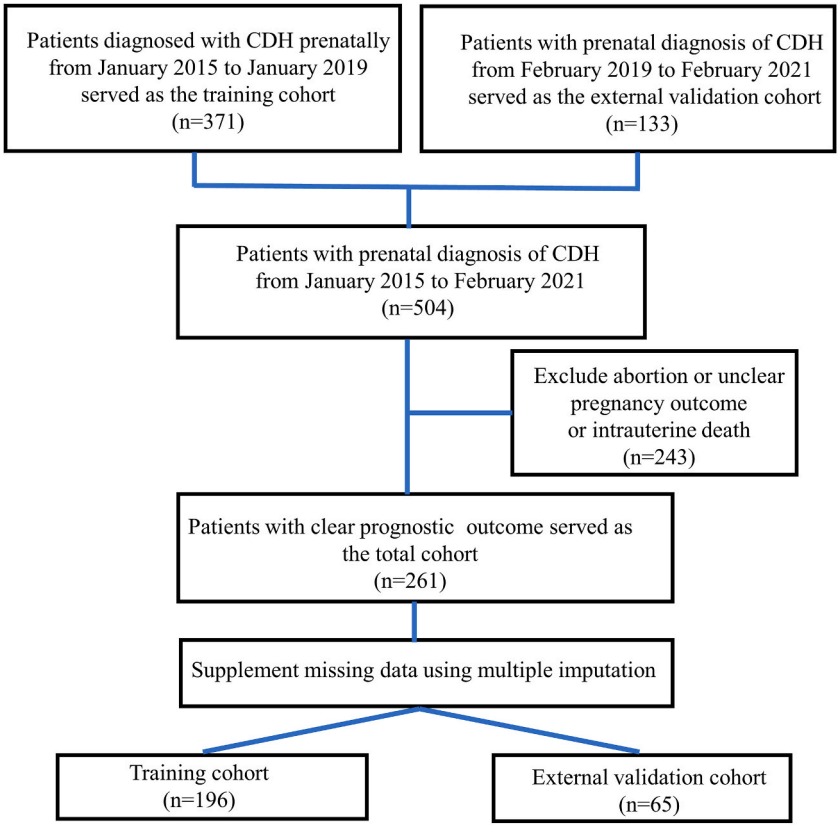


Fig. 1. Flowchart of enrolled patients and grouping criteria.

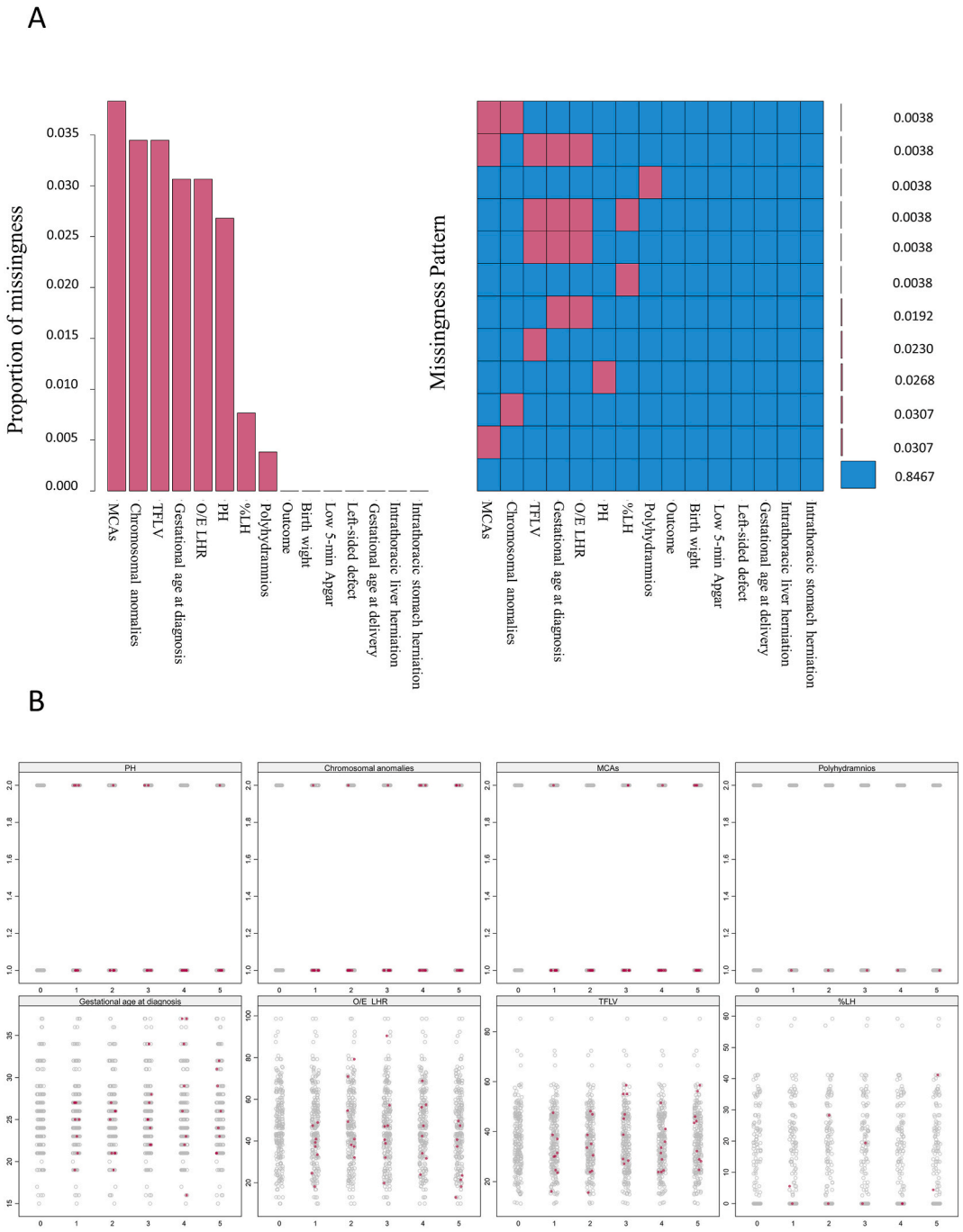


Fig. 2. Determining missing data patterns and imputing data. (A) The proportion of missing in each variable. Each row on the right panel represents a missing pattern, with red representing missing and blue representing non-missing. For example, the second row represents 3.07% of the patterns in which only MCAs variable is missing and no other variables are missing. (B) The distribution of values after imputation of missing variables. Each panel is the original data of one variable and the data generated after 5 imputations. The grey dots represent the original data and the interpolated values are the red dots. It can be seen in the figure that the red dots follow the grey dots fairly well, including the gaps in the distribution.

remaining patient characteristics did not differ between groups (Table 2).

Table 3 summarizes the differences in the characteristics of survivors and non-survivors in the training cohort. A univariable analysis indicated that liver herniation into the thorax ($P < 0.001$) and %LH ($P < 0.001$) were associated with the outcomes of CDH but not gastric herniation into the thorax ($P = 0.789$). Patients with different outcomes did not have different chromosomal anomalies,

Table_1
Values for each of the independent variables to calculate the total Brindle score.

Model Variable	Value
Low Birth Weight	1
Low 5-min Apgar	1
Missing 5-min Apgar	2
Severe Pulmonary Hypertension at Birth	2
Major Cardiac Anomalies	2
Chromosomal Anomalies	1
Total CDH Risk Score	***0–8***

Table_2
Characteristics of patients with CDH in the training and validation cohort.

Characteristics	After imputation processing			*P*
N (%) or median(IQR)	Total cohort (n = 261)	Training cohort (n = 196)	External validation cohort (n = 65)	
Outcome (survival, n%)	87.0%	86.2%	89.2%	0.533
Birth wight (g)	2960(505)	2970(517)	2930(424)	0.229
PH (n%)	25.3%	24.5%	27.7%	0.607
Low 5-min Apgar (n%)	17.6%	16.3%	21.5%	0.339
Left-sided defect (n%)	82.0%	82.7%	80.0%	0.630
Gestational age at diagnosis (wk)	24(5)	24(5)	24(5)	0.652
Gestational age at delivery (wk)	38(2)	38(2)	38(2)	0.208
Polyhydramnios (n%)	41.4%	39.3%	47.7%	0.233
Chromosomal anomalies (n%)	14.9%	13.3%	20.0%	0.187
MCAs (n%)	20.7%	24.5%	9.2%	0.008*
Intrathoracic liver herniation (n%)	35.2%	38.3%	26.2%	0.077
%LH	0(15.2%)	0(17.425)	0(4.005)	0.089
Intrathoracic stomach herniation (n%)	56.7%	54.6%	63.1%	0.232
TFLV	35.98(17.97)	35.94(18.282)	36.21(17.815)	0.570
O/E LHR	47.00(22.96)	46.92(23.400)	47.02(23.950)	0.571

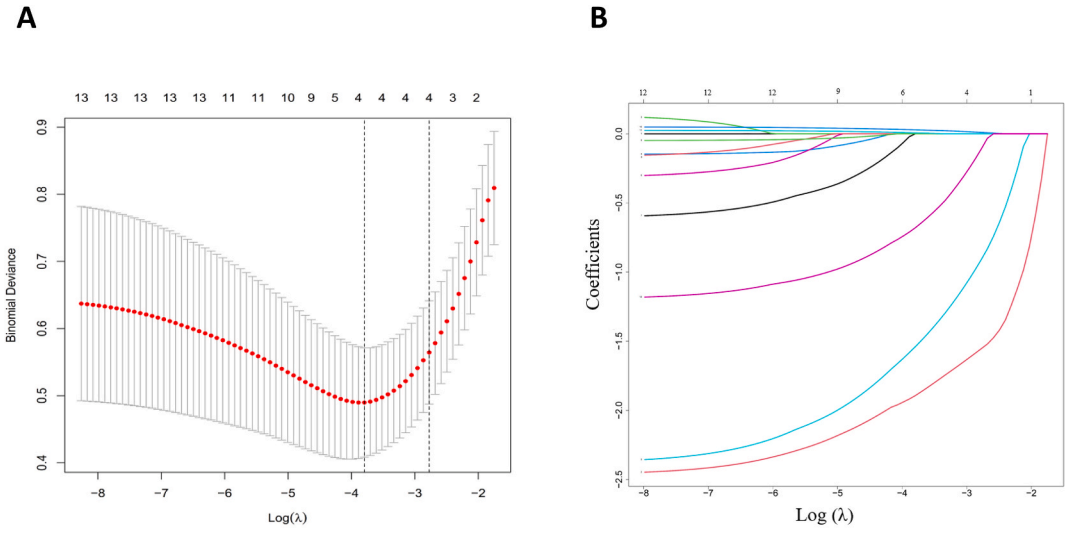
Interquartile range (IQR), pulmonary hypertension (PH), major cardiac anomalies (MCAs), the percentage of liver herniation (%LH), total fetal lung volume (TFLV), observed-to-expected lung-to-head ratio (O/E LHR). Data are presented as median (interquartile range).

Table_3
Comparison of prenatal and postnatal predictors of 12-month mortality between CDH survivors and non-survivors by univariable and multivariable Logistic regression analysis.

Variables	Survivors (n = 227)	Non-survivors (n = 34)	Univariable analysis			Multivariable analysis		
N(%) or median(IQR)			OR	95% *CI*	*P*	OR	95% *CI*	*P*
Birth wight (g)	2990(440)	2710(710)	1.002	1.001–1.003	<0.001*	1.000	0.999–1.002	0.818
PH (n%)	18.1%	73.5%	0.079	0.034–0.183	<0.001*	0.177	0.057–0.551	0.003*
Chromosomal anomalies (n%)	15.0%	14.7%	1.022	0.370–2.824	0.967	0.477	0.109–2.080	0.324
Apgar score <7 at 5 min (n%)	11.0%	61.8%	0.077	0.034–0.172	<0.001*	0.260	0.076–0.894	0.033*
Left-sided defect (n%)	81.9%	82.4%	1.029	0.400–2.645	0.953	2.101	0.390–11.325	0.388
Gestational age at diagnosis (wk)	24(5)	24.5(6.25)	1.000	0.918–1.090	0.994	0.975	0.849–1.121	0.726
Gestational age at delivery (wk)	38(2)	38(3)	1.175	0.960–1.438	0.117	0.812	0.583–1.130	0.216
Intrathoracic liver herniation (n%)	30.8%	64.7%	0.243	0.114–0.519	<0.001*	3.486	0.357–34.070	0.283
Polyhydramnios (n%)	39.6%	52.9%	0.584	0.283–1.205	0.145	0.933	0.312–2.791	0.901
Intrathoracic stomach herniation (n%)	56.4%	58.8%	0.905	0.435–1.881	0.789	1.612	0.510–5.095	0.416
MCAs (n%)	18.9%	32.4%	0.489	0.221–1.078	0.076	0.491	0.140–1.716	0.265
TFLV	37.22(16.80)	26.05(14.90)	1.078	1.038–1.120	<0.001*	1.019	0.996–1.075	0.497
%LH	0(9.6)	21.70(36.70)	0.928	0.904–0.952	<0.001*	0.908	0.841–0.980	0.013*
O/E LHR	48.20(21.50)	25.75(20.13)	1.080	1.049–1.112	<0.001*	1.057	1.015–1.101	0.007*

Interquartile range (IQR), pulmonary hypertension (PH), major cardiac anomalies (MCAs), the percentage of liver herniation (%LH), total fetal lung volume (TFLV), observed-to-expected lung-to-head ratio (O/E LHR). Data are presented as median (interquartile range). * denotes $P < 0.05$.

diaphragmatic defect location, gestational age at diagnosis, gestational age at delivery, polyhydramnios, or MCAs. A multivariable logistic regression analysis showed that %LH had the potential to be included in the final prediction model. ($P = 0.013$) %LH as a continuous variable ($P = 0.013$) was superior to the dichotomous variable intrathoracic liver herniation ($P = 0.283$).



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Variables	Survivors(n=169)	Non−survivors(n=27)	OR(95%CI)	ß	P
O/E LHR	48.2(21.25)	24.3(22.53)	1.060(1.023−1.106)	0.058	0.003
%LH	0(9.95)	24.6(36.7)	0.939(0.901−0.975)	−0.063	0.002
MCAs	22.49%	37.04%	0.718(0.194−2.823)	−0.331	0.623
Low 5−min Apgar	8.88%	44.44%	0.124(0.034−0.416)	−2.086	0.001
PH	17.75%	66.67%	0.139(0.038−0.459)	−1.971	0.002
Chromosomal Anomaly	13.02%	14.81%	0.607(0.121−3.790)	−0.499	0.56

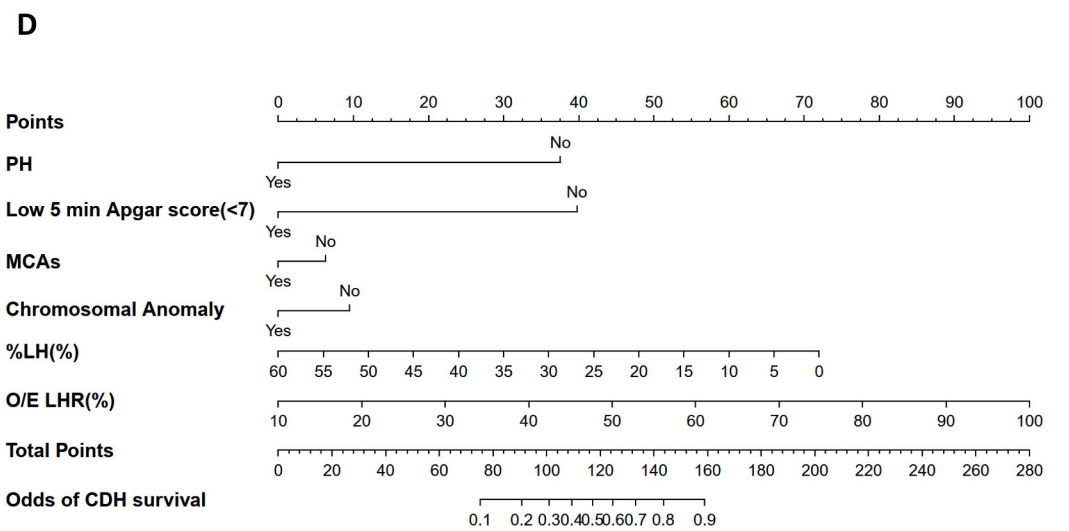

Fig. 3. Establishment of nomogram for predicting CDH survival odds. (A) After the 10-fold cross validation, tuning parameter (λ) selection in Lasso model via minimum criteria, four factors were finally screened. (B) The LASSO regression coefficient plot with 14 features. And optimal λ resulted in 4 nonzero coefficients including O/E LHR, %LH, Low 5-min Apgar score and PH. (C) The forest plot of 6 variables for the new model CCDH score, which includes OR values, 95% CIs, and *P* values obtained by Logistic regression. Values to the left of the invalid line, such as PH, imply a negative correlation with CDH survival. O/E LHR is positively correlated with CDH. (D) According to the clinical characteristics of a CDH patient, the scores for each independent predictor can be obtained and summed. The total score obtained is projected downward to obtain the probability of survival for this patient.

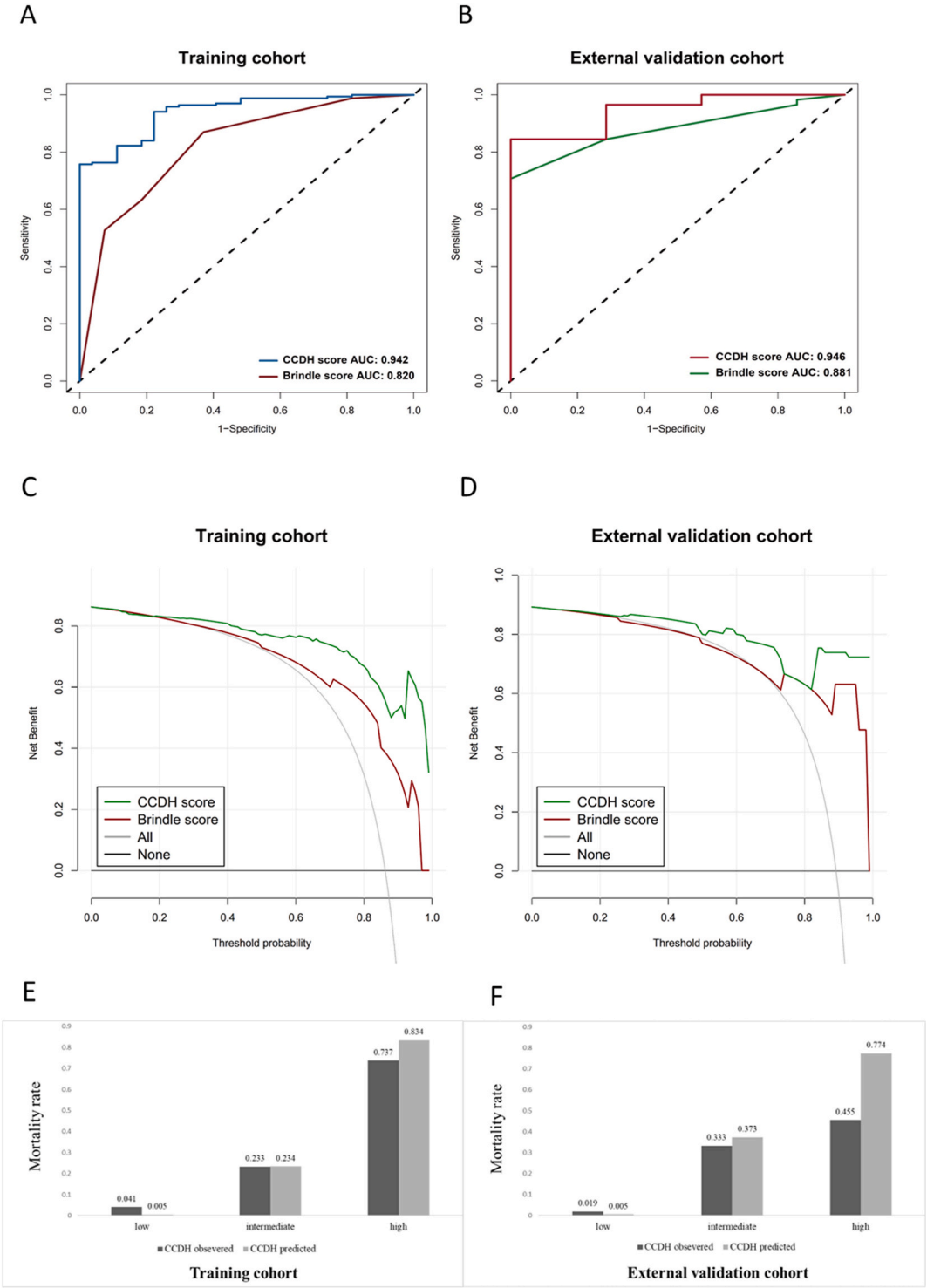

Fig. 4. The performance of CCDH score and compare it with Brindle score. (A, B) Receiver operating characteristic (ROC) curves corresponding to CCDH score and Brindle score in training cohort and external validation cohort. (C, D) The decision curves of net benefit of CCDH score and Brindle score in training cohort and external validation cohort. The solid grey line represents the net benefit for all patients, the solid black line means the net benefit for no patient. (E, F) Actual and predicted mortality rates for different risk groups in CCDH score included in the training cohort and external validation cohort.

2.2. Development of the nomogram

From the 14 potential predictors, four predictors, PH, O/E LHR, %LH, and Apgar score <7 at 5 min, were screened out and included in the final model by a LASSO regression analysis (Fig. 3A and B), which is consistent with the variables screened out in the multivariate logistic analysis (Table 2). Moreover, the *P*-values of chromosomal abnormalities and MCAs were 0.56 and 0.623, respectively. Chromosomal abnormalities and MCAs were included in the final model after discussion with an expert group comprising pediatric intensivists, neonatologists, and fetal medicine specialists for their significant treatment decisions (Fig. 3C). The nomogram model was constructed using R software and was named the "CCDH score" (Chinese Congenital Diaphragmatic Hernia score) (Fig. 3D). In the CCDH score, each factor is assigned a weighted total score, which indicates the probability of survival of patients with CDH. For example, the absence of cardiac malformations is associated with a score of 10, whereas 30% of LH is associated with a score of 35. The higher the sum of the scores for the six predictors, the higher the chance of survival.

2.3. Performance and validation of the nomogram

The maximum VIF of the predictors for the training cohort was 1.079, which was less than 1.25, indicating that the model did not exhibit multicollinearity. The model was highly discriminative, with a C-index of 0.941 (95% CI: 0.904–0.977) and AUC of 0.942 (95% CI: 0.906–0.978) (Fig. 4A and B) and $\chi^2 = 4.498$ and $P = 0.810$ for the Hosmer–Lemeshow test, demonstrating the agreement between the actual and observed probabilities of the results. Internal validation reached the same conclusion (C-index = 0.914).

To avoid overfitting, it is necessary to use cohorts other than developing predictive models to evaluate model performance. For external validation, the relevant clinical data of the 65 patients with CDH were incorporated into the CCDH score for calculation. The C-index was 0.946 (95% CI: 0.896–0.996), and AUC was 0.946 (95% CI: 0.907–0.980), and the model had strong discrimination (Fig. 4A and B). For the Hosmer-Lemeshow test, $\chi^2 = 7.291$ and $P = 0.399$, indicating that the model was well-calibrated.

2.4. Comparison between CCDH score and Brindle score

The Hosmer-Lemeshow test showed good consistency in the Brindle score in the Chinese population ($P = 0.322$ for the training cohort and $P = 0.296$ for the external validation cohort). The AUC of the CCDH score (0.942; 95% CI: 0.906–0.978) in the training cohort was greater than that of the Brindle score (0.820; 95% CI: 0.734–0.906), and the same was true in the external validation cohort (0.946 and 95% CI: 0.907–0.980 vs. 0.881 and 95% CI: 0.792–0•969) (Fig. 4A and B). This indicates that in Chinese patients with CDH, the Brindle score performed well, but the CCDH score had better discriminative power. Additionally, the CCDH score had a higher overall net benefit in the training cohort and external validation (Fig. 4C and D).

The CCDH scores of 159 and 117 corresponded to fatality rates of 10% and 50%, respectively. We suggest that these scores can be used as cutoff values to divide patients with CDH into three subgroups. Based on the total score (0, 1, 2, or 3), Brindle et al. identified infants at low, intermediate, and high risk of death (<10%, approximately 20%, and approximately 50%, respectively) [7]. The three subgroups, divided according to the CCDH score, were compared between the actual and predicted death probabilities (Fig. 4E and F). Actual mortality was similar to the predicted mortality for both models. In the external validation cohort, the predictions of both models might have overestimated the likelihood of adverse outcomes in the high-risk group.

3. Discussion

In this study, we retrospectively analyzed the relevant clinical data of 261 patients with CDH. The Brindle score has been externally validated in a Chinese population. We found that the Brindle score is applicable to the Chinese population; however, there is room for optimization. Our study established a new predictive model, the CCDH score, which was presented as a nomogram. Through internal and external validations, CCDH appears to have better predictive power than the Brindle score, enabling individualized and systematic real-time assessment and risk prediction in patients.

Several CDH-related predictive models have been proposed. The SNAP-II score is based on the Canadian Neonatal Network Database, and its validity has been recognized by many medical centers in the United States and Europe [5,11]. SNAP-II is mainly used to evaluate the overall condition of critically ill children and involves a comprehensive evaluation of vital signs, the nervous system, acid-base balance, and the respiratory system. This scoring method is suitable for prognostic assessment in all critically ill children and lacks specificity in children with CDH. In contrast, the CCDH score involves relevant clinical indicators of CDH with strong specificity, and the number of indicators that need to be collected for calculation is small and easy to obtain, making it a fast and simple evaluation model.

Schultz et al. conducted a retrospective study of 88 children with CDH in two centers in the United States, obtained the WHSRPF equation using statistical methods, and validated the model with the data of 849 children with CDH in CDHSG [12]. This model can be used to evaluate the prognosis of children with CDH with an AUC of 0.87. In 2009, Sinha et al. studied prognostic indicators in 86 children with CDH from a single center in the United Kingdom and found that BOI-d1 on the first day after birth could be used to evaluate prognosis [13]. The effectiveness of BOI-d1 has also been validated by four European medical centers [14]. The main disadvantage was that WHSRPF and BOI-d1 mainly evaluated the respiratory system, including relatively single indicators. The CDHSG rule contains only two variables: postnatal weight and the 5-min Apgar score after birth [6,15]. The 5-min Apgar score after birth may have poor accuracy owing to the large error of the different measuring personnel. The CCDH score covers many factors that affect the outcome of neonates with CDH, including genetic factors and cardiac malformations, and the combination of multiple factors

avoids the influence of the subjectivity of individual scores. This is an advantage of the CCDH score compared with these three models.

Although the Brindle score appeared to be valid, some variables were not useful in the Chinese population, which may have affected the model's predictive performance. Brindle et al. speculated that an infant with a missing Apgar score at 5 min might be undergoing resuscitation or intubation, implying that the infant is sick. However, this situation did not fit our study; therefore, this parameter was excluded.

It may be advantageous to combine prenatal and postnatal variables to increase the power of the new prediction rules. Different prenatal variables were tested using this model. Surprisingly, TFLV had no added value to the model, and in earlier studies, TFLV played a role in predicting survival. Measuring TFLV has potential limitations; increased pulmonary crowding and chest compression within the uterus affect reproducibility and learning curves [16]. Calculating TFLV has a significant inter-observer error, requiring skill and experience [17,18].

Most patients in our study were not born preterm, and fetuses with low birth weights (<1500 g) were not present. Therefore, the low-birth-weight parameter was excluded. Birth weight was not included as a continuous variable in the new model CCDH score, although a univariable analysis revealed that birth weight was associated with outcomes in patients with CDH. This is one of the differences between the Brindle score [7] and the other prediction rule [9]. Whether body weight is associated with CDH outcomes remains controversial [13]. We cannot rule out that the difference may be due to the small number of patients included in the study or bias due to patient origin. Some patients included in the study were from remote districts with relatively poor medical conditions. Visiting our hospital for treatment is a choice of parents after careful consideration, and this may filter out some patients whose conditions are not optimistic and whose parents lack confidence in future treatment. Therefore, we are currently working with medical centers in other regions to collect more patient information and verify the effectiveness of the CCDH score.

Undeniably, the CCDH score has some flaws and requires further improvement. CDH is associated with chromosomal abnormalities, which often significantly impact mortality [19,20]. In the model, we retained chromosomal anomalies, although their association with mortality was insignificant. Some patients may have abnormal chromosomal microarray results, but it is difficult to determine whether these results are related to CDH due to limitations in the current level of research. However, because this study was retrospective, we included all patients with chromosomal array abnormalities.

The Brindle and CCDH scores may slightly overestimate the mortality for the high-risk group, while the possibility of clinical management decisions being changed by this difference is relatively small, as there is still a very distinct, significant difference between the three risk groups. However, this requires more data and further verification combined with the actual clinical situation.

Moreover, except for pulmonary dysplasia and PH, impaired lung function is a non-negligible factor that leads to the death of patients with CDH. The parameter of an Apgar score <7 at 5 min in the CCDH score is subjective and cannot accurately reflect the tolerance of the blood gas level in newborns. A parameter that can better reflect a patient's respiratory function should be determined as a future research direction. In 2016, Snoek et al. showed that the combined model of SNAP-II and Brindle might better stratify CDH severity in children and assess their prognosis [21]. This prompted us to explore the clinical significance of the parameters represented by each prediction model, and each had its strengths, which may generate a more concise and perfect predictive model. Perhaps, the variable included in the SNAP-II score, oxygenation index PaO2/FiO2 instead of the Apgar score <7 at 5 min in CCDH, will better predict the survival outcome of CDH patients.

Compared with the Brindle score, the CCDH score combining the six indicators of PH, O/E LHR, %LH, Apgar score <7 at 5 min, MCAs, and chromosomal anomalies had better predictive performance in Chinese individuals. This model can guide clinicians in making critical clinical decisions on related issues and improving maternal and infant outcomes. However, it is necessary to expand the sample size and incorporate more factors to correct the bias and optimize and increase the scope and accuracy of the model. It is worth noting that combining the CCDH score with the actual situation of individuals and comprehensive consideration can ensure the safety of mothers and babies.

4. Materials and methods

4.1. Study design

From January 2015 to February 2021, 504 patients were diagnosed with CDH on the three campuses of Guangzhou Women and Children's Medical Center. After excluding 243 patients with terminated pregnancy, intrauterine death, or unclear pregnancy results and supplement missing data by multiple imputation, 261 patients were included in the study (total cohort). A total of 196 patients diagnosed between January 2015 and January 2019 were used as the training cohort for model development. Patients diagnosed from February 2019 to February 2021 were used to externally validate the model (Fig. 1). All patients were followed up for one year postpartum. This study was retrospective, did not require signed informed consent, and was approved by the Ethics Committee of Guangzhou Women and Children's Medical Center (approval number: 157B00).

4.2. Data acquisition

To validate the Brindle score, the data collected met the definitions used by the developers of Brindle et al.: low birth weight (<1500 g), Apgar score <7 or no Apgar score at 5 min, severe PH defined as a right-to-left shunt or systemic pulmonary artery pressure estimated on the first echocardiogram, chromosomal abnormalities defined as any abnormality in the chromosomal array, and major cardiac abnormalities, classified as all abnormalities except the patent foramen ovale, patent ductus arteriosus, atrial septum defects, and ventricular septal defects [7] (Table 1).

Brindle score. Birth weight was included as a continuous variable to further improve the model. After reviewing the literature and seeking clinical expert advice, the following prenatal variables were included as candidates for developing the CCDH score: location of the defect in diaphragmatic hernia [22], polyhydramnios [23], gestational age at diagnosis [24], gestational age at delivery [25], O/E LHR [26], TFLV [17], whether the liver herniated into the thoracic cavity [27], intrathoracic stomach herniation [28], and percentage of liver herniation (%LH) [27]. %LH was defined as the ratio of herniated liver volume to TFLV.

The outcome of patients with CDH was "survival" defined as survival at the one-year postpartum follow-up. %LH was defined as 0% if the liver did not herniate into the thorax. O/E LHR and TFLV were measured using ultrasonography and MRI at the first diagnosis, and %LH was calculated from the last prenatal MRI examination. Whether the liver or stomach herniated into the chest during the last antenatal ultrasound was used as a binary variable. TFLV, O/E LHR, and %LH values were calculated prospectively by experienced radiologists blinded to patient information and outcomes and were reviewed by senior imaging professors.

4.3. Statistical analysis

Statistical analysis was performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA) and R 4.0 (R Foundation for Statistical Computing, Vienna, Austria), with a p-value less than 0.05 indicating statistical significant. Missing data patterns were analyzed using R software, and five groups of post-supplementation data were generated by multiple imputations [29]. A function strip plot was used to judge the effect of data supplementation. According to the Alpha coefficient in the reliability analysis, the best populated dataset was selected as the "Total cohort". The following R packages were used: VIM and MICE packages.

To describe the baseline characteristics of patients with CDH, the median and interquartile range (IQR) were used for continuous variables, and percentages were used for categorical variables. The baseline characteristics of the training and external validation cohorts were compared using Pearson's χ^2 test or Fisher's exact test for categorical variables and the Mann-Whitney U test for continuous variables. Univariable and multivariable logistic regression analyses were used to determine variables associated with the outcomes of patients with CDH. We filtered the variables and built the models.

To avoid the problem of multicollinearity in independent variables, LASSO regression was used to filter variables. All variables were included in the LASSO algorithm for variable filtering. A 10-fold cross-validation method was used to determine the adjustment parameter lambda in the least absolute shrinkage and selection operator (LASSO) regression. We optimized LASSO by lambda within one standard error (SE) so that the variables whose coefficients were not zero under the condition of the special parameter lambda could be obtained [30]. The variables screened by LASSO were used to build a visual nomogram and a predictive model. Multicollinearity can lead to difficulties in model interpretation; therefore, the variance inflation factor (VIF) was calculated to determine whether the model had multicollinearity. The predictive power was evaluated using the C-index, area under the receiver operating characteristic curve (AUC), and the Hosmer-Lemeshow test. The models were internally validated using bootstrap repeated sampling (1000 times). The following R packages were used: glmnet, rms, and ROCR.

Author contribution statement

Wen Ding: Performed the experiments; Analyzed and interpreted the data; Wrote the paper.

Huiying Wu: Conceived and designed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Data availability statement

Data will be made available on request.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Abbreviations

% LH	Percentage of liver herniation
AUC	Area under the receiver operating characteristic curve
BOI (d1)	Best oxygenation index on day 1
CDH	Congenital diaphragmatic hernia
CDHSG	Congenital Diaphragmatic Hernia Study Group
LASSO	Least absolute shrinkage and selection operator

MCAs	Major cardiac abnormalities
MICE	Multivariate Imputation by Chained Equations
O/E LHR	Observed-to-expected lung-to-head ratio
PH	Pulmonary hypertension
SNAP-II	Score for Neonatal Acute Physiology-Perinatal Extension II
TFLV	Total fetal lung volume
VIF	Variance inflation factor
VIM	Visualization and Imputation of Missing values
$WHSR_{PF}$	Wilford Hall/Santa Rosa clinical prediction formula

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