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Outcomes of Congenital Diaphragmatic Hernia in the modern era of management

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Abstract

Objective To identify clinical factors associated with pulmonary hypertension and mortality in patients with congenital diaphragmatic hernia (CDH).

Study design A prospective cohort of neonates with a diaphragm defect identified at one of seven collaborating medical centers was studied. Echocardiograms were performed at one month and three months of age and analyzed at a central core by two cardiologists independently. Degree of pulmonary hypertension and survival were tested for association with clinical variables using Fischers exact test, chi-square and regression analysis.

Results 220 patients met inclusion criteria. Worse pulmonary hypertension measured at one month of life was associated with higher mortality. Other factors associated with mortality were need for extracorporeal membrane oxygenation (ECMO), patients inborn at the treating center and patients with a prenatal diagnosis of CDH. Interestingly, patients with right sided CDH did not have worse outcomes.

Conclusions Severity of pulmonary hypertension is associated with mortality in CDH. Other factors associated with mortality were birth weight, gestational age at birth, inborn status and need for ECMO.

Keywords

Congenital Diaphragmatic Hernia; Pulmonary Hypertension; Survival; Treatment

Congenital diaphragmatic hernia (CDH) is one of the most common major congenital anomalies, with an incidence of 1 in 3000 live births worldwide (1). Patients with CDH have significant morbidity and mortality. The leading cause of CDH related morbidity and mortality is respiratory failure resulting from pulmonary hypoplasia and pulmonary hypertension (PH). Ventilatory management of neonates with CDH has almost universally changed to a strategy of gentle ventilation and permissive hypercarbia as suggested by Wung et al (2). Over the last 10-15 years, average survival for CDH has improved from 50% to 70-80% and even up to 90% in some institutions (3,4,5).

Several centers have shown that survival of patients with CDH is directly correlated with severity of pulmonary hypertension (6,7). These studies have demonstrated that persistent, sustained severe pulmonary hypertension is associated with significantly worse survival and increased need for ECMO. Moreover, treatment of pulmonary hypertension in these patients has demonstrated improved outcomes (5,6,8). Right sided CDH has been classically associated with worse overall survival. Here we present data from a prospective, multicenter CDH birth cohort that identifies clinical factors associated with outcomes for survival and pulmonary hypertension in CDH.

Methods

Subjects were recruited as part of the DHREAMS (Diaphragmatic Hernia Research & Exploration; Advancing Molecular Science) study (http://www.cdhgenetics.com). The DHREAMS study is a prospective cohort of neonates with a diaphragm defect identified at one of seven collaborating medical centers. Columbia University began enrollment in January, 2005, and recruitment at six other sites (Washington University Medical Center/St. Louis Children's Hospital, University of Pittsburgh, Cincinnati Children's Hospital and Medical Center / University of Cincinnati, Omaha Children's Hospital / University of Nebraska, University of Michigan / CS Mott Children's Hospital and Vanderbilt University) began from 2009 to 2010. Eligibility criteria for the CDH birth cohort were that the child was born or transferred into a participating institution within the first week of life and had a radiologically confirmed CDH diagnosis. Isolated CDH was defined as a CDH without an associated additional birth defect. Pulmonary hypoplasia, cardiac displacement and intestinal herniation were considered to be part of the diaphragm defect sequence and were not considered to be an additional malformation. The study was approved by the institutional review boards at each participating institution. Study data were collected and managed using REDCap (Research Electronic Data Capture) tools, hosted at Columbia University, which is a secure, web-based application designed to support data capture for research studies, providing: (1) an intuitive interface for validated data entry; (2) audit trails for tracking data manipulation and export procedures; (3) automated export procedures for seamless data downloads to common statistical packages; and (4) procedures for importing data from external sources.

Echocardiograms (echo) were performed at one month and three months of age. One month echos were defined as echos performed between 14-45 days of age, and 3 month echos were performed between 60 to 180 days of age. Echocardiograms were centrally read, by two cardiologists independently, to qualitatively assess the degree of pulmonary hypertension using the following echo parameters: 1. Tricuspid regurgitant (TR) gradient, 2 shunt gradient across a patent ductus arteriosus or inter-ventricular communication, 3 ventricular septal position (normal/ flattening or posterior bowing in systole as well as flattened or paradoxic septal motion, 4 the presence or absence of right ventricular (RV) dysfunction, and 5. RV hypertrophy and RV dilatation.

Right ventricular systolic pressure (RVSP) was estimated using the modified Bernoulli equation $4V^2$: (V is tricuspid regurgitant jet velocity obtained by continuous wave Doppler). Because RA pressure is 0-3 mm Hg in infants, it is not usually considered in the equation when RVSP is estimated in this age group. A RV pressure estimate less than half of the systolic blood pressure at the time of echo, based on TR gradient was quantified as mild (or no) PH, 1/2 to 2/3 systemic as moderate, and greater than 2/3 systemic as severe. In the absence of TR, ventricular septal position and motion and RV function and size were used to roughly estimate the severity of PH. The presence of bidirectional shunting or right to left shunting at the ductal or VSD level was also quantified as severe PH (systemic or suprasystemic pressures in the right heart).

Independent reads between the two cardiologists were compared for inter-observer variability. There was 100% concordance in reading between the two readers for all subjects in the severe group. There was < 5% disagreement in the moderate and mild group when there was no tricuspid regurgitation present to get an accurate pressure estimate in the right ventricle. Any discordant read was re-reviewed by the two readers and a consensus was obtained based upon additional subjective criteria. These included right ventricular hypertrophy, right ventricular function, ventricular septal position and septal motion obtained from additional echocardiographic images from the subxiphoid and apical planes.

A clinical genetic evaluation was performed on each subject. A genetic diagnosis was defined as the presence of a pathogenic cytogenetic or molecular genetic abnormality.

Statistical analyses

The primary outcomes were pulmonary hypertension at 1 and 3 months and mortality, defined as death prior to discharge. Pulmonary hypertension was categorized into three categories: none/mild, moderate and severe. Descriptive analysis was performed. Data are reported as frequencies, means and standard deviation. Associations of selected variables with the outcomes were assessed with chi-squared tests, Fisher's exact tests, logistic regression models and proportional odds models. A multiple logistic regression analysis was conducted to examine the association between mortality and gestational age, birth weight, inborn/outborn status, primary/patch repair and occurrence of postoperative complication as predictors based on simple analysis of associations between two variables. Multiple proportional odds models were similarly used for one month pulmonary hypertension and the same set of predictors. Statistical analysis was performed using SAS 9.2. For our analysis a $p<0.05$ was used as a cutoff.

Results

A total of 220 of the 313 eligible cases born at participating centers during the study time period consented to enrollment in the DHREAMS study (Table I). The average gestational age was 37 weeks. White, non-Hispanic patients comprised 54.5% of the study population. 56.8 % were male. 84.1% of the diaphragmatic lesions were left sided. 61.8% of the patients had an isolated CDH. Of the patients with other anomalies, congenital heart disease was the most common in 21.4% of the entire cohort. A genetic evaluation was completed on 204 of the 220 patients (93%). 5% of the patients in our study had a genetic diagnosis that was associated with their CDH. The genetic diagnoses included 2 cases of Trisomy 21, 1 case of Trisomy 18, 1 case of mosaic Trisomy 18, 1 case of mosaic Trisomy 8, 3 cases with deletions (size ranged from 3.4 – 24Mb) at 8p23, 1 case with a 18.26Mb duplication at 11p23.1 and 4.28Mb duplication at 22q11, 1 case with 6.79Mb deletion at 13q33, and one case with a WT1 mutation consistent with Fraiser syndrome. 76.4% of the patients were diagnosed prenatally. 63.6% of the patients were born at the treating hospital. The average age at time of repair was 8 days. The average overall hospital stay was 50 days and 31.8% of the babies required ECMO. In an effort to ensure that there was not significant inter-institution variability in CDH management and outcomes, we compared survival to discharge, survival prior to obtaining the one month echo, the percentage requiring ECMO and the percentage with severe PH measured at one month at each institution. There was no significant difference in any of these parameters between the institutions (data not shown).

Pulmonary Hypertension

PH was classified into 3 categories: none/mild, moderate, or severe based upon the echocardiograms at 1 and 3 months of age. Of the 220 newborns enrolled in the study, 138 patients had an echocardiogram performed at one month of life (Table II). One month echocardiograms were not available for 82 patients. 17 patients died prior to 14 days of life, and 65 patients did not have an echo within the prescribed time frame. A prenatal diagnosis of CDH, patch repair, and post- operative complications were all positively associated with more severe pulmonary hypertension at one month. Not surprisingly, patients who required ECMO had significantly worse PH. Patients with right sided CDH had comparable PH at one month to those with left sided lesions. In simple proportional odds models, birth weight and ECMO duration were positively associated with PH at 1 month (Table III; available at www.jpeds.com). Using multiple proportional odds models, we found that low birth weight,

patch repair and need for ECMO were positively associated with more severe PH at one month (data not shown).

113 patients had an echocardiogram at 3 months (Table IV). Three month echos were not available for 107 patients. 40 patients died prior to 60 days of life, and 67 patients did not have an echo within the prescribed time frame. Patch repair, a non-isolated CDH and a genetic diagnosis were all associated with worse PH at 3 months of age. Right sided CDH was not associated with more severe PH at 3 months. Using simple proportional odds models, birth weight was associated with decreased odds of severe PH at 3 months (Table V; available at www.jpeds.com).

Survival/Mortality

The overall mortality at discharge in our cohort was 23.6% (52/220). The overall mortality for black children enrolled was 50% (data not shown). Though patients with a right sided CDH required ECMO more often than those with a left sided CDH (p=0.04) we did not find a difference in need for a patch repair mortality between left and right sided CDH (Table VI).

The mortality at discharge in children with mild PH at one month was 1.4%, those with moderate PH was 7.4% and those with severe PH 56.1% (p<0.0001). A prenatal diagnosis of CDH was associated with an increased risk of death prior to discharge when compared to those who were not diagnosed until after delivery. Inborn status was associated with increased mortality compared with patients born outside of the treating center. Those who were transferred in had a lower proportion of deaths at discharge than those who were inborn (p=0.02). The survival in patients with an isolated CDH was no different than those with another associated congenital anomaly although there was a trend toward improved survival with isolated CDH (80.2% vs 70.2%, p=0.09). However, the diagnosis of complex congenital heart disease (defined as a coarctation, interrupted arch, transposition of the great vessels, truncus arteriosus, total anomalous pulmonary venous return, hypoplastic left heart syndrome, single ventricle or double outlet right ventricle) in combination with CDH was associated with mortality. Patients who had a genetic diagnosis also had higher mortality.

Of the repaired patients 61.4% required a patch repair of whom 76% were alive at discharge compared with 95% alive after a primary repair (p=0.0004). Patients who had any major post-operative complication (intra ventricular hemorrhage, abdominal compartment syndrome, abdominal/ incisional hernia, hemothorax, sepsis, chylothorax, or organ failure) had higher mortality (34.9%) when compared to those who did not (8.1%, p<0.001). Of those that required ECMO 36/70 (51%) were alive at discharge versus 132/150 (88%) of those that did not require ECMO (p<0.0001). Using simple logistic regression, gestational age at birth, birth weight and duration of ECMO were associated with discharge status (Table VII; available at www.jpeds.com). Using multiple logistic regression need for ECMO and occurrence of postoperative complication were associated with mortality (data not shown)

Discussion

Recent advances in the post-natal care of children with CDH at specialized centers have improved survival and decreased the need for ECMO [3]. However, with improved survival, many of the long term morbidities of CDH have been exposed. The leading cause of morbidity and mortality in patients with CDH is severe hypoxic respiratory failure, resulting from pulmonary hypoplasia and abnormal pulmonary vascular development and vasoreactivity, leading to PH (3,9,10). Recent studies have correlated the severity of PH with mortality. In the series by Dillon et al, all patients with CDH with suprasystemic PH

died, and all patients with CDH with none or mild pulmonary hypertension survived (6). However, Kinsella et al have since shown that with judicious and timely use of vasodilator therapy, both prior to and, after surgery, long term survival is possible in these infants, despite severe PH beyond the neonatal period(8,11).

In our study, patients with more severe PH at 1 month of life had a higher incidence of post-operative complications. Patients who had any major post-operative complication also had a worse survival. These data clearly point to an association between postoperative complications and mortality. It is unclear if patients who are “sicker” and have worse survival will also have more post-operative complications or if post-operative complications lead to a worse outcome or both.

In our study, patients with prenatal diagnosis of CDH had worse PH at 1 month of life. Prenatal diagnosis of CDH as well as an earlier gestational age at diagnosis have been shown previously to portend a worse prognosis (12,13). In our cohort, for those diagnosed prenatally, the gestational age at diagnosis did not correlate with PH, measured at 1 or 3 months of life or survival. However in the entire cohort, the gestational age at birth did correlate with survival. Interestingly patients transferred from an outside, referring institution to one of the 7 treating centers had improved survival relative to those delivered at the treating center independent of PH status. These results directly contradict those of the recently published series from Canada (14). We can speculate that those patients born at an outside institution and who are well enough to be transferred are more likely to survive whereas, those patients near death were not transferred resulting in a selection bias among those transferred. These data need to be more thoroughly interrogated to determine which factors are most predictive of survival in patients transferred from outside institutions.

In 2001 the international CDH registry published a formula that can be used to predict outcome in patients with CDH. The formula utilized birth weight and 5 minute APGAR (15). In our study, birth weight was significantly associated with survival as well as the degree of PH measured at both 1 and 3 months of life by a simple regression analysis. A greater birth weight may be an indication of a more robust child, which could explain these findings. Moreover, several studies have indicated that lung to head ratio (LHR) measured prenatally as well as the prenatal position of the fetal liver, either “up” into the defect or not, have prognostic significance in CDH (16,17). As part of the DHREAMS database we collected LHR measurements as well as liver position on prenatal ultrasound. Unfortunately of the 145 subjects with a prenatally diagnosed left sided CDH only 115 had the liver location assessed at an point during gestation and only 55 had an LHR measured between 24 and 28 weeks of gestation leaving too small a sample size for analysis. We hope that with additional data acquisition we will be able to analyze these parameters in the future.

Most previous reports have shown that a right sided CDH portends a worse outcome. Though the patients in our study with a right sided CDH did have a greater need for ECMO, they did not have either worse PH, measured at 1 or 3 months of age, or decreased survival when compared to left sided CDH. It is difficult to definitively determine the etiology of these findings, but our findings and those of Schaible (18) may be reason enough for practitioners seeing these patients during prenatal counseling to be cautious in predicting a dismal prognosis for right sided CDH.

In our study a patch repair was associated with worse survival and more severe PH. The need for a patch repair is a gross indicator of the size of the diaphragmatic defect. Our data indicates that size of diaphragmatic defect does correlate, negatively, with outcome and warrants further investigation into prenatal predictors of the size of the diaphragmatic defect and, presumably, lung volumes.

ECMO continues to be an integral part of the treatment in patients with CDH. Though there were no specific ECMO criteria across this study, and each center used their own institutional criteria for inclusion and contraindication, there was no difference in the percentage of patients who required ECMO between the centers (p=0.56, data not shown). In our study ECMO was used approximately 30% of the time and was associated with a 51% survival. Most likely we are treating sicker children with ECMO and though the overall outcomes are worse, ECMO likely improves survival in these patients.

Complex congenital heart disease was associated with worse survival but was not associated with severity of PH at either 1 or 3 months of life. This suggests that complex CHD is an independent risk factor associated with survival independent of PH. Similarly, patients with an associated genetic diagnosis had significantly worse survival than those without but did not have worse PH. Using a simple logistic regression birth weight and ECMO use were associated with the degree of PH. These factors, in addition to gestational age at birth, were all associated with survival.

One limitation of our study is that treatment for these patients was not standardized across all the centers. In order to determine whether there were gross differences between the study centers we looked at various clinical parameters. Though there were no gross differences between the centers, it is possible that there was variation between the study sites that could have resulted in some of the findings. Moreover there was a significant number of patients who were eligible for the study but were not enrolled. One could speculate that this is because a significant number of these patients died prior to enrollment in the study, which could have affected our results. In addition, a number of patients did not have their echos performed during the prescribed time period. Survival in our study was defined as survival to discharge and it is possible that differences in survival in these patients will be evident as longer term follow is obtained. As part of the DHREAMS research project we will be following these children longitudinally and will be reporting these results when they are acquired in the near future. The definitions of PH we used for our study are based on echocardiogram observations. Though the echos were reviewed consistently by the same reviewers they were performed by various technicians at all seven centers which could have led to deviations in our data.

Here we have shown that complex associated heart disease, as well as an associated genetic diagnosis, portend a worse survival in patients with CDH independent of degree of PH. We have demonstrated that birth weight appears to be a significant predictor of outcome in these patients, associated with both pulmonary hypertension and overall survival. Patients in our study born outside of a treating center and referred into one of the study centers did better when compared with those born at the site. Our study demonstrates that a right sided CDH does not necessarily portend a worse prognosis. These findings are important in helping practitioners discuss prognosis with families recently diagnosed with CDH. Our studies also indicate areas of investigation for future studies.

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Abbreviations

CDH	Congenital Diaphragmatic Hernia
echo	Echocardiogram
ECMO	Extracorporeal membrane oxygenation
PH	pulmonary hypertension
RV	right ventricular
RVSP	right ventricular systolic pressure
TR	tricuspid regurgitation

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TABLE 1

Patient characteristics (N = 220); n (%)

Ethnicity	
White, non-Hispanic	120 (54.5)
White, Hispanic	37 (16.8)
Black	12 (5.5)
Asian	19 (8.6)
Other/ Mixed ethnicity	25 (11.4)
Unknown	7 (3.2)
Sex	
Male	125 (56.8)
Female	95 (43.2)
Side of lesion	
Left	185 (84.1)
Right	31 (14.1)
Other	4 (1.8)
Isolated CDH	136 (61.8)
Congenital heart disease	47 (21.4)
Simple shunt	31 (14.1)
Complex heart disease	13 (5.9)
Pulmonary stenosis	3 (1.4)
Genetic diagnosis	11 (5.0)
Prenatal diagnosis	168 (76.4)
Inborn	140 (63.6)
Gestational age, weeks*	37 (1.8)
Birth weight, z-score*	-0.6 (0.9)
ECMO	70 (31.8)
Duration, days*	11 (6)
Inhaled nitric oxide	112 (50.9)
Repaired	202 (91.8)
Primary diaphragm repair	78 (38.6)
Diaphragm patch repair	124 (61.4)
Postop complications	66 (32.7)
Age at repair, days*	8 (8)
NICU stay, days*	50 (47)

ECMO: Extracorporeal membrane oxygenation

*Mean (SD)

TABLE 2

Pulmonary hypertension at 1 month ECHO (N = 138); n (%)

	None/mild (N=70)	Moderate (N=27)	Severe (N=41)	p value*
Gender				0.9
Male, n = 71	36 (50.7)	15 (21.1)	20 (28.1)	
Female, n = 67	34 (50.8)	12 (17.9)	21 (31.3)	
Inborn				0.3
Yes, n = 89	41 (46.1)	20 (22.5)	28 (31.5)	
No, n = 49	29 (59.2)	7 (14.3)	13 (26.5)	
Prenatal diagnosis				0.03
Yes, n = 109	49 (45)	24 (22)	36 (33)	
No, n = 29	21 (72.4)	3 (10.3)	5 (17.2)	
Side of lesion				0.4
Right, n = 24	10 (41.7)	7 (29.2)	7 (29.2)	
Left, n = 113 (Other, n = 1)	60 (53.1)	20 (17.7)	33 (29.2)	
Repair type				0.0004
Primary, n = 40	31 (77.5)	4 (10)	5 (12.5)	
Patch, n = 97 (Not repaired, n = 1)	39 (40.2)	23 (23.7)	35 (36.1)	
Postop complication				0.01
Yes, n = 47	18 (38.3)	8 (17)	21 (44.7)	
No, n = 90 (Not repaired, n = 1)	52 (57.8)	19 (21.1)	19 (21.1)	
ECMO				<0.0001
Yes, n = 52	12 (23.1)	12 (23.1)	28 (53.9)	
No, n = 86	58 (67.4)	15(17.4)	13 (15.1)	
Isolated CDH				0.3
Yes, n = 88	49 (55.7)	16 (18.2)	23 (26.1)	
No, n = 50	21 (42)	11 (22)	18 (36)	
Congenital heart disease				0.6
Yes, n = 28	12 (42.9)	6 (21.4)	10 (35.7)	
No, n = 110	58 (52.7)	21 (19.1)	31 (28.2)	
Complex CHD				0.5
Yes, n = 7	4 (57.1)	0	3 (42.9)	
No, n = 131	66 (50.4)	27 (20.6)	38 (29)	
Genetic diagnosis				0.3
Yes, n = 5	1 (20)	1 (20)	3 (60)	
No, n = 133	69 (51.9)	26 (19.6)	38 (28.6)	

ECMO: Extracorporeal membrane oxygenation

CDH: Congenital diaphragmatic hernia

CHD: Congenital heart disease

*Chi-squared test; Fisher's exact test used when expected cell count less than 5

TABLE 3

Association with pulmonary hypertension at 1 month ECHO

	OR*	95% CI	p value
Gestational age at diagnosis, weeks, n = 104	1.0	0.9 - 1.0	0.5
Gestational age at birth, weeks, n = 138	0.8	0.7 - 1.0	0.08
Birth weight, z score, n = 138	0.7	0.5 - 0.9	0.02
ECMO duration, days, n = 52	1.3	1.1 - 1.5	0.001
Age at repair, days, n = 137	1.0	0.98 - 1.1	0.3

ECMO: Extracorporeal membrane oxygenation

*Simple proportional odds models

TABLE 4

Pulmonary hypertension at 3 months ECHO (N = 113); n (%)

	None/mild (N=93)	Moderate (N=5)	Severe (N=15)	p value*
Sex				1.0
Male, n = 63	52 (82.5)	3 (4.8)	8 (12.7)	
Female, n = 50	41 (82)	2 (4)	7 (14.0)	
Inborn				0.9
Yes, n = 67	54 (80.6)	3 (4.5)	10 (14.9)	
No, n = 46	39 (84.8)	2 (4.4)	5 (10.9)	
Prenatal diagnosis				0.1
Yes, n = 85	68 (80)	3 (3.5)	14 (16.5)	
No, n = 28	25 (89.3)	2 (7.1)	1 (3.6)	
Side of lesion				0.2
Right, n = 19	14 (73.7)	2 (10.5)	3 (15.8)	
Left, n = 92 (Other, n = 2)	78 (84.8)	3 (3.3)	11 (12)	
Repair type				0.006
Primary, n = 44	42 (95.5)	1 (2.3)	1 (2.3)	
Patch, n = 69	51 (73.9)	4 (5.8)	14 (20.3)	
Postop complication				0.4
Yes, n = 34	26 (76.5)	1 (2.9)	7 (20.6)	
No, n = 79	67 (84.8)	4 (5.1)	8 (10.1)	
ECMO				0.1
Yes, n = 36	26 (72.2)	2 (5.6)	8 (22.2)	
No, n = 77	67 (87)	3 (3.9)	7 (9.1)	
Isolated CDH				0.02
Yes, n = 71	64 (90.1)	2 (2.8)	5 (7)	
No, n = 42	29 (69.1)	3 (7.1)	10 (23.8)	
Congenital heart disease				0.1
Yes, n = 22	15 (68.2)	2 (9.1)	5 (22.7)	
No, n = 91	78 (85.7)	3 (3.3)	10 (11)	
Complex CHD				0.4
Yes, n = 6	4 (66.7)	0	2 (33.3)	
No, n = 107	89 (83.2)	5 (4.7)	13 (12.2)	
Genetic diagnosis				0.047
Yes, n = 5	2 (40)	1 (20)	2 (40)	
No, n = 108	91 (84.3)	4 (3.7)	13 (12)	

ECMO: Extracorporeal membrane oxygenation

CDH: Congenital diaphragmatic hernia

CHD: Congenital heart disease

*Chi-squared test; Fisher exact test used when expected cell count less than 5

TABLE 5

Association with pulmonary hypertension at 3 month ECHO

	OR*	95% CI	p value
Gestational age at diagnosis, weeks, n = 83	1.0	0.9 - 1.1	0.6
Gestational age at birth, weeks, n = 113	0.9	0.7 – 1.2	0.6
Birth weight, z score, n = 113	0.4	0.2 – 0.7	0.0008
ECMO duration, days, n = 36	1.0	0.9 – 1.1	0.8
Age at repair, days, n = 113	1.0	1.0 - 1.1	0.04

ECMO: Extracorporeal membrane oxygenation

*Simple proportional odds models

TABLE 6

Discharge status alive or dead (N = 220); n (%)

	Alive (N=168)	Dead (N=52)	p value*
Sex			0.9
Male, n = 125	95 (76)	30 (24)	
Female, n = 95	73 (76.8)	22 (23.2)	
Inborn			0.02
Yes, n = 140	100 (71.4)	40 (28.6)	
No, n = 80	68 (85)	12 (15)	
Prenatal diagnosis			0.0001
Yes, n = 168	118 (70.2)	50 (29.8)	
No, n = 52	50 (96.1)	2 (3.9)	
Side of lesion			0.3
Right, n = 31	26 (83.9)	5 (16.1)	
Left, n = 185 (Other, n = 4)	141 (76.2)	44 (23.8)	
Repair type			0.0004
Primary, n = 78	74 (94.9)	4 (5.1)	
Patch, n= 124 (Not repaired, n = 18)	94 (75.8)	30 (24.2)	
Postop complication			<0.0001
Yes, n = 66	43 (65.2)	23 (34.9)	
No, n = 136 (Not repaired, n = 18)	125 (91.9)	11(8.1)	
ECMO			<0.0001
Yes, n = 70	36 (51.4)	34 (48.6)	
No, n = 150	132 (88)	18 (12)	
Isolated CDH			0.09
Yes, n = 136	109 (80.2)	27 (19.9)	
No, n = 84	59 (70.24)	25 (29.8)	
Congenital heart disease			0.1
Yes, n = 47	32 (68.1)	15 (31.9)	
No, n = 173	136 (78.6)	37 (21.4)	
Complex CHD			0.003
Yes, n = 13	5 (38.5)	8 (61.5)	
No, n = 207	163 (78.7)	44 (21.3)	
Genetic diagnosis			0.004
Yes, n = 11	4 (36.4)	7 (63.6)	
No, n = 209	164 (78.5)	45 (21.5)	

ECMO: Extracorporeal membrane oxygenation

CHD: Congenital heart disease

*Chi-squared test; Fisher exact test used when expected cell count less than 5

TABLE 7

Association with alive discharge status

	OR*	95% CI	p value
Gestational age at diagnosis, weeks, n = 161	1.0	1.0 - 1.1	0.3
Gestational age at birth, weeks, n = 220	1.3	1.1 - 1.5	0.002
Birth weight, z score, n = 220	1.6	1.1 - 2.2	0.01
ECMO duration, days, n = 70	0.9	0.8 - 0.99	0.03
Age at repair, days, n = 202	1.0	0.9 - 1.0	0.4

ECMO: Extracorporeal membrane oxygenation

*Simple logistic regression models