Prenatal prognosis in isolated congenital diaphragmatic hernia

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Background and Objective

Prenatal identification of the severity of pulmonary hypoplasia associated with isolated congenital diaphragmatic hernia (CDH) remains a challenge. Some CDH research has used ultrasonography or magnetic resonance imaging (MRI). The recent prospective multicenter study by Gorincourt et al of 77 fetuses with isolated CDH investigated the correlation between fetal lung volume (FLV) measured by MRI and postnatal mortality. However, postnatal management varied widely between centers, perhaps affecting postnatal outcomes.

We retrospectively reviewed records at our prenatal center for 79 live-born neonates prenatally diagnosed with isolated CDH to evaluate the relationship between fetal ultrasound factors, FLV measured by MRI, and postnatal outcome. Our purpose was to evaluate these factors as predictors of postnatal mortality in a large group of infants receiving the same treatments.

Materials and Methods

Between Jan. 2000-Nov. 2005, 118 patients were referred to the fetal medicine center of Necker Hospital in Paris after antenatal diagnosis of CDH. We identified 99 pregnancies with isolated CDH in which 79 live-born infants were admitted to the neonatal intensive care unit (NICU).

Potential prognostic features prospectively recorded from a detailed prenatal sonographic examination included gestational age at diagnosis, hernia location (which side), amniotic fluid volume (normal vs polyhydramnios, defined as a pocket of fluid ≥8 cm), stomach position, thoracic liver herniation with left CDH, and the left ventricle (LV)/right ventricle (RV) index at a mean gestational age of 32.1 weeks (range, 22-37 weeks). In 62 cases, the FLV ratio was measured by MRI during the third trimester (mean, 31.7 weeks; range, 27-37), as described previously by Mahieu-Caputo et al. During the last 2 years of the study, ultrasound was used to measure the ratio of fetal lung area to head circumference (lung to head ratio [LHR]) in 28 cases of left CDH at 22-28 weeks' gestation.

All babies received the same initial ventilator treatment with high-frequency oscillation performed with sufentanil and midazolam sedation. Muscle-paralyzing agents were avoided. Persistent pulmonary hypertension was managed by high forced inspiratory oxygen and inhaled nitric oxide. Neonates underwent surgical repair only after respiratory and hemodynamic stabilization had been achieved. The treatment protocol did not include prenatal corticosteroids, exogenous surfactant therapy, or extracorporeal membrane oxygenation (ECMO).

OVERVIEW

Prenatal magnetic resonance imaging measurement of fetal lung volume ratio appears to be the most accurate prognostic factor for left and right congenital diaphragmatic hernia.

Results

Mean gestational age at birth was 38.4 weeks (range, 32-41) and mean birthweight was 3017 g (range, 1665-4210). Of the 79 neonates, 54 were male (68%, sex ratio 2:1); 13 were right (16.5%) and 66 were left CDH (83.5%). None had an anterior or bilateral diaphragmatic hernia or an associated anomaly diagnosed after birth.

During NICU treatment, the survival rate of the 79 patients was 63.3% (range, 53.5-74.9%) at 1 month. No deaths occurred after this period. Of the total 29 deaths, 24 were preoperative and 5 were postoperative. Severe uncontrolled persistent pulmonary hypertension was the cause of 28 deaths; the remaining death was caused by septic shock.

We found that age at ultrasound diagnosis, polyhydramnios, and the LV/RV index were not associated with mortality (Table). However, neonatal mortality was significantly associated with the side of the hernia, intrathoracic position of the stomach and the liver, and the LHR and FLV ratios. An FLV ratio of 30% appeared to be the threshold below which mortality risk was worse and above which survival rate was better. This threshold had a 60.8% positive predictive value, 71.8% negative predictive value, 56% sensitivity, and 75.7% specificity. In a multivariate analysis of data for the 28 neonates who had antenatal LHR and MRI measures, only the LHR and the FLV ratio were significant independent predictors of survival (Table).

Comment

The aim of this study was to identify potential prenatal factors predictive of postnatal mortality in a series of 79 patients with isolated CDH managed in the same center during pregnancy and the postnatal period. MRI measurement of the FLV ratio was the most accurate prognostic factor for left and right CDH. Intrathoracic liver and LHR were also accurate predictors of left CDH.

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TABLE
Prenatal factors and risk of mortality in isolated CDH

	n	RR (95% CI)	*P* value	Adjusted RR (95% CI)[a]	*P*
Gestational age at diagnosis[a]	76	0.94 (0.87-1.01)	.088		
Side of the hernia[b]	79	0.36 (0.16-0.82)	.011		
Intrathoracic stomach[b]	66	ND	.043		
Intrathoracic liver[b]	66	3.14 (1.33-7.40)	.006	0.83 (0.15-4.61)	.83
Polyhydramnios[b]	79	1.08 (0.57-2.27)	.83		
RV/LV index[a]	65	0.74 (0.05-10.40)	.83		
LHR[a]	28	0.36 (0.17-0.77)	.009	0.43 (0.19-0.94)	.034
FLV ratio[a]	62	0.53 (0.37-0.74)	.0003	0.41 (0.19-0.85)	.018
FLV greater than 30%[b]	62	0.37 (0.17-0.81)	.010		

CI, confidence interval; *ND*, not determined because all nonsurvivors had an intrathoracic stomach.

[a] Cox proportional-hazard model. Relative risk (RR) was calculated for a 0.5 increase of LHR; RR was calculated for a 10% increase of FLV ratio.

[b] Log rank test. For intrathoracic stomach and intrathoracic liver, RR was calculated only for left CDH.

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We failed to confirm the purported significance of some previously reported predictors, such as age at antenatal diagnosis, polyhydramnios, and LV/RV ratio.

As reported previously, outcome in right-sided CDH was worse. The presence of intraabdominal stomach may be one of the most accurate predictors of outcome in left CDH. In our series, the 100% survival rate of infants with intraabdominal stomach confirms previous reports of survival rates greater than 90%. However, the practical value of this finding is limited because intraabdominal stomach was uncommon (9 of 66 cases).

Our study confirms the influence of antenatal herniation of the liver on the neonatal outcome of left CDH. In multivariate analyses that included fetal lung size, liver position was not a significant independent predictor of outcome. However, our 28-subject sample size may be too small to support a powerful multivariate analysis.

Although the predictive value of LHR is controversial, it was a strongly significant predictive factor of outcome in this study, despite our small sample size. We also found that the FLV ratio was significantly correlated with mortality, as Gorincourt et al similarly reported. They found a significant survival gap when the FLV ratio was less than 25%, as compared with less than 30% in our study. During pregnancy, this information may help parents to anticipate the severity of their fetus's disease. However, our statistical data are not sufficient to guide accurately prenatal counseling in individual cases.

The goal of LHR and FLV measures is to evaluate pulmonary hypoplasia by estimating fetal pulmonary volume. This step, however, does not provide a functional evaluation of pulmonary vasculature, as shown in our series by the postnatal death of 1 infant with LHR greater than 1.5 and 5 infants with FLV 40% or greater vs the survival of 2 infants with LHR less than 1 and 1 infant with FLV less than 20%.

The postnatal survival rate in our study did not differ from those reported with the use of ECMO. We did not offer this therapy because of its reportedly poor outcome and severe morbidity. However, comparing survival rates between institutions that use different therapeutic modalities is not really informative if disease severity between populations is not estimated.

We have shown that prenatal investigations such as fetal ultrasound and MRI permit the analysis of anatomic factors with a statistical predictive value for the outcome. We propose using these prenatal factors to characterize the severity of pulmonary hypoplasia in neonates with isolated CDH managed in different institutions. A stratification scheme based on these prenatal parameters should be designed to allow better comparison of outcome data from different NICUs.

We conclude that some prenatal factors may help clinicians to evaluate the outcome of infants with CDH. Because none of these factors can establish prognosis accurately during pregnancy, all should be used with caution in prenatal management. However, these factors could be used to estimate postnatal risks in populations with isolated CDH. Doing so would allow clinicians to compare different therapeutic modalities with greater accuracy and improve the quality of therapeutic research in the future.

CLINICAL IMPLICATIONS

- Magnetic resonance imaging (MRI) measurement of the fetal lung volume ratio was the most accurate prognostic factor for left and right congenital diaphragmatic hernia (CDH).
- Intrathoracic liver and lung to head ratio were accurate prognostic factors for left CDH.
- No individual factor observed with fetal ultrasound and MRI can accurately predict neonatal survival in isolated CDH.
- Combined factors could be used to estimate the risks for populations with isolated CDH and to compare postnatal therapies more accurately. ■