

Liver position and lung-to-head ratio for prediction of extracorporeal membrane oxygenation and survival in isolated left congenital diaphragmatic hernia

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BACKGROUND AND OBJECTIVE

Depending on the severity of disease, congenital diaphragmatic hernia (CDH) forces families into making difficult choices that include whether to terminate the pregnancy, undergo experimental fetal intervention, or receive standard postnatal therapy with or without extracorporeal membrane oxygenation (ECMO).

Understanding the natural history of CDH is crucial in the management of the disease. The most widely used prenatal predictors of postnatal outcome are liver position and right lung area-to-head circumference ratio (LHR). We sought to determine the ability of liver position and LHR to assist in the prediction of survival rates and the need for ECMO in fetuses with isolated left CDH that receive both prenatal and postnatal care at a single institution.

MATERIALS AND METHODS

We examined all prenatal patient records with a referral diagnosis of CDH to the Center for Fetal Diagnosis and

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Presented at the 27th Annual Clinical Meeting of the Society for Maternal-Fetal Medicine, San Francisco, CA, Feb. 5-10, 2007.

Cite this article as: Hedrick HL, Danzer E, Merchant A, et al. Liver position and lung-to-head ratio for prediction of extracorporeal membrane oxygenation and survival in isolated left congenital diaphragmatic hernia. *Am J Obstet Gynecol* 2007;197:422.e1-422.e4.

0002-9378/free

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doi: 10.1016/j.ajog.2007.07.001



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OVERVIEW

Liver position was highly predictive of outcome in cases of congenital diaphragmatic hernia, regardless of gestational age or right lung area-to-head circumference ratio.

Treatment at the Children's Hospital of Philadelphia from January 1996 through January 2006. Data collected retrospectively from patient charts included gestational age (GA) at evaluation, results of prenatal imaging and chromosomal studies, surgical interventions, and clinical outcomes. The principal outcome variable was survival rate. Secondary measures were the need for ECMO, type of repair, number of days of ventilator support, and number of days of initial hospitalization.

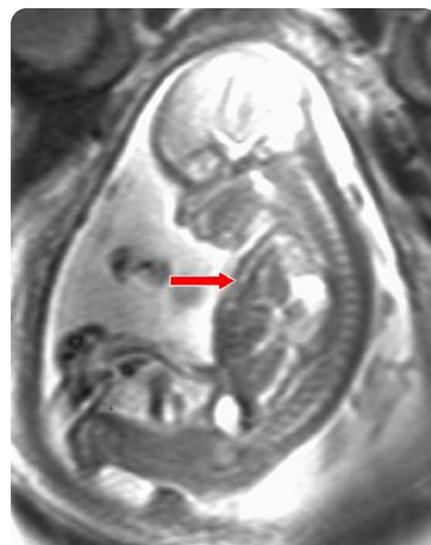
Fetal liver position was determined by ultrasound evaluation and confirmed by magnetic resonance imaging (MRI; **Figure**). Liver position was considered "up" if any portion was in the chest above the normal level of the diaphragm and "down" if the liver was completely within the abdomen. In left CDH, the right lung area was measured by sonography as an estimate of right lung size and mediastinal shift at the level of the atria on a transverse scan of the fetal thorax, as previously described by Metkus et al.

RESULTS

In the final study group, we reviewed the prenatal and postnatal records of 89 patients with isolated left CDH who received both prenatal and postnatal care at our institution. Median GA at initial evaluation was 24.3 weeks (range, 19.1-36.1 weeks). Overall survival rate was 66.3% at a median follow-up of 57.8

FIGURE

Ultrafast fetal MRI



Ultrafast fetal MRI shows liver herniation into the left chest (*arrow*).

Hedrick. Liver position and lung-to-head ratio for prediction of extracorporeal membrane oxygenation and survival in isolated left congenital diaphragmatic hernia. *AJOG* 2007.

months (range, 8 months to 10 years). No patient died after 1 year of age.

Liver position was intrathoracic in 49 of 89 fetuses (55%). ECMO was required in 39 of 49 fetuses (80%) with liver up vs 10 of 40 fetuses (25%) with liver down ($P < .0001$). Survival rate was 45% for fetuses with liver up vs 93% for fetuses with liver down ($P < .00005$). Liver position was highly predictive of both the need for ECMO ($P = .006$) and survival rates ($P = .001$) at all GAs of evaluation. In addition, the liver up patients had a longer ventilator duration (median, 29 days) than liver down patients (median, 18.5 days; $P = .0016$). We observed no significant differences in lengths of stay between the liver up and liver down groups.

Median LHR was 1.2 mm (range, 0.5–3.6 mm). Mean LHR among survivors was 1.45 ± 0.56 mm; mean LHR among nonsurvivors was 1.1 ± 0.36 mm ($P = .0028$). Independent of GA at time of initial measurement, low LHR (<1.0 mm) predicted increased incidence of ECMO (75%; $P = .036$) and lower survival rate (35%; $P = .0003$). When measured at <24 weeks of gestation ($n = 41$), LHR was not predictive of outcome (need for ECMO, $P = .108$; survival rate, $P = .150$). When measured at >24 weeks of gestation ($n = 48$), LHR was predictive of the need for ECMO ($P = .027$) and correlated with survival rates but did not reach statistical significance ($P = .07$). The incidences of the need for ECMO and survival rates for liver position and LHR are summarized in the Table. When liver position was analyzed with LHR, the latter was not predictive of need for ECMO ($P = .277$) or survival rate ($P = .129$).

Overall GA at delivery (cesarean section, 17/89; 19%) was 37.8 ± 1.4 weeks and did not differ significantly between survivors and nonsurvivors ($P = .5$). Deaths were the result of multisystem organ failure in a setting of pulmonary hypertension ($n = 9$), central nervous system bleed ($n = 10$), or persistent pulmonary hypertension ($n = 11$). Seven patients died before surgery to repair the diaphragm. Gore-Tex patch repair was performed in 57 of 82 patients who underwent surgery (70%). Four additional patients underwent muscle flap repair. One patient subsequently required Gore-Tex patch repair at 1 month of age. The number of days on ventilation did not correlate with survival rate ($P = .952$).

COMMENT

This study represents a 10-year experience of prenatal and postnatal care at a single high-volume institution with standardized methods of prenatal assess-

TABLE

The incidence of need for ECMO and survival for the variables liver position and LHR

Variable	ECMO (%) ^{*†}	Survival (%) ^{* ‡}
Liver up (49/89; 55%)	80	45
Liver down (40/89; 45%)	25	93
Lung-to-head circumference ratio <1 (20/89)	75	35
Lung-to-head circumference ratio >1 (69/89)	49	75

* $P < .05$, comparison of liver up vs liver down and lung-to-head circumference ratio <1 vs >1 .

† Need for ECMO compared by Fisher's exact test.

‡ Kaplan-Meier curve.

ment and postnatal management. We conclude that liver position is the best prenatal predictor of both the need for ECMO and survival rates in isolated left CDH. In this series, which analyzed the largest number of patients to date from a single institution with standardized prenatal and postnatal care, liver position was highly predictive of outcome, regardless of GA or LHR. The liver up-down approach, if measured by ultrafast fetal MRI, is simple and highly reproducible and requires no subjectivity. In the future, if we accurately quantify the degree of liver herniation, we may be able to further risk stratify patients based on outcomes.

LHR has been controversial because of the variability between observers from institution to institution and over time among the same observers. In our experience, LHR alone was predictive of survival and the need for ECMO but was not predictive when used in conjunction with liver position or at a GA of <24 weeks. The reasons for the inability of LHR to predict outcome early in gestation may be related to the small relative size of the lungs. As the fetus grows, the relative differences between lung sizes become more pronounced.

Timing of prognosis is of paramount importance for families who must decide whether to terminate or to authorize a

fetal intervention. Although we continue to use LHR in our prenatal counseling as an additional piece of information that is related to contralateral lung size, we are cautious in drawing any conclusions regarding its significance at <24 weeks of gestation.

In summary, LHR findings alone should not be used to counsel families on mid gestational management choices that are related to termination or fetal intervention.

CLINICAL IMPLICATIONS

- In isolated left congenital diaphragmatic hernia, liver position is the best prenatal predictor of both survival rate and the need for extracorporeal membrane oxygenation.
- Liver-to-head circumference ratio alone is predictive of survival and the need for extracorporeal membrane oxygenation but is not predictive when used in conjunction with liver position or at <24 weeks of gestation.
- Liver-to-head circumference ratio findings alone should not be used to counsel families regarding mid gestational management choices that are related to termination or fetal intervention. ■