Journal of Pediatric Surgery (2011) **46**, 1873–1880

ELSEVIER

Journal of Pediatric Surgery

www.elsevier.com/locate/jpedsurg

Original articles

Prenatal risk stratification for isolated congenital diaphragmatic hernia: results of a Japanese multicenter study

Noriaki Usui[a,*], Yoshihiro Kitano[b], Hiroomi Okuyama[c], Mari Saito[d], Kouji Masumoto[e], Nobuyuki Morikawa[b], Hajime Takayasu[b], Tomoo Nakamura[f], Satoshi Hayashi[f], Motoyoshi Kawataki[g], Hiroshi Ishikawa[g], Keisuke Nose[h], Noboru Inamura[i], Haruhiko Sago[f]

[a]*Department of Pediatric Surgery, Osaka University Graduate School of Medicine, Osaka, Japan*
[b]*Division of Surgery, National Center for Child Health and Development, Tokyo, Japan*
[d]*Division of Clinical Research, National Center for Child Health and Development, Tokyo, Japan*
[f]*Department of Maternal-Fetal and Neonatal Medicine, National Center for Child Health and Development, Tokyo, Japan*
[c]*Department of Pediatric Surgery, Hyogo College of Medicine, Hyogo, Japan*
[e]*Department of Pediatric Surgery, Kyushu University, Fukuoka, Japan*
[g]*Department of Perinatal Care, Kanagawa Children's Medical Center, Yokohama, Japan*
[h]*Department of Pediatric Surgery, Osaka Medical Center and Research Institute for Maternal and Child Health, Osaka, Japan*
[i]*Department of Pediatric Cardiology, Osaka Medical Center and Research Institute for Maternal and Child Health, Osaka, Japan*

Received 9 March 2011; revised 9 May 2011; accepted 6 June 2011

Key words:
Congenital diaphragmatic hernia;
Prenatal diagnosis;
Risk stratification;
Prognostic classification;
Multicenter study

Abstract

Background/Purpose: The aim of this study was to establish a prenatal prognostic classification system for risk-stratified management in fetuses with isolated congenital diaphragmatic hernia (CDH).

Methods: A multi-institutional retrospective cohort study of isolated CDH, diagnosed prenatally in fetuses delivered during the 2002 to 2007 period at 5 participating institutions in Japan, was conducted. The risk stratification system was formulated based on the odds ratios of prenatal parameters for mortality at 90 days. The clinical severity in CDH infants were compared among the stratified risk groups.

Results: Patients were classified into the 3 risk groups: group A (n = 48) consisted of infants showing liver-down with contralateral lung–to–thorax transverse area ratio (L/T) ratio ≥0.08; group B of infants showing liver-down with L/T ratio <0.08 or liver-up with L/T ratio ≥0.08 (n = 35), and group C of infants showing liver-up with L/T ratio <0.08 (n = 20). The mortality at 90 days in groups A, B, and C were 0.0%, 20.0%, and 65.0%, respectively. The intact discharge rates were 95.8%, 60.0%, and 5.0%, respectively. This system also accurately reflected the clinical severity in CDH infants.

Conclusions: Our prenatal risk stratification system, which demonstrated a significant difference in postnatal status and final outcome, would allow for accurate estimation of the severity of disease in fetuses with isolated CDH, although it needs prospective validation in a different population.

* Corresponding author. Tel.: +81 6 6879 3753; fax: +81 6 6879 3759.
E-mail address: usui@pedsurg.med.osaka-u.ac.jp (N. Usui).

0022-3468/$ – see front matter © 2011 Elsevier Inc. All rights reserved.
doi:10.1016/j.jpedsurg.2011.06.007

Congenital diaphragmatic hernia (CDH) remains one of the most challenging anomalies facing pediatric surgeons and neonatologists, as it has a broad spectrum of severities dependent on components of pulmonary hypertension and hypoplasia of the lungs. An accurate prenatal severity assessment is essential for standardization of prenatal and postnatal care for individual cases because severity directly affects mortality and morbidity. Prenatal prognostic classification of CDH would provide the family with more precise information about the course of treatment and allow a management protocol based on risk to be established. This may minimize excessive treatment and medical expenses for low-risk patients while maximizing effective management in high-risk patients.

Several prenatal prognostic parameters for fetal CDH have previously been proposed by other investigators [1-14]. It has been validated by multiple centers that the presence of liver herniation is among the most reliable predictors of severity and mortality in CDH [1-6]. Stomach position was also studied as a prognostic indicator along with liver herniation [8-10]. Moreover, estimation of fetal lung size or evaluation of fetal lung characteristics has reportedly been used for severity prediction [11-18]. Among these fetal lung assessments, the lung area–to–head circumference ratio (LHR) is the most commonly used as a prenatal prognostic factor [8,11,18]. However, LHR is no longer considered to be independently predictive of survival by several investigators [2,19-21] because it has been shown to increase according to gestational age [15,16,22,23]. The observed to expected LHR has been proposed to provide a constant value throughout the gestational period [22], but in that study, this value was standardized by the normal lung size value of each population corresponding to gestational age without taking individual fetal growth into consideration.

In contrast, the contralateral lung–to–thorax transverse area ratio (L/T ratio) appears to be a reliable predictive parameter in fetal CDH, as it was originally reported to be constant throughout the gestational period in normal fetuses [12], and is reportedly not strongly influenced by gestational age even in fetuses with CDH [15,16]. Although combining several reliable prognostic parameters including the L/T ratio may contribute to the establishment of a prenatal risk stratification system for fetal CDH, such approaches have not been successful to date. The aim of this study was to establish a prenatal prognostic classification system for risk-stratified management of fetuses with isolated CDH based on a combination of fetal ultrasonographic findings including liver position and L/T ratio.

1. Materials and methods

1.1. Patient selection and data collection

We conducted a multicenter retrospective review of the medical records of 117 fetuses with isolated CDH, diagnosed prenatally, born at 5 participating centers during the period between January 2002 and December 2007 [10,24]. Patients with serious associated anomalies such as major cardiac malformations and chromosomal abnormalities were excluded. Two cases with bilateral diaphragmatic hernia and 12 without L/T ratio measurements were excluded from the analysis. All 103 eligible patients were managed by maternal transport, with immediate resuscitation followed by neonatal intensive care mostly with high-frequency oscillatory ventilation. In all institutions, the blood gas parameter goals were $Paco_2$ < 60 to 70 mm Hg and preductal Spo_2 > 90%, under the concept of permissive hypercapnia [25] and permissive hypoxia. All institutions had extracorporeal membrane oxygenation (ECMO) and nitric oxide inhalation (iNO) capability, which were initiated according to the clinical decisions of each institution; indication criteria were not defined prospectively. Diaphragmatic repair was performed when respiratory and circulatory functions had stabilized. As the criteria of preoperative stabilization were not defined prospectively, operability of each patient was determined according to the clinical decisions of each institution. This study was approved by the institutional review boards of all 5 participating centers.

The primary outcome measure was mortality at 90 days. Prenatal ultrasonographic findings including polyhydramnios, fetal liver position, fetal stomach position, and the L/T ratio were collected at 3 times, according to gestational age at diagnosis: the earliest determination before 30 weeks of gestation, between 30 and 35 weeks of gestation, and after 35 weeks of gestation. Polyhydramnios was regarded as positive if the maximal vertical pocket was more than 8 cm. Only those patients with obvious liver herniation (ie, whose liver occupied more than one third of the thoracic space) were regarded as liver-up. Those with slight liver herniation or with liver herniation first recognized during surgery were regarded as liver-down. Fetal stomach position was categorized as contralateral stomach herniation, defined as more than half of the stomach having herniated into the contralateral thoracic cavity (equivalent to grade 3 in our previous report [10]) or others. The L/T ratio was measured at the transverse section containing the 4-chamber view of the heart by ultrasonography [12]. Briefly, the L/T ratio was defined as the area of the contralateral lung, which was determined by tracing around the contralateral lung, divided by the area of the thorax surrounded by the inner border of the bilateral ribs, the sternum, and the vertebra [15]. The cutoff value of the L/T ratio was set at 0.08 based on our previous studies [15,16,26]. Polyhydramnios, liver-up, and contralateral stomach herniation were categorized as positive if 1 of the 3 determinations was positive. The L/T ratio value was represented by the minimal value of 3 determinations, as in our previous report [16].

Postnatal factors, including sex, gestational age at birth, birth weight, mode of delivery, hernia side, Apgar scores at 1 and 5 minutes, preductal arterial blood gas data within