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Congenital diaphragmatic hernia: prognostic indices in the fetal endoluminal tracheal occlusion era

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Abstract

Introduction: Management of congenital diaphragmatic hernia (CDH) in the UK now includes the possibility of fetal endoluminal tracheal occlusion (FETO) for poor prognosis fetuses. The objective of this study was to investigate the value of variables previously thought prognostic in the FETO era.

Methods: A retrospective single-centre study was performed of all infants with CDH born between January 1994 and December 2007. Fetal endoluminal tracheal occlusion was available and had been used with parental consent for fetuses with lung-to-head ratio (LHR) of 1.0 or less and a liver-up position from 2002. Univariate analysis was used to predict survival (to leave hospital) using both prenatal (eg, polyhydramnios) and perinatal variables [eg, best oxygenation index on day 1, or BOI (d1)] and their dependence tested in a logistic regression model. Data were quoted as medians (range). $P < .05$ was regarded as significant.

Results: Eighty-six infants with CDH (1994-2002, n = 35 and 2002-2007, n = 51 "FETO era") were studied. Successful FETO intervention was performed in 31 infants.Univariate analysis showed liver position, birth weight, LHR, and BOI (d1) were significant prognostic predictors (all $P < .05$); however, only BOI (d1) retained significance using logistic regression analysis (odds ratio, 21; 95% confidence interval, 6-74; $P < .001$). Best oxygenation index on day 1 was then used as a surrogate marker for outcome to test the relationship with LHR (available since 2002) and showed a significant inverse correlation ($r_s = -0.5$; $P < .001$). There was no difference in median BOI (d1) between the FETO group and all those treated expectantly (40 [34-1046] vs 59 (23-581); $P = .3$].

Conclusion: Best oxygenation index on day 1 is the best early postnatal predictor of survival. The more recently evaluated prenatal index, LHR, has an observable relationship with BOI (d1) when it is used as a surrogate marker of outcome.

Antenatally detected congenital diaphragmatic hernia (CDH) is a complex anomaly with reported survival varying from 60% to 66% in recent series [1,2]. Better postnatal care has improved expectation of survival perhaps by a greater appreciation of the role of various factors such as:

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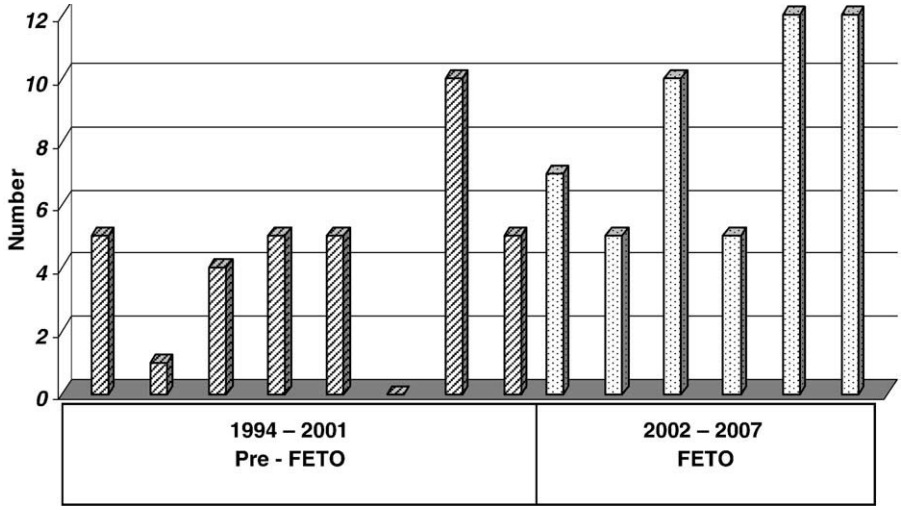

Fig. 1 Live-born infants with CDH (by year) (pre-FETO era = 1994-2001, FETO era = 2002-2007).

barotrauma and adoption of gentle ventilation strategies; pulmonary vasodilator therapy; delayed operation and the role of extracorporeal membrane oxygenation (ECMO). However, there remains a cohort of affected infants with apparently lethal pulmonary hypoplasia. To try and change outcome for these infants, a programme of fetal endoscopic tracheal occlusion (FETO) has been adopted in some European centres. Initial reports have suggested benefit if consistently applied to poor prognosis fetuses [3,4]; however, the method of evaluation of prognosis still appears to excite controversy.

The aim of this study was to investigate the value of prognostic variables in the FETO era.

1. Materials and methods

Kings College Hospital and the co-located Harris Birthright Research Centre for Fetal Medicine are tertiary centres for the management of antenatally diagnosed surgical malformations such as CDH. After confirmation of diagnosis, amniocentesis and chromosomal analysis were routinely offered together with full ultrasound serial scanning. Since 2002, this has included assessment of the lung-to-head ratio (LHR), defined as ratio of contralateral lung cross-sectional area-to-head circumference. Fetal endoluminal tracheal occlusion has now been available at our institution since January 2002 and, after informed parental consent, was offered for "poor prognosis" fetuses with isolated CDH (defined as LHR ≤1.0 and a liver-up position). Briefly, this involves single-port fetoscopy (1.2-mm fetoscope within 3-mm sheath) at 26 to 28 weeks under locoregional anaesthesia, fetal analgesia and immobilisation, followed by manipulation of a detachable balloon (GVB 16, MicroVasys, Paris, France) through the mouth and larynx. The balloon is then inflated and detached to achieve complete tracheal occlusion. During this period of study, a number of methods of balloon removal were used. Initially, this included the ex utero intrapartum treatment procedure at ~38 weeks gestation but was later replaced by direct US-guided balloon puncture at ~34 weeks and near-term induced-vaginal delivery [3,4].

Retrospective analysis of all live-born infants with CDH was performed, both during the FETO era (January 2002-December 2007) and in the preceding 8-year period (May 1994-December 2001) to provide a suitable comparison group. Prenatal (ie, polyhydramnios, side of defect, liver position, LHR) and perinatal variables [ie, birth weight, Apgar score, day 1 best oxygenation index, or BOI (d1)] were determined. The latter variable was calculated from best blood gas on day 1 of life as [fractional inspired O_2 (as %) ×

Table 1 Univariate analysis of infants with CDH, 1994 to 2007

Variable	n	Survival (%)	*P*
Left/right	76/10	59 vs 60	1.0
Liver position (up/down)	58/28	52 vs 79	.03
Polyhydramnios (present/absent)	21/61	59 vs 55	.79
LHR [a] (>1.0 vs ≤1.0)	12/36	92 vs 47	.01
Birth weight (>2.7 vs ≤2.7 kg)	57/28	68 vs 43	.03
Apgar (5 min) (> 5 vs ≤5)	40/10	80 vs 57	.32
BOI (d1) (≤82 vs >82) [b]	46/38	91 vs 18	<.001

[a] LHR only available from 2002 (n = 48).

[b] Alternate units—if mm Hg is used for Pao_2, then value for BOI (d1) should be divided by 7.5; that is, cutoff of 82 will be equivalent to 11.

Table 2 Binary logistic regression analysis of infants (1994-2007)

Variable	Odds ratio (95% CI)	*P*
Liver position (up/down)	2.32 (0.4-10.8)	.28
Birth weight (>2.6 vs ≤2.6 kg)	1.49 (0.3-5.8)	.57
BOI (d1) [a] (≤82 vs >82)	21.3 (6-74)	<.001

[a] Alternate units—if mm Hg is used for Pao_2, then value for BOI (d1) should be divided by 7.5; that is, cutoff of 82 will be equivalent to 11.