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Fetal lung-to-head ratio in the prediction of survival in severe left-sided diaphragmatic hernia treated by fetal endoscopic tracheal occlusion (FETO)

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KEY WORDS
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Objective: The objective of the study was to investigate the value of fetal lung area to head circumference ratio in the prediction of the postnatal outcome in left-sided congenital diaphragmatic hernia treated by fetoscopic endoluminal tracheal occlusion.

Study design: The lung area to head circumference ratio was measured before fetoscopic endoluminal tracheal occlusion in 28 fetuses with congenital diaphragmatic hernia at 25 to 29 weeks. Regression analysis was used to investigate the effect on survival of lung area to head circumference ratio, gestation at fetoscopic endoluminal tracheal occlusion, gestation at delivery, preterm amniorrhexis following fetoscopic endoluminal tracheal occlusion, and prenatal removal of the balloon.

Results: The median lung area to head circumference ratio prior to fetoscopic endoluminal tracheal occlusion was 0.7 (range 0.5 to 0.9). The median gestation at delivery was 34 (range 27 to 39) weeks, and there were 16 survivors (57%). Only lung area to head circumference ratio provided significant prediction of survival, which increased from 17% for lung area to head circumference ratio of 0.4 to 0.5 to 62% for lung area to head circumference ratio of 0.6 to 0.7 and 78% for lung area to head circumference ratio of 0.8 to 0.9.

Conclusion: In congenital diaphragmatic hernia treated by fetoscopic endoluminal tracheal occlusion, postnatal survival can be predicted by the lung area to head circumference ratio measured prior to the procedure.

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Prenatally diagnosed isolated, left-sided congenital diaphragmatic hernia (CDH) is associated with a high postnatal death rate, primarily because of pulmonary hypoplasia and/or hypertension.[1-3] Furthermore, the mortality rate is substantially higher if there is intrathoracic herniation of the liver than in cases in which there is no such herniation (about 50% versus 25%).[4]

In fetuses with intrathoracic herniation of the liver, measurement of the fetal lung area to head circumference ratio (LHR), at 22 to 28 weeks of gestation, provides useful prediction of subsequent survival. Thus, in a multicenter study of 86 fetuses with left-sided CDH and liver herniation, which were managed expectantly and were live born after 30 weeks of gestation, the survival rate increased from 0% for those with LHR of 0.4 to 0.7 to about 15% for LHR of 0.8 to 0.9, 65% for LHR of 1.0 to 1.5, and 83% for LHR of 1.6 or more.[4]

Tracheal occlusion (TO) prevents egress of pulmonary fluid leading to lung tissue stretch and triggers growth of airways and pulmonary vessels.[5,6] The timing and duration of the occlusion are crucial for the quality and response of airways and pulmonary vessels, and sustained TO leads to a decreased number of type II alveolar cells, the surfactant-producing cell in the lung.[7-10] In sheep, TO in the late canalicular phase with prenatal reversal (plug-unplug sequence or temporary TO), is associated with in utero recovery of the type II alveolar cell population.[8] Preliminary clinical experience suggests that in fetuses with severe left-sided CDH, the chances of survival are improved by fetoscopic endoluminal tracheal occlusion (FETO) with a balloon, which is inserted at 25 to 29 weeks of gestation.[11-13]

In this study we aimed to investigate the potential value of the fetal LHR, measured at 23 to 29 weeks before fetal intervention, in the prediction of postnatal survival after FETO. We also examined the effect on survival of preterm prelabor amniorrhexis (preterm premature rupture of membranes [PPROM]), which is commonly observed after FETO, gestation at delivery, extra corporeal membrane oxygenation (ECMO) and whether the balloon was removed perinatally or prenatally to allow for in utero recovery.

Material and methods

This was a prospective ongoing study of patients with severe CDH treated with FETO at the Fetal Medicine Centres of the University Hospital Gasthuisberg, Leuven, Belgium; King's College Hospital, London, United Kingdom; and Vall d'Hebron Hospital, Barcelona, Spain. In all cases the patients were assessed and received counseling by a multidisciplinary team composed of fetal medicine specialists, neonatologists, and pediatric surgeons. The study was approved by the local Ethics Committees and/or Committee on Innovative Technologies, and all patients give written informed consent to the procedure.

The entry criteria for fetal surgery are singleton pregnancy with severe CDH in an otherwise anatomically and chromosomally normal fetus. For both left- and right-sided CDH, it is necessary that there is intrathoracic herniation of the liver and that LHR is less than 1.0. In all centers measurement of the LHR was as described by Metkus et al,[14] which essentially involved first obtaining a transverse section of the fetal chest demonstrating the 4-chamber view of the heart and second, multiplying the longest diameter by the longest perpendicular of the contralateral lung.

The procedure of FETO is performed under combined spinal-epidural anesthesia with fetal analgesia and immobilization, as previously described.[11] Essentially, a 1.2-mm endoscope within a 3.0-mm sheath (Karl Storz, Tüttlingen, Germany) is introduced into the trachea to position a detachable balloon between the carina and vocal cords. In the first 24 hours after the procedure, the patients are treated with bed rest, low-molecular-weight heparin, pain relief on demand, cefazolin, and nifedipine. Ultrasound examination to confirm the endotracheal presence of the inflated balloon and to monitor lung growth is performed every 1 to 2 weeks. Whenever preterm delivery is anticipated, a course of corticosteroids is administered and active tocolysis is attempted, unless contraindicated.

The balloon is removed either prenatally, by fetal tracheoscopy in a way described as for placement of the balloon, or ultrasound-guided puncture with a 20G needle inserted through the maternal abdomen or tracheoscopy at the time of delivery by ex utero intrapartum treatment or immediately after vaginal delivery.[12] Patients are allowed to deliver at the referring institution with facilities for neonatal intensive care and pediatric surgery, according to the local protocols. Postnatal therapy includes endotracheal intubation and mechanical ventilation, use of high-frequency oscillatory ventilation, inhaled nitric oxide for refractory pulmonary hypertension, and where ECMO available as a salvage in eligible cases and delayed surgical repair.

The participating centers provided outcome data, which were entered into a central CDH registry at the Fetal Medicine Unit at the University Hospital of Leuven, Belgium. We searched the database to identify all consecutive cases of isolated, left-sided diaphragmatic hernia treated by FETO before 30 weeks of gestation and fulfilling the following criteria: (1) live birth with no major defect and (2) either postnatal survival to at least 3 months after discharge from the hospital or postnatal death caused by pulmonary hypoplasia and/or hypertension.

Statistical analysis

Regression analysis was used to investigate the effect on survival of LHR, gestation at FETO and gestation at delivery in weeks, PPROM (yes or no), or antenatal