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Current consequences of prenatal diagnosis of congenital diaphragmatic hernia

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Abstract

Background: Today, the diagnosis of congenital diaphragmatic hernia (CDH) can readily be made in the prenatal period during screening ultrasound examination. Patients ought to be referred to rule out associated anomalies, and in isolated cases, prognosis is poor when the liver is intrathoracic and the lung-to-head ratio (LHR) is less than 1. In these patients, prenatal intervention aiming to reverse pulmonary hypoplasia can be considered.

Methods: We present our current algorithm for counselling patients presenting with CDH. Patients with a poor prognosis are offered percutaneous fetal endoluminal tracheal occlusion (FETO) with a balloon, inserted at 26 to 28 weeks. We report on the evolution of technique and results in a consecutive homogeneous case series and compare outcome in cases with similar severity managed in the postnatal period.

Results: Within a period of 28 months, FETO was performed between 26 and 28 weeks in 24 fetuses with severe left-sided CDH. Under general (n = 5), epidural (n = 17) or local (n = 2) anesthesia, the balloon was successfully positioned at first surgery (23/24) with a mean operation time of 20 minutes (range, 3-60 minutes). There were no serious maternal complications or direct fetal adverse effects. In the first 2 weeks after FETO, LHR increased from 0.7 to 1.7. Premature prelabour rupture of the membrane (PPROM) occurred in 16.7% and 33.3% at 28 and 32 weeks or earlier, respectively. Gestational age at delivery was 33.5 weeks. Patency of airways was restored either in the prenatal (n = 12) or perinatal period (n = 12).

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Early (7 days) and late (28 days) survival, and survival at discharge were 75% (18/24), 58.3% (14/24) and 50% (12/24), respectively. Half of nonsurvivors (n = 6) died of pulmonary hypoplasia and hypertension, in combination with PPROM and preterm delivery (n = 4) and balloon dislodgement (n = 2), which coincided with a short tracheal occlusion (TO) period (12 days). In the other 6, TO period was comparable to that in the 12 survivors (47 vs 42 days, respectively). In that group of 6 babies, only 2 died of pulmonary problems. Late neonatal survival (28 days) was higher with prenatal vs perinatal balloon retrieval 83.3% vs 33.3% ($P = .013$). In a multicentre study validating the criteria, survival till discharge in 37 comparable cases was 9% (3/32) and 13% (5/37) of parents opted for termination.

Conclusion: Fetuses with isolated left-sided CDH, liver herniation, and LHR of less than 1 have a poor prognosis. Percutaneous FETO is minimally invasive and may improve the outcome in these highly selected cases. Airways can be restored before birth, allowing vaginal delivery and return to the referring tertiary unit and may improve survival rate. The procedure carries a risk for PPROM, although that may decrease with experience.

Congenital diaphragmatic hernia (CDH) is a surgically correctable anatomical defect with unknown etiology. It sporadically occurs with an incidence of 1 of 2500 to 1 of 5000 of newborns, depending on whether stillbirths are included or not. Eighty-four percent of lesions are left-sided (LCDH), 13% right-sided (RCDH), and 2% bilateral. In just less than half of the cases, there are associated anomalies. The defect is believed to arise in the embryological period ("first hit"), and during further gestation, lung development is impaired ("second hit") [1]. Whether the anomaly is a primary pulmonary or diaphragmatic pathology remains a source of debate. As a consequence, CDH lungs have fewer alveoli, thickened alveolar walls, increased interstitial tissue, markedly diminished alveolar airspace, and gas-exchange surface area. Parallel to airway changes, pulmonary vasculature is abnormal, with a reduced number of vessels, adventitial thickening, medial hyperplasia, and peripheral extension of the muscle layer into the smaller intra-acinary arterioles [2].

The above morphological changes have a tremendous postnatal functional impact: pulmonary hypoplasia leads early on to ventilatory insufficiency, and in survivors, vascular alterations lead to variable degrees of persistent pulmonary hypertension (PPHN). Until the 1990s, the cornerstone of neonatal management was emergency repair of the defect and aggressive control of PPHN. Later on, these 2 tenets were questioned, and today "gentle ventilation" (preservation of spontaneous respiration, permissive hypercapnia and avoidance of high ventilation pressure) followed by delayed surgery have been shown to improve results [3]. High-frequency oscillatory ventilation, liquid ventilation, extracorporeal membrane oxygenation, the use of corticoids and/or surfactant and have been proposed, but there role is being debated.

Survival largely depends on the presence of associated anomalies, which can be structural, chromosomal, or syndromal. They are independent predictors of survival, with less than 15% of babies surviving in this group [4,5]. For isolated cases, survival is better, but exact rates remain a matter of debate. In a 1998 report from the CDH study group, an overall survival of 65% was reported, which was also our experience [4]. A number of highly specialised centres report rates higher 80% with specific local protocols [6]. However, in larger European surveys, mortality rates in antenatally diagnosed isolated and live-born cases remain approximately 30%, as is today [5,7]. Improved survival rates may, at least in part, reflect increasing termination rates as well as selection bias. Survivors may have gastrointestinal, pulmonary, orthopaedic, and neurological morbidity, but this has been much less studied, and so far could not be predicted from prenatal findings. The observation that nonsurvivors usually die of the consequences of pulmonary hypoplasia and that no postnatal therapy can address this successfully has been the basis of the concept of prenatal interventions directed to improve lung development.

1. Prenatal diagnosis of congenital diaphragmatic hernia

Modern ultrasound allows prenatal diagnosis of CDH. The diaphragm can be visualised with modern high-resolution equipment already in the first trimester. Its absence is usually suggested by the intrathoracic presence of abdominal viscera and as a consequence displacement, compression, and ill development of thoracic organs. On longitudinal scanning, a defect in the posterior aspect of the diaphragm may be seen, at least for the most common Bochdalek type of hernia. For LCDH, mediastinal shift and rightwards displacement of the heart can be seen, and in most cases, a fluid-filled stomach or bowels are later on present within the thoracic cavity. An important feature to look for is presence of (a portion of) the liver in the thorax. Doppler interrogation of the umbilical vein and hepatic vessels may be helpful in this respect. With RCDHs, the right lobe of the liver usually herniates into the chest, combined with mediastinal shift to the left. Because a high proportion of cases will have associated anomalies, the sonographer should look for these. The variety of anomalies is wide and includes cardiac, central nervous system, renal, and gastrointestinal anomalies. Chromosomal