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Severe diaphragmatic hernia treated by fetal endoscopic tracheal occlusion

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KEYWORDS: congenital diaphragmatic hernia; fetal therapy; fetal tracheal occlusion; lung-to-head ratio; pulmonary hypoplasia

ABSTRACT

Objectives *To examine operative and perinatal aspects of fetal endoscopic tracheal occlusion (FETO) in congenital diaphragmatic hernia (CDH).*

Methods *This was a multicenter study of singleton pregnancies with CDH treated by FETO. The entry criteria for FETO were severe CDH on the basis of sonographic evidence of intrathoracic herniation of the liver and low lung area to head circumference ratio (LHR) defined as the observed to the expected normal mean for gestation (o/e LHR) equivalent to an LHR of 1 or less.*

Results *FETO was carried out in 210 cases, including 175 cases with left-sided, 34 right-sided and one with bilateral CDH. In 188 cases the CDH was isolated and in 22 there was an associated defect. FETO was performed at a median gestational age of 27.1 (range, 23.0–33.3) weeks. The first eight cases were done under general anesthesia, but subsequently either regional or local anesthesia was used. The median duration of FETO was 10 (range, 3–93) min. Successful placement of the balloon at the first procedure was achieved in 203 (96.7%) cases. Spontaneous preterm prelabor rupture of membranes (PPROM) occurred in 99 (47.1%) cases at 3–83 (median, 30) days after FETO and within 3 weeks of the procedure in 35 (16.7%) cases. Removal of the balloon was prenatal either by fetoscopy or ultrasound-guided puncture, intrapartum by* ex-utero *intrapartum treatment, or postnatal either by tracheoscopy or percutaneous puncture. Delivery was at 25.7–41.0 (median, 35.3) weeks and before 34 weeks in 65 (30.9%) cases. In 204 (97.1%) cases the babies were live born and 98 (48.0%) were discharged from the hospital alive. There were 10 deaths directly related to difficulties with removal of the balloon. Significant prediction of survival was provided by the o/e LHR and gestational age at delivery. On the basis of the relationship between survival and o/e LHR in expectantly managed fetuses with CDH, as reported in the antenatal CDH registry, we estimated that in fetuses with left CDH treated with FETO the survival rate increased from 24.1% to 49.1%, and in right CDH survival increased from 0% to 35.3% (*$P < 0.001$*).*

Conclusions *FETO in severe CDH is associated with a high incidence of PPROM and preterm delivery but a substantial improvement in survival. Copyright © 2009 ISUOG. Published by John Wiley & Sons, Ltd.*

INTRODUCTION

Prenatally diagnosed congenital diaphragmatic hernia (CDH) is associated with a high postnatal mortality rate, owing to the coexistence of other major defects or various combinations of pulmonary hypoplasia and persistent pulmonary hypertension[1–5]. The outcome of fetuses with CDH may be improved by fetal endoscopic tracheal occlusion (FETO) with a balloon[6,7]. During pregnancy, the fetal lungs secrete fluid into the airways, which is drained to the amniotic cavity during fetal breathing movements[8]. FETO prevents egress of pulmonary fluid leading to lung tissue stretch, triggering lung growth of airways and also inducing vascular changes[9–11]. Since 2001, we have been offering FETO clinically to fetuses with CDH with a poor predicted survival rate, based on their lung measurements.

In this study we present our entire experience with FETO. We aimed to report on the technical aspects of insertion and removal of the balloon, and intraoperative and postoperative complications. We further explored

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which antenatal factors predicted postnatal survival in the population with isolated CDH.

METHODS

This is a prospective and ongoing study in singleton pregnancies with CDH treated by FETO at the Fetal Medicine Centers of the University Hospital Gasthuisberg, Leuven, Belgium, King's College Hospital, London, UK, and Clinic Hospital, Barcelona, Spain (referred to as the FETO consortium)[6]. 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 were severe CDH on the basis of sonographic evidence of intrathoracic herniation of the liver and low lung area to head circumference ratio (LHR)[6]. Measurement of the LHR was as described by Metkus *et al*., which essentially involves obtaining a transverse section of the fetal chest demonstrating the four-chamber view of the heart and then, in the lung contralateral to the CDH, multiplying the longest diameter by the longest perpendicular diameter[12]. A study of 650 normal fetuses has shown that, between 12 and 32 weeks of gestation, there is an 18-fold increase in lung area, but only a fourfold increase in head circumference[13]. Consequently, the left and right LHR increase exponentially with gestation. In order to eliminate the effect of gestation we introduced the observed to expected (o/e) LHR[14]. The entry criterion for the study was an o/e LHR equivalent to an LHR of 1 or less. The o/e LHR that is equivalent to an LHR of 1 decreases linearly with gestation from 32% at 23 weeks to 23% at 33 weeks for left CDH, and from 43% at 23 weeks to 32% at 33 weeks for right CDH.

We aimed to perform FETO only in cases of isolated CDH. However, the procedure was also carried out in a few cases with associated cardiac defects, cystic adenomatoid malformation or pleural effusions, following individual case discussion by a multidisciplinary team and taking into account the postnatal perspectives and the patient's wishes.

The FETO procedure was performed under combined fetal analgesia and immobilization (fentanyl, pancuronium and atropine) and maternal general, spinal–epidural or local anesthesia. The technique has been described in detail previously[6]. Essentially, a 1.3-mm endoscope within a 3.0-mm sheath (Karl Storz, Tüttlingen, Germany) was introduced into the trachea to position a detachable balloon between the carina and vocal cords. Ultrasound examination to confirm the endotracheal presence of the inflated balloon and to monitor lung growth was performed every 1–2 weeks. Whenever preterm delivery was anticipated, a course of corticosteroids was administered and active tocolysis was attempted, unless contraindicated.

The balloon was removed either prenatally, by fetal tracheoscopy as described for placement of the balloon or by ultrasound-guided puncture with a 20-G needle inserted through the maternal abdomen, or by tracheoscopy at the time of delivery by *ex-utero* intrapartum treatment (EXIT), or by tracheoscopy or ultrasound-guided needle puncture through the neck of the neonate immediately after vaginal delivery. After removal of the tracheal occlusion the patients were allowed to deliver at the referring institution with facilities for neonatal intensive care and pediatric surgery, according to the local protocols.

Each referral center provided their data on all cases of CDH treated by FETO.

Statistical analysis

Regression analysis was used to investigate the effect on spontaneous rupture of the membranes within 3 weeks after FETO of the duration of FETO in minutes, operator experience, gestational age at the time of FETO in days, side of CDH (left or right or bilateral), placental location (anterior or posterior), method of anesthesia (local, spinal–epidural or general), number of fetoscopic balloon insertion procedures and o/e LHR. Similarly, regression analysis was used to investigate the effect on delivery before 34 weeks of the above variables and of preterm prelabor rupture of the membranes (PPROM) (yes or no). Regression analysis was also used to investigate the effect on survival of site of CDH, o/e LHR, gestational age at the time of FETO and gestational age at delivery, PPROM, duration of tracheal occlusion, interval between removal of the balloon and delivery, and operator experience.

The difference between the observed survival rates in fetuses with FETO and their estimated expected survival rate with expectant management during pregnancy based on the antenatal registry[14] was performed using the Chi-square test.

Statistical analysis was performed with SPSS for Windows version 16 (SPSS, Chicago, IL, USA).

RESULTS

A FETO procedure was carried out in a total of 210 cases of CDH between October 2001 and October 2008. The median maternal age was 31 (range, 18–48) years. The CDH was left-sided in 175 cases, right-sided in 34 and bilateral in one. In 188 cases the CDH was isolated, in six there was an associated cardiac defect (three with aortic stenosis, two with coarctation of the aorta and one with severe mitral atresia), in eight there was cystic adenomatoid malformation of the lung, and in six there were large pleural effusions. In all cases antenatal fetal karyotyping either in our centers or in the referral hospitals was reported as being normal but in two cases deletion of chromosome 8 was diagnosed after delivery. There was also one case of Goldenhar syndrome that was diagnosed postnatally but this case is included in the isolated CDH group because the condition does not affect the prognosis, in terms of either pulmonary development or survival. The o/e LHR, measured within a few days before FETO, was 8–30% (median, 20%) for left CDH, 16–45% (median, 30%) for right CDH and 19% for the case with bilateral CDH.

Insertion of the balloon

FETO was performed at a median gestational age of 27.1 (range, 23.0–33.3) weeks (Figure 1). The aim was to perform the procedure at 26–29 weeks but this varied according to the gestational age at referral, and was positively related to the o/e LHR ($P = 0.015$). The placenta was anterior in 100 cases and posterior in 110. In the first eight cases general anesthesia was given but subsequently either regional ($n = 160$) or local ($n = 42$) anesthesia was used. The median duration of FETO was 10 (range, 3–93) min. The duration of FETO decreased significantly with operator experience, defined as the number of cases previously done by a given operator ($P = 0.018$).

Successful placement of the balloon at the first procedure was achieved in 203 (96.7%) cases. In three cases it was not possible to enter the trachea owing to fetal position and/or mobility but this was successful during a second FETO 4–7 days later. In another four cases the first FETO was complicated by tracheal laceration and the procedure was abandoned to allow time for healing. In three of these cases a balloon was inserted successfully during a second FETO 8–14 days later. In the fourth case with tracheal laceration the parents declined the offer of a second FETO. Therefore, 209/210 fetuses were treated with an endotracheal balloon.

In 17/209 (8.1%) cases follow-up scans demonstrated that 1–63 (median, 28) days after FETO there was no visible balloon within the trachea. This was probably because of spontaneous deflation and/or expulsion. In 9/17 cases a second balloon was inserted successfully by FETO. Therefore, in total a second FETO was carried out in 16 cases (three for failed first attempt, three for tracheal laceration at the first FETO and nine because of spontaneous expulsion of the balloon).

Additional intrauterine interventions

In addition to FETO the six fetuses with effusions and one of the cases of cystic adenomatoid malformation were treated by placement of a thoracoamniotic shunt. During the course of the pregnancy 18 cases developed severe polyhydramnios that was treated by amniodrainage.

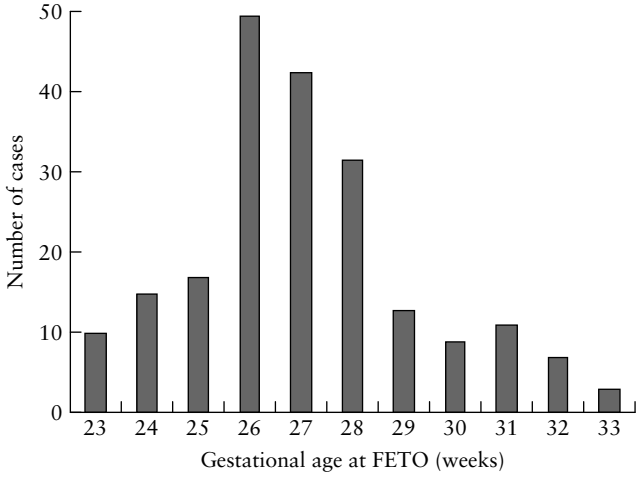

Figure 1 Gestational age at the time of fetal endoscopic tracheal occlusion (FETO) in 210 consecutive cases.

Removal of the balloon

Removal of the balloon was prenatal in 146 cases, either by fetoscopy ($n = 106$) or ultrasound-guided puncture ($n = 40$), intrapartum by EXIT in 14 cases, and postnatal in 34 cases either by tracheoscopy ($n = 21$) or percutaneous puncture ($n = 13$). In 16 cases there was no need to remove the balloon because of failed insertion in one case, spontaneous deflation of the balloon in 10 cases, and fetal death or termination of pregnancy in five cases (there was another fetal death after removal of the balloon, see below).

The balloon was removed electively by fetoscopy, ultrasound-guided puncture or EXIT in 85/194 (43.8%) cases at 33.7–38.7 (median, 34.3) weeks (Table 1). In the 85 cases of elective removal of the balloon, there was subsequent delivery within 7 days in 26 (30.6%) cases, including 20 (23.5%) in which there was spontaneous onset of labor. The other six were delivered electively.

In the other 109 (56.2%) cases removal of the balloon was an emergency procedure at 26.0–36.3 (median, 33.0) weeks either prenatally or postnatally because of spontaneous rupture of membranes, the development of polyhydramnios or spontaneous preterm labor and delivery. In 80 cases, this was before 34 weeks (73.4%) and in 38 (34.9%) cases it was before 32 weeks.

Preterm prelabor rupture of membranes

PPROM occurred in 99 (47.1%) of the 210 cases, including four cases in which two FETOs were performed, eight that had amniodrainage or polyhydramnios and 17 in which a second fetoscopy was performed for elective removal of the balloon. The interval between the first fetoscopy and membrane rupture was 3–83 (median, 30) days and it was within 3 weeks of the procedure in 35 (16.7%) cases.

Regression analysis demonstrated that significant prediction of PPROM within 3 weeks of FETO was provided by the duration of FETO in minutes (OR, 1.026; 95% CI, 1.004–1.048; $P = 0.020$) (Table 2) and

Table 1 Method of balloon removal

Reason	*Method*	n
Elective	EXIT	3
	Fetoscopic removal	71
	Ultrasound-guided puncture	11
Emergency	EXIT	11
	Fetoscopic removal	35
	Ultrasound-guided puncture	29
	Postnatal tracheoscopic removal	21
	Postnatal puncture through the neck	13

EXIT, *ex-utero* intrapartum treatment.

Table 2 Rate of preterm prelabor rupture of the membranes (PPROM) in relation to duration of fetal endoscopic tracheal occlusion (FETO) in 204 cases of diaphragmatic hernia resulting in live birth

Duration of FETO (min)	n	*PPROM within 3 weeks of FETO* (n *(%))*
1–10	111	12 (10.8)
11–20	49	9 (18.4)
21–30	18	4 (22.2)
> 30	26	9 (34.6)

anesthesia (general vs. regional or local: OR, 5.583; 95% CI, 1.294–24.1; $P = 0.021$; local vs. regional: $P = 0.113$), but not operator experience ($P = 0.188$), gestational age at FETO ($P = 0.073$), side of CDH ($P = 0.944$), placental location ($P = 0.111$), number of FETOs ($P = 0.213$) or o/e LHR ($P = 0.189$).

Maternal complications

Procedure-related maternal complications occurred in seven cases. In one case there was an intra-amniotic hemorrhage from puncture of the placenta with the trocar, which required treatment with a maternal blood transfusion. In five cases PPROM was complicated by chorioamnionitis which occurred 3, 12, 14, 24 and 42 days after FETO. The pregnancies were treated successfully with intravenous antibiotics and delivery.

Gestational age at delivery

Delivery was at a median gestational age of 35.3 (range, 25.7–41.0) weeks (Figure 2). Delivery was before 34 weeks in 65 (30.9%) cases and before 32 weeks in 36 (17.1%). These early preterm deliveries included four fetal deaths or terminations of pregnancy (see below) and one elective delivery at 30 weeks for severe pre-eclampsia. After exclusion of these five cases the median gestational age at delivery was 35.4 (range, 26.0–41.0) weeks.

Regression analysis including the remaining 205 cases demonstrated that significant prediction of delivery before 34 weeks was provided by occurrence of PPROM (OR, 5.002; 95% CI, 2.527–9.901; $P < 0.001$) and gestational age at FETO (OR, 0.975; 95% CI, 0.953–0.997; $P = 0.028$) but not by side of CDH ($P = 0.394$), duration of FETO ($P = 0.225$), placental location ($P = 0.559$), method of anesthesia ($P = 0.135$), number of FETOs ($P = 0.720$), o/e LHR ($P = 0.673$) or operator experience ($P = 0.472$). Similarly, regression analysis demonstrated that significant prediction of delivery before 32 weeks was provided by occurrence of PPROM (OR, 5.850; 95% CI, 2.215–15.451; $P < 0.0001$), gestational age at FETO (OR, 0.949; 95% CI, 0.919–0.981; $P = 0.002$) and side of CDH (right OR, 3.256; 95% CI, 1.194–8.881; $P = 0.021$), but not duration of FETO ($P = 0.335$), placental location ($P = 0.995$), method of anesthesia ($P = 0.615$), number of FETOs ($P = 0.262$), o/e LHR ($P = 0.446$) or operator experience ($P = 0.332$).

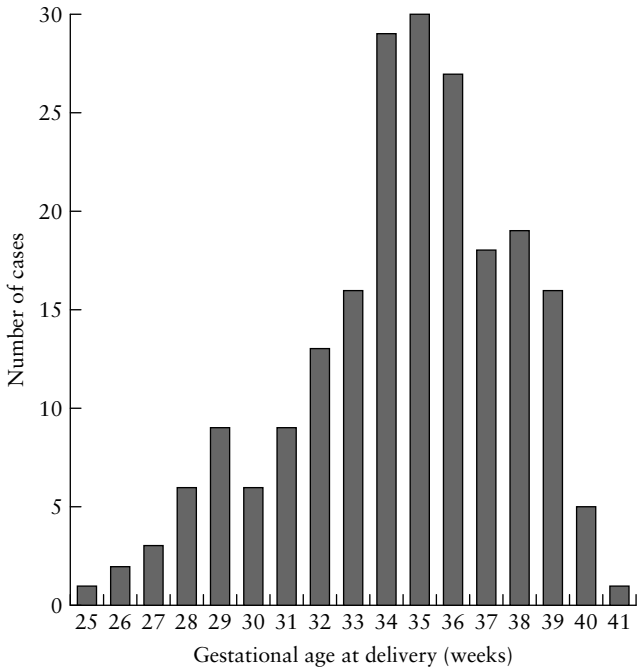

Figure 2 Gestational age at delivery.

Pregnancy outcome

There were four fetal deaths. One of these occurred within 24 h of FETO following an episode of unexplained severe bradycardia. There were another three unexplained deaths at 32, 50 and 73 days, following uncomplicated procedures and an unremarkable postoperative course.

In two cases termination of pregnancy was performed. In one case there was spontaneous rupture of the membranes 10 days after FETO performed at 24 weeks and the parents did not want to continue with the pregnancy. In another case of FETO at 24 weeks, intra-amniotic bleeding was noted at the site of entry of the fetoscope but this was thought to be of maternal origin because there was no obvious change in the fetal heart rate. However, a follow-up scan 3 weeks later demonstrated severe brain damage with a shrunken echogenic cortex and dilatation of the lateral ventricles and subarachnoid space. This pregnancy was terminated at the request of the parents.

In 204 cases the babies were liveborn at 26.0–41.0 (median, 35.3) weeks and in 98 (48.0%) cases the babies survived following surgery and were discharged from hospital alive. Survival rate according to the side of CDH and the presence or absence of other abnormalities is shown in Table 3. The survival rate was 49.4% for isolated left CDH and 37.9% for isolated right CDH.

In 106 cases the babies died at 1–194 (median, 1) days of age. There were 10 deaths directly related to difficulties in removal of the balloon, two cases of chromosomal abnormalities (deletions of chromosome 8) which were missed on prenatal karyotyping, and 94 deaths mainly due to problems arising from various combinations of pulmonary hypoplasia, pulmonary hypertension and prematurity.

Table 3 Survival to discharge from hospital according to side of the hernia and associated defects in 210 fetuses with diaphragmatic hernia treated by fetal endoscopic tracheal occlusion

Hernia type	n	*Survival (*n *(%))*
Left sided	175	86 (49.1)
Isolated	158	78 (49.4)
Plus cardiac defect	6	3 (50.0)
Plus cystic adenomatoid malformation	7	4 (57.1)
Plus pleural effusion	2	1 (50.0)
Plus deletion of chromosome 8	2	0 (0)
Right sided	34	12 (35.3)
Isolated	29	11 (37.9)
Plus cystic adenomatoid malformation	1	0 (0)
Plus pleural effusion	4	1 (25.0)
Bilateral	1	0 (0)

Details on the postnatal course and outcome will be provided in a separate publication.

Estimated impact of fetal endoscopic tracheal occlusion on survival

In a multicenter study of Fetal Medicine Units on the antenatal findings and postnatal outcome of fetuses diagnosed with isolated CDH and undergoing expectant antenatal management, the data are entered in a central Antenatal CDH Registry at the Fetal Medicine Unit in the University Hospital of Leuven, Belgium. In this registry there are 161 cases of isolated left CDH with intrathoracic herniation of the liver that were liveborn at 31–42 (median, 38) weeks of gestation and 85 (52.8%) were discharged from hospital alive. In all cases the LHR was measured antenatally as described by Metkus *et al.*[12] and in each fetus the observed LHR was expressed as an o/e LHR. Regression analysis demonstrated a significant linear association between o/e LHR and postnatal survival (survival rate (%) = (258 × (o/e LHR (%))−28.68)/100; $r = 0.974$, $P < 0.0001$). In the registry there were also eight cases of isolated right CDH with an o/e LHR < 45% and none of these survived after delivery at 35–41 (median, 38) weeks.

On the basis of the regression equation of survival from o/e LHR in the expectantly managed fetuses in the registry, the estimated survival rate in our 175 fetuses with left CDH treated by FETO was 24.1%. The observed survival rate was 49.1%, which was significantly higher than the expected rate ($P < 0.001$). Similarly, in the fetuses with right CDH the observed survival rate of 35.3% in our 34 fetuses was significantly higher than the expected survival rate of 0% ($P < 0.001$).

Prediction of survival in isolated congenital diaphragmatic hernia

In this analysis we included the 144 cases of left CDH and 28 of right CDH in which the condition was isolated and the babies were liveborn. We excluded the terminations of pregnancy, the intrauterine deaths, the case with bilateral CDH, the cases with effusions, cardiac defects, cystic adenomatoid malformation and chromosomal abnormalities, and the neonatal deaths due to problems related to removal of the balloon.

The survival rates for left and right CDH according to o/e LHR, gestation at FETO, gestational age at delivery, duration of tracheal occlusion and presence or absence of PPROM are given in Table 4.

In the left CDH group logistic regression analysis demonstrated that significant prediction of postnatal survival was provided by both o/e LHR (OR, 1.490 E4; 95% CI, 4.8–4.6 E7; $P = 0.019$) and gestational age at delivery in days (OR 1.024; 95% CI, 1.007–1.042; $P = 0.007$) but not gestational age at FETO ($P = 0.602$), duration of tracheal occlusion ($P = 0.064$), interval between balloon removal and delivery ($P = 0.304$), incidence of PPROM ($P = 0.112$) or operator experience ($P = 0.845$).

Regression analysis demonstrated that for right CDH there was no significant association between survival and either o/e LHR ($P = 0.744$), gestational age at FETO ($P = 0.966$), gestational age at delivery ($P = 0.254$), duration of tracheal occlusion ($P = 0.301$), interval between balloon removal and delivery ($P = 0.495$), incidence of PPROM ($P = 0.187$) or operator experience ($P = 0.347$).

DISCUSSION

This multicenter study on FETO has demonstrated the feasibility of this method of fetal therapy, and documented the technical problems associated with the procedure, postoperative complications and pregnancy outcome. It further documented significant predictors for survival following FETO in left- and right-sided isolated CDH.

In open fetal surgery that necessitates hysterotomy > 25% of women require intensive care and > 10% have blood transfusions[15]. In contrast, FETO is a minimally invasive intrauterine procedure, none of our patients was admitted to the intensive care unit and only one had a blood transfusion. Chorioamnionitis developed in about 2% of our cases; this occurred after membrane rupture and the pregnancies were treated with antibiotics and delivery thereby avoiding maternal sepsis. In a previous report of 80 multiple pregnancies undergoing endoscopic selective cord coagulation there was one case of chorioamnionitis with maternal sepsis, leading to termination of pregnancy[16].

Successful placement of the balloon at the first procedure was achieved in 97% of cases, with the failures being a consequence of either inability to enter the trachea or tracheal laceration leading to abandonment of the operation. Difficulties in accessing the trachea and insertion of the balloon, reflected in the duration of the procedure, contributed to both PPROM and early delivery before 34 weeks. In contrast, other procedure-related factors such as gestational age at FETO, placental

Table 4 Survival to discharge from hospital according to side of the hernia, observed to expected lung area to head circumference ratio (LHR), gestational age at fetal endoscopic tracheal occlusion (FETO), duration of tracheal occlusion and preterm prelabor rupture of membranes (PPROM) in 172 liveborn fetuses with isolated unilateral diaphragmatic hernia treated with FETO in which there were no problems with balloon removal

	Left-sided hernia		*Right-sided hernia*	
Variable	n	*Survival* (n *(%))*	n	*Survival* (n *(%))*
Total	144	78 (54.2)	28	11 (39.3)
Observed to expected LHR (%)				
≤ 15	15	3 (20.0)	—	—
16–20	53	31 (58.5)	2	0 (0)
21–25	56	30 (53.6)	5	2 (40.0)
26–30	20	14 (70.0)	9	6 (66.7)
> 30	—	—	12	3 (25.0)
Gestational age at FETO (weeks)				
23–25	28	15 (53.6)	4	1 (25.0)
26–29	93	51 (54.8)	19	9 (47.4)
30–33	23	12 (52.2)	5	1 (20.0)
Gestational age at delivery (weeks)				
25–29	10	1 (10)	2	0 (0)
30–31	4	1 (25.0)	6	2 (33.3)
32–33	22	13 (59.1)	2	0 (0)
34–41	108	63 (58.3)	18	9 (50)
Duration of tracheal occlusion (weeks)				
< 1	3	0 (0)	2	0 (0)
1–4	37	17 (45.9)	8	3 (37.5)
> 4	104	61 (58.7)	18	8 (44.4)
PPROM				
PPROM and delivery < 34 weeks	27	10 (37.0)	6	2 (33.3)
No PPROM and delivery < 34 weeks	9	5 (55.6)	4	0 (0)
PPROM and delivery ≥ 34 weeks	39	21 (53.8)	10	6 (60.0)
No PPROM and delivery ≥ 34 weeks	69	42 (60.9)	8	3 (37.5)

site, method of anesthesia and number of FETOs did not have such effects.

Complications associated with FETO relate, first, to the need for complete and persistent tracheal occlusion and, second, to timely removal of the tracheal obstruction before or soon after delivery. In about 8% of cases there was spontaneous deflation and subsequent expulsion of the balloon. In half of such cases the deflation occurred within a few days of FETO and a second insertion was necessary to ensure lung growth. In the other half there was effective tracheal occlusion for several weeks and it was felt unnecessary to insert a new balloon. The currently used balloon is manufactured for vascular occlusion, where such a problem has no direct consequences on its effectiveness. The extent to which this problem can be overcome by a better design of balloon remains to be seen.

A more serious problem relates to removal of the balloon. It was generally aimed to remove the balloon electively, either by fetoscopy or ultrasound-guided puncture, at around 34–36 weeks. However, elective reversal of occlusion was possible in fewer than half of the cases because in the majority of patients removal became an emergency, either because of PPROM or spontaneous preterm labor and delivery. In 5% of cases difficulties in removal of the balloon had a major contribution to neonatal death. The following strategies should be considered to reduce this complication. First, elective removal of the balloon should be undertaken in all cases at 34 weeks. Had this been carried out in our cases the need for an emergency procedure would not have been avoided but it would have been reduced by about 25%. However, removal of the balloon itself may precipitate preterm delivery, which occurred within 7 days of the procedure in about 25% of our cases. Second, obstetricians and neonatologists should be trained to puncture the balloon by needling through the neck of the neonate immediately after vaginal delivery and use this as a first-line strategy rather than aiming to remove the balloon by tracheoscopy. Third, parents should be advised to stay near or in hospitals with expertise in balloon removal for the whole duration of fetal tracheal occlusion. However, such a policy would be unacceptable to most patients and it requires permanent availability of several fetal medicine or neonatal specialists. Fourth, there is a need to develop a balloon with an attached thread that is left outside the fetal mouth. However, pulling on a thread is unlikely to achieve removal of an inflated balloon and could result in trauma to the upper airways and oropharynx. A better alternative is that of pulling on a thread to open the valve and deflate the balloon. We have so far been unsuccessful in finding a company that would produce such a balloon.

A common complication associated with FETO is PPROM, with an overall prevalence of 47% and within 3 weeks of the procedure in about 15% of cases. In patients with rupture of membranes there was a five-fold increase in risk of delivery before 34 weeks. The

only significant predictors of membrane rupture were the duration of FETO, which probably reflects the difficulty of the operation, and method of anesthesia, with general compared with local or regional anesthesia being associated with a fivefold increase in risk. Experimental studies involving the insertion of a collagen plug to seal the fetoscopy-induced membrane defect have reported promising results, but the extent to which such therapy is beneficial in humans treated by FETO remains to be seen[17,18].

In four (1.9%) of our cases treated by FETO there was an unexplained fetal death. This rate is similar to the 1.7% (9/543) reported in the registry of expectantly managed fetuses with isolated CDH as well as other studies[14].

In 97% of cases treated by FETO the babies were liveborn, and about half of these survived following surgery and were discharged from hospital alive. An important determinant of survival was the side of CDH, with substantially better results for left- than right-sided hernias. In the entire pooled experience of isolated left CDH, independent predictors of survival were severity of pulmonary hypoplasia reflected in o/e LHR and gestational age at delivery, increasing from about 15% for delivery before 32 weeks to about 60% at 32 weeks or more. In the case of right CDH no significant predictors of postnatal survival could be identified, presumably because of the small number of cases examined. Survival in the limited number of cases with associated anomalies was as good as for cases with isolated CDH.

The data comparing the survival of fetuses with severe CDH treated with FETO with those managed expectantly suggest that FETO is associated with a substantial improvement in both left- and right-sided CDH. However, this now needs to be tested in a randomized study.

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