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Morbidity in children after fetoscopic endoluminal tracheal occlusion for severe congenital diaphragmatic hernia: Results from a multidisciplinary clinic

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ABSTRACT

Background: Although fetoscopic endoluminal tracheal occlusion (FETO) was recently shown to improve survival in a multicenter, randomized trial of severe congenital diaphragmatic hernia (CDH), morbidity outcomes remain essentially unknown. The purpose of this study was to assess long-term outcomes in children with severe CDH who underwent FETO.

Methods: We conducted a prospective study of severe CDH patients undergoing FETO at an experienced North American center from 2015-2021 (NCT02710968). This group was compared to a cohort of non-FETO CDH patients with severe disease as defined by liver herniation, large defect size, and/or ECMO use. Clinical data were collected through a multidisciplinary CDH clinic. Statistics were performed with t-tests and Chi-squared analyses ($p \leq 0.05$).

Results: There were 18 FETO and 17 non-FETO patients. ECMO utilization was 56% in the FETO cohort. Despite significantly lower median observed/expected lung-to-head ratio (O/E LHR) in the FETO group, [FETO: 23% (IQR:18-25) vs. non-FETO: 36% (IQR: 28-41), $p<0.001$], there were comparable survival rates at discharge (FETO: 78% vs. non-FETO: 59%, $p = 0.23$) and at 5-years (FETO: 67% vs. non-FETO: 59%, $p = 0.53$) between the two cohorts. At a median follow up of 5.8 years, metrics of pulmonary hypertension, pulmonary morbidity, and gastroesophageal reflux disease improved among patients after FETO. However, most FETO patients remained on bronchodilators/inhaled corticosteroids (58%) and were feeding tube dependent (67%).

Conclusions: These North American data show that prenatal tracheal occlusion, in conjunction with a long-term multidisciplinary CDH clinic, is associated with acceptable long-term survival and morbidity in children after FETO.

Level of Evidence: Level III

1. Introduction

Congenital diaphragmatic hernia (CDH) is a major anatomic anomaly characterized by loss of diaphragmatic domain, with resultant herniation of abdominal viscera into the thoracic cavity during fetal life. The phenotypic consequences of CDH on the developing fetus result in varying degrees of pulmonary hypoplasia, pulmonary hypertension, and cardiac dysfunction at birth [1]. At the most severe end of the CDH clinical spectrum, the presence of intrathoracic liver herniation and reduced lung size, as measured by the observed/expected lung-to-head ratio (O/E LHR) <25-30%, have been shown to be associated with poor outcomes, including

Abbreviations: CDH, Congenital diaphragmatic hernia; ECMO, extracorporeal membrane oxygenation; FDA, Food and Drug Administration; FETO, Fetoscopic endoluminal tracheal occlusion; GERD, Gastroesophageal reflux disease; HCO3, Bicarbonate; IDE, Investigational device exemption; O/E LHR, Observed/Expected lung-to-head ratio; PaO2, Partial pressure of oxygen; PaCO2, Partial pressure of carbon dioxide; PH, Pulmonary hypertension; PO, Per os, by mouth; PPROM, Preterm premature rupture of membranes; TOTAL, Tracheal Occlusion to Accelerate Lung Growth.

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mortality rates in excess of 60-80% under expectant fetal management [2–4].

In the most severely affected fetuses, temporary fetoscopic endoluminal tracheal occlusion (FETO) was recently shown in a European-based multicenter randomized trial to provide a significant survival benefit (40%) compared to those who received no fetal intervention (15%) [3]. However, for CDH fetuses with moderate disease, a separate randomized trial failed to demonstrate improved survival after FETO [5]. Despite the important findings of these landmark studies, there remain several important unanswered questions regarding the efficacy and role of FETO in CDH when translated to centers outside of Europe. First, it remains unclear how contemporary neonatal outcomes after FETO might differ compared to outcomes in those with comparable prenatal disease severity but who did not receive FETO [6]. The enhanced integration of prenatal and postnatal care services, greater standardization in postnatal care protocols, and more liberal use of extracorporeal membrane oxygenation (ECMO) at most North American centers might suggest different early postnatal outcomes after FETO [6–9]. Second, the long-term morbidities after FETO, including pulmonary, cardiac, gastrointestinal, and neurocognitive sequelae, have remained essentially unknown among CDH survivors [10–12].

In this study, our objective was to evaluate long-term outcomes in CDH patients who underwent FETO at an experienced North American center. Our group hypothesized that FETO would be associated with high survival rates after discharge as well as improved long-term morbidity when managed within an established multidisciplinary outpatient CDH clinic.

2. Methods

2.1. Study design and inclusion criteria

After obtaining institutional review board approval (IRB00127299), a retrospective review of prospectively collected data was performed on all CDH patients managed at the Johns Hopkins Children's Center (JHCC) between 2015 and 2021. In this integrated health care delivery model, fetuses were managed by the Center for Fetal Therapy, a quaternary care unit within the Department of Gynecology & Obstetrics at the Johns Hopkins Hospital. Postnatal patients were subsequently treated at the JHCC during their initial hospitalization and followed as an outpatient in a multidisciplinary CDH clinic at the adjacent Kennedy Krieger Institute.

2.2. Study cohort

Children with severe CDH were identified prenatally based on O/E LHR with evidence of intrathoracic liver herniation. For the cohort that underwent FETO, inclusion criteria were: (1) severe, left or right sided CDH as determined by O/E LHR <30%, (2) intrathoracic liver herniation, (3) normal karyotype, (4) singleton pregnancy, (5) absence of additional anatomic anomalies, (6) maternal age >18 years, (7) absence of any maternal contraindication to fetoscopic surgery, and (8) maternal compliance to follow the FETO care pathway [6]. Exclusion criteria for FETO included: (1) severe maternal comorbidity, (2) uterine anomaly increasing risk of preterm premature rupture of membranes (PPROM), (3) placenta previa, and/or (4) preterm labor or cervical shortening <15 mm within 24 hours of FETO [6]. Details on fetoscopy and 30-day outcomes for a subgroup of these FETO patients have been previously published as a non-randomized prospective trial (NCT02710968) with U.S. Food and Drug Administration (FDA) investigational device exemption (IDE) [6]. A non-FETO cohort, which was used as a comparison group of severe CDH children within our institution, included prenatal patients that were ineligible for FETO based on O/E LHR measurements. Additional inclusion criteria for the non-FETO cohort were: (1) ECMO utilization and/or (2) Type C/D defect size with intrathoracic liver herniation. Patients with evidence of prenatal cardiac anomalies were excluded.

All CDH patients were managed postnatally under the same CDH treatment algorithm, which emphasized ventilation management strategies minimizing barotrauma, ECMO support when indicated, CDH repair with Goretex patch when clinically stable, and aggressive management of pulmonary hypertension [6]. All patients were followed in our multidisciplinary clinic at 3–12-month intervals by a team consisting of a pediatric surgeon, cardiologist, pulmonologist, physical medicine specialist, and additional developmental providers as needed.

2.3. Study outcomes

Study outcomes included overall mortality, as determined by the most recent outpatient appointment or admission, and metrics of long-term morbidity with a focus on pulmonary status, echocardiographic data on pulmonary hypertension, gastrointestinal issues, and need for additional procedures.

2.4. Data analysis

Statistical analyses were performed with STATA 16.1. A p-value $\leq$0.05 was considered statistically significant. Proportional distribution of categorical variables was evaluated by Chi-Square or Fisher's exact test as appropriate. Continuous variables were assessed with Student's t-tests.

3. Results

3.1. Prenatal and birth characteristics

There were 35 patients with severe CDH, of which 18 underwent FETO and 17 were non-FETO patients. Prenatal O/E LHR are shown for FETO patients pre- and post-intervention in comparison to non-FETO patients at early and later gestational ages (Fig. 1). The median initial O/E LHR for FETO patients was significantly less than non-FETO patients [23% (IQR, 18-25) vs. 36% (IQR, 28-41), respectively; p<0.001]. At later gestational ages, the O/E LHR was comparable between the two cohorts [53% (IQR, 42-61) vs. 49% (IQR, 35-65), respectively; p = 0.33].

Baseline characteristics of the study population are shown in Table 1. Patients in both cohorts had comparable gestational ages and birthweights. There was a trend towards increased cardiac anomalies requiring surgical intervention in the FETO cohort in comparison to the non-FETO patients (17% vs 0%, respectively; p = 0.08). Of those in the FETO group, the diagnoses that required cardiac surgery included Tetralogy of Fallot, ventricular septal defect, and atrial septal defect.

3.2. In-hospital clinical course

Patients in both cohorts had more severe pulmonary hypertension at the time of birth, with 73% of FETO patients and 70% of non-FETO patients having two-thirds systemic to suprasystemic right ventricular pressure at their initial echocardiogram (p = 0.40) (Table 2). This decreased to 25% and 18%, respectively, at the time of discharge (p = 0.66). Given our inclusion criteria for non-FETO patients, there was a lower ECMO rate among FETO patients compared to the non-FETO group (56% vs. 88%, respectively; p = 0.03). There was trend towards less time on ECMO in those FETO patients that required ECMO [FETO: 6 (IQR, 5-13) days vs. non-FETO: 11 (IQR, 9-26) days, p = 0.07]. Of those patients that were repaired,

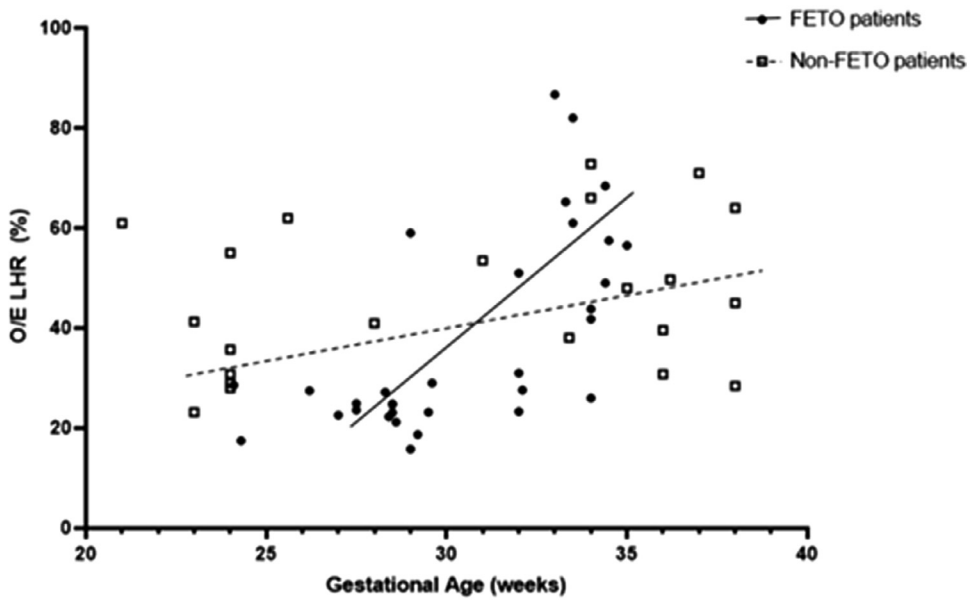

Fig. 1. Observed/expected lung-to-head ratio (O/E LHR) values pre-FETO and post-FETO in comparison to early and late gestation O/E LHR in non-FETO patients.

Table 1
Baseline characteristics of patient population.

	FETO n = 18	Non-FETO n = 17	*p-value*
Gender			0.85
Male	10 (56)	10 (59)	
Female	8 (44)	7 (41)	
Race			0.10
Non-Hispanic White	11 (65)	6 (43)	
Non-Hispanic Black	0 (0)	4 (30)	
Hispanic	2 (12)	1 (7)	
Asian	2 (12)	3 (21)	
Unknown	3 (17)	3 (18)	
Year			0.79
2015	1 (6)	3 (18)	
2016	3 (17)	2 (12)	
2017	4 (22)	4 (24)	
2018	5 (28)	2 (12)	
2019	1 (6)	1 (6)	
2020	3 (17)	2 (12)	
2021	1 (6)	3 (18)	
Early gestational age O/E LHR	23 (18-25)	36 (28-41)	<0.001
Late gestational age O/E LHR	53 (42-61)	49 (35-65)	0.33
Inborn	18 (100)	17 (100)	1.00
Chromosomal anomalies	1 (6)	3 (18)	0.28
Cardiac anomalies*	3 (17)	0 (0)	0.08
Birthweight (kg)	3 (2-3)	3 (2-3)	0.20
Gestational age (weeks)	38 (35-39)	38 (37-39)	0.36
Apgar score at 1-minute	4 (2-6)	2 (1-5)	0.31
Apgar score at 5-minute	7 (5-8)	6 (4-8)	0.23
Delivery type			0.94
Vaginal	13 (70)	11 (65)	
Caesarean	5 (28)	6 (35)	

Values listed as n (%) vs. median (interquartile range (IQR)); O/E LHR = Observed/Expected Lung-to-head ratio.

* Cardiac anomalies were defined as those anomalies requiring surgical intervention.

defect size was similar, with most patients having Type C and D defects (100% vs. 81% in FETO and non-FETO patients, respectively, p = 0.29). There was a trend towards higher patch repair in FETO patients (100% vs. non-FETO: 81%, p = 0.09).

3.3. Mortality and morbidity at discharge

FETO survivors were hospitalized for a significantly longer period [FETO: 112 (IQR, 49-152) days vs. non-FETO: 48 (IQR, 22-80)

Table 2
In-hospital and surgical data of FETO and non-FETO patients.

	FETO n = 18	Non-FETO n = 17	*p-value*
Pulmonary hypertension at birth			0.40
None	1 (6)	0 (0)	
<2/3 systemic	1 (6)	2 (12)	
2/3 - systemic	10 (56)	6 (35)	
Suprasystemic	3 (17)	6 (35)	
PH without quantitative data	0 (0)	1 (6)	
Unknown	3 (17)	2 (12)	
ECMO	10 (56)	15 (88)	0.03
Days on ECMO	6 (5-13)	11 (9-26)	0.07
Parameters prior to ECMO			
pH	7.2 (7.1-7.3)	7.2 (7.0-7.2)	0.25
PaO2 (mmHg)	48 (36-84)	35 (30-41)	0.05
PaCO2 (mmHg)	56 (47-61)	58 (55-82)	0.14
HCO3 (mEq/L)	22 (18-24)	24 (21-26)	0.24
Lactate (mmol/L)	3 (3-7)	2 (1-2)	0.03
Surgical repair	18 (100)	16 (94)	0.13
Side defect			0.18
Left	16 (89)	12 (71)	
Right	2 (11)	5 (30)	
Intrathoracic liver herniation	17 (94)	12 (75)	0.11
Defect size			0.29
A	0 (0)	2 (13)	
B	0 (0)	1 (6)	
C	12 (67)	8 (50)	
D	6 (33)	5 (31)	
Patch repair	18 (100)	13 (81)	0.09
Days intubated	49 (23-55)	29 (9-26)	0.23
Number of PH medications during admission	4 (3-5)	4 (3-6)	0.34
Pulmonary hypertension prior to discharge			0.66
None	4 (25)	4 (24)	
<2/3 systemic	8 (50)	3 (18)	
2/3 - systemic	3 (19)	2 (12)	
Suprasystemic	1 (6)	1 (6)	
PH without quantitative data	0 (0)	1 (6)	
Unknown	2 (11)	6 (35)	

Values listed as n (%) vs. median (interquartile range (IQR)); PH = pulmonary hypertension; PaO2 = partial pressure of oxygen; PaCO2 = partial pressure of carbon dioxide; HCO3 = bicarbonate.

Table 3
Morbidity and mortality at discharge for FETO patients and non-FETO patients.

	FETO n = 18	Non-FETO n = 17	*p-value*
In-hospital survival	14 (78)	10 (59)	0.23
Length of stay (days)	112 (49-152)	48 (22-80)	0.03
Weight at discharge (kg)	5 (4-6)	5 (4-6)	0.92
Discharge location			0.05
Home	9 (64)	4 (40)	
Transfer to another hospital	1 (7)	5 (50)	
Transfer to rehabilitation facility	4 (29)	1 (10)	
Additional operations			
Gastrostomy tube	5 (28)	1 (6)	0.10
Fundoplication	5 (28)	5 (31)	0.81
Small bowel obstruction	3 (17)	1 (6)	0.60
Sildenafil	10 (71)	9 (90)	0.27
Bosentan	4 (29)	3 (30)	0.94
Treprostinil	3 (21)	2 (20)	0.93
Bronchodilator/inhaled corticosteroids	11 (79)	6 (60)	0.32
Supplemental oxygen	5 (36)	2 (20)	0.69
Tracheostomy at discharge	2 (14)	1 (10)	0.76
Diuretic	11 (79)	8 (80)	0.93
Number of gastrointestinal medications at discharge	2 (1-2)	1 (0-2)	0.30
Antacid	13 (93)	6 (60)	0.05
Erythromycin	9 (64)	3 (30)	0.10
Feeding at discharge*			0.04
PO	1 (7)	1 (10)	
Nasogastric/nasoduodenal tube	2 (14)	6 (60)	
Gastrostomy/jejunostomy	11 (79)	3 (30)	
Anti-epileptic medication	2 (14)	1 (10)	0.75

Values listed as n (%) vs. median (interquartile range (IQR)); PO = per os, by mouth; antacids as defined by proton pump inhibitors or H2 antagonists.
* Feeding defined as ≥50% nutrition obtained through listed access.

Table 4
Long-term morbidity and mortality data for FETO patients and non-FETO patients.

	FETO n = 12	Non-FETO n = 9+	*p-value*
Overall survival*	12 (67)	10 (59)	0.53
Overall recurrence*	5 (28)	2 (12)	0.27
Follow-up (years)	6 (1-7)	4 (1-7)	0.88
Sildenafil	5 (42)	5 (56)	0.53
Bosentan	2 (17)	0 (0)	0.20
Treprostinil	0 (0)	0 (0)	1.00
Bronchodilator/inhaled corticosteroids	7 (58)	6 (67)	0.70
Supplemental oxygen	1 (8)	0 (0)	0.40
Tracheostomy	1 (8)	1 (11)	0.72
Diuretic	3 (25)	3 (33)	0.68
Number gastrointestinal medications at most-recent follow-up	0 (0-1)	0.5 (0-1)	0.57
Antacid	5 (42)	2 (22)	0.35
Erythromycin	4 (33)	1 (11)	0.24
Feeding at most-recent follow-up++			0.95
PO	3 (25)	2 (25)	
Nasogastric/nasoduodenal tube	1 (8)	1 (13)	
Gastrostomy/jejunostomy	8 (67)	5 (63)	
Anti-epileptic medication	0 (0)	0 (0)	1.00

Values listed as n (%) vs. median (interquartile range (IQR)); PO = per os, by mouth.
+ 1 of 10 surviving non-FETO patients was lost to follow-up.
* Data representative of overall survival and recurrence in the entire cohort (n = 18 in FETO and n = 17 in non-FETO cohort).
++ Feeding defined as ≥50% nutrition obtained through listed access.

days, p = 0.03]. There were similar survival rates at the time of discharge in FETO patients compared to non-FETO patients (78% vs. 59%, p = 0.23). There were increased rates of discharge to home (64% vs. 40%, p = 0.05) after FETO when compared to their non-FETO counterparts (Table 3). Most patients in both cohorts were discharged with sildenafil (FETO: 71% vs. non-FETO: 90%, p = 0.27) and bronchodilators/inhaled corticosteroids (FETO: 79% vs. non-FETO: 60%, p = 0.32). A small cohort of patients were discharged with a tracheostomy (FETO: 14% vs. non-FETO: 10%, p = 0.76) or with supplemental oxygen (FETO: 36% vs. non-FETO: 20%, p = 0.69). Patients in both cohorts required antacids at discharge, with increased usage in FETO patients (FETO: 93% vs. non-FETO: 60%, p = 0.05). There was also a significantly increased number of FETO patients who had a gastrostomy/jejunostomy prior to discharge (FETO: 79% vs. non-FETO: 30%, p = 0.04).

3.4. Mortality and morbidity at long-term follow-up

FETO patients were followed for a median of 5.8 years and non-FETO patients were followed for a median of 4.4 years (p = 0.88) (Table 4). At that point, the survival rates in both cohorts remained relatively stable (FETO: 67% vs. non-FETO: 59%, p = 0.53). There were two FETO patients that died after discharge secondary to chronic lung disease. At the most recent follow-up, sildenafil use decreased by 29% in FETO patients and 34% in non-FETO patients (p = 0.53). Patients in the FETO cohort decreased their bronchodilator/inhaled corticosteroid use by 21%, whereas patients in the non-FETO cohort increased their use by 7% (p = 0.70). The number of patients requiring tracheostomy or supplemental oxygen decreased in both cohorts. Antacid use decreased in both cohorts (p = 0.35). There was a 12% decrease in ≥50% gastrostomy/jejunostomy feeds among FETO patients, but a 33% increase in non-FETO patients. This led to nearly identical gastrostomy/jejunostomy rates at the most recent follow-up (FETO: 67% vs. non-FETO: 63%, p = 0.95).

4. Discussion

Previous feasibility studies and the recent, multicenter randomized trial (Tracheal Occlusion to Accelerate Lung Growth, TOTAL) have shown that FETO improves neonatal survival in a severe group of CDH patients when compared to expectant prenatal management [3,4,6,7]. However, there have been no published cohort studies evaluating mortality and quality of life beyond one year after FETO [12]. In this study, we provide data from an experienced North American center showing that FETO was associated with a 67% survival rate after a median follow-up of more than five years. Our study also demonstrates improved disease morbidity over time based on serial evaluations within a multidisciplinary CDH clinic composed of pediatric surgeons, pulmonologists, cardiologists, and other specialty providers. Moreover, our mortality data and longer-term morbidity outcomes after FETO compared quite favorably to non-FETO cohorts with severe disease reported elsewhere [13,14] and to our own non-FETO CDH cohort that had prenatal evidence of more moderate disease.

To our knowledge, the data presented in this study is the first to demonstrate a persistent survival benefit after discharge in children undergoing FETO for severe CDH. There was a 78% survival rate to discharge after a median length of stay of 112 days. The long-term survival rate of 67% at our center was appreciably higher than the 40% 6-month survival rate reported in the severe TOTAL trial and the 33-53% survival rates reported in prior single institution studies on severe CDH [3,4,15,16]. One potential explanation for our increased survival after FETO may have been inadvertent selection of FETO patients with less severe disease. However, since our patient selection for FETO was dictated by established IDE guidelines, there is little evidence that we selected for a healthier FETO cohort. Our FETO population had a median O/E LHR of 23% with a 94% rate of intrathoracic liver herniation, whereas the O/E LHR was 21% with a 90% liver herniation rate in the severe TOTAL trial [3]. We speculate that our increased long-term survival after

FETO may be related to avoidance of preterm deliveries, enhanced integration of prenatal and postnatal care, greater standardization and multidisciplinary input in postnatal critical care, and/or more liberal use of ECMO [9]. The integration of prenatal/postnatal care and acute postnatal management of infants within our CDH program have been previously described [6]. Our ECMO survival rates after FETO were comparable to the non-FETO cohorts studied in prior reports [17]. Of the 56% of neonates requiring ECMO, the median ECMO run was only six days, and 60% survived to discharge. In those who required ECMO, prior fetal intervention did not appear to independently worsen outcomes.

Despite high disease severity within our FETO cohort, various morbidity metrics, focusing on pulmonary hypertension (PH), oxygen status, gastroesophageal reflux disease (GERD), enteral feeding status, and seizures, uniformly showed gradual improvement over time. PH significantly improved over the course of admission, with most patients having two-thirds systemic - systemic right ventricular pressure at birth to less than two-thirds systemic pressure at discharge. After discharge, the use of two different PH agents, sildenafil and bosentan, significantly decreased in FETO patients, with all patients being weaned off treprostinil at follow up. Prior reports in non-FETO CDH children have shown that an O/E LHR $\leq$45% directly correlated with severe initial PH that nearly resolved over the course of five years [18]. Despite having a significantly lower initial O/E LHR among our FETO patients, our data followed the same trends in PH resolution as the non-FETO CDH patients in our study and those reported in prior literature [18]. The use of bronchodilators/inhaled corticosteroids and supplemental oxygen decreased significantly over the follow-up period as well. Fifty-eight percent of FETO survivors remained on bronchodilators/inhaled corticosteroids, and 8% still required oxygen at the most recent appointment. This is consistent with rates of 59% and 6%, respectively, observed in prior reports at 1-year [12]. Taken together, these findings suggest that most FETO survivors are not long-term "pulmonary cripples," but there remains a continued need for pulmonary pharmacotherapies and supplemental oxygen in a small subset of these patients.

As reported by previous investigators in fetal CDH [11,12,19], we found that FETO with severe CDH was also associated with substantial levels of severe GERD. Over a quarter of FETO children required fundoplication after their CDH repair, and nearly half were managed with antacids at the most recent follow-up. The 42% long-term utilization rate of antacids is comparable to reports of long-term GERD rates of 42-47% in both FETO and non-FETO patients [11,12]. While GERD often improved over time, there was a persistent need for long-term enteral feeding access, with gastrostomy and jejunostomy tube rates remaining >60% at the most recent follow-up. This is notably higher than previous reports of 15-18% at 1-year follow up in FETO patients [12]. This may be secondary to our institutional practice patterns to facilitate safe outpatient enteral access as the non-FETO comparison group had >60% rates of gastrostomy/jejunostomy tubes as well. Overall, the gastrointestinal morbidity of CDH was evident at long-term follow up despite improvements in cardiopulmonary status. Quality of life studies relating to CDH sequelae have been contradictory [20], and specific studies on the gastrointestinal sequelae after FETO warrant further evaluation.

The results of this study must be interpreted in the context of its limitations. First, it is a small, retrospective, single institution cohort study and therefore is vulnerable to the bias and inaccuracies of previously collected data and lacks statistical power to perform subgroup analyses. We would encourage multicenter, prospective studies with other North American centers to further validate our results. Second, our institutional comparison group of non-FETO patients cannot be considered as a control group since it was generated in a nonrandomized, post hoc fashion based on both established prenatal and postnatal predictors of disease severity, including need for ECMO and large defect size with intrathoracic liver herniation [21–24]. Although we believe this comparison group is more valuable than using a cohort of historical controls under expectant fetal management, the ideal comparison group would have been composed solely of fetuses who were eligible for FETO but declined the procedure through an informed consent process. Unfortunately, this was not possible since nearly all mothers referred to our institution with an eligible fetus desired FETO. Third, longer follow up on the FETO cohort will be necessary to provide essential information on neurocognitive outcomes, an important morbidity metric not assessed in our study [25]. Finally, our results may not be generalizable to other pediatric referral centers elsewhere because of differences in fetal surgical expertise, perinatal care integration, post-discharge multidisciplinary care, and other factors [26].

5. Conclusions

This study addresses the impact of FETO on long-term morbidity and mortality in severe CDH patients. We were able to follow these patients through our multidisciplinary clinic to trend their overall survival, medication utilization, and enteral feeding status as a surrogate for sequalae burden. The use of fetoscopic intervention, in conjunction with collaborative postnatal care, was associated with improved morbidity compared to their status at discharge at a median follow up of five years. These data should be invaluable for prenatal counseling of families interested in long-term FETO outcomes. Moreover, it offers further evidence that a dedicated FETO program in North America can produce long-term results with acceptable outcomes in appropriately selected patients.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jpedsurg.2022.09.042.

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