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Postnatal care setting and survival after fetoscopic tracheal occlusion for severe congenital diaphragmatic hernia: A systematic review and meta-analysis

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ABSTRACT

Background: Fetoscopic endoluminal tracheal occlusion (FETO) was recently shown to improve postnatal survival in a multicenter, randomized controlled trial of infants with severe congenital diaphragmatic hernia (CDH). However, the external validity of this study remains unclear given a lack of standardization in postnatal management approaches. The purpose of this study was to evaluate the impact of an integrated prenatal and postnatal care setting on survival outcomes in severe CDH after FETO.

Study design: A systematic review, meta-analysis, and individual participant analysis of FETO outcomes in severe CDH were conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines. The primary outcome was survival to discharge. Subgroup analyses of patients managed in integrated versus nonintegrated settings were performed to identify predictors of outcome.

Results: The review generated five studies (n = 192) for the meta-analysis of FETO versus expectant prenatal management. These data revealed a significant survival benefit after FETO that was restricted to an integrated setting (OR 2.97, 95% Confidence Interval 1.69–4.26). There were nine studies (n = 150) for the individual participant analysis, which showed that FETO managed in an integrated setting had significantly increased survival rates when compared to FETO treated in a nonintegrated setting (70.7% vs. 45.7%, p = 0.003). Multi-level logistic regression identified increased availability of extracorporeal membrane oxygenation (ECMO) as the strongest determinant of postnatal survival (OR=18.8, p = 0.049).

Conclusion: This systematic review shows that institutional integration of prenatal and postnatal care is associated with the highest overall survival in children with severe CDH. These data highlight the importance of a standardized, multidisciplinary approach, including access to ECMO, as a critical postnatal component in optimizing FETO outcomes in CDH.

Introduction

Congenital diaphragmatic hernia (CDH) is a major developmental anomaly characterized by partial or complete absence of the hemidiaphragm, allowing for herniation of abdominal viscera into the thoracic cavity during fetal life. Children born with CDH have respiratory distress at birth secondary to varying degrees of pulmonary hypoplasia and pulmonary hypertension, and those at the most severe end of the clinical spectrum are at the highest risk for mortality and long term morbidity, including pulmonary, gastrointestinal, and neurocognitive sequelae [1]. The risk for neonatal respiratory failure and mortality can be estimated by prenatal imaging based on lung size and intrathoracic liver herniation [2,3]. In severe fetal CDH, as defined by an observed/expected lung-to-head ratio (O/E LHR) <25–30%, dismal survival rates as low as 5–15% in the absence of fetal intervention have been reported [4,5].

Temporary fetoscopic endoluminal tracheal occlusion (FETO) is a prenatal intervention for patients with CDH that increases intrapulmonary airway pressure and induces lung stretch to stimulate fetal lung growth prior to delivery [6]. FETO has been shown to

Abbreviations: FETO, Fetoscopic endoluminal tracheal occlusion; CDH, congenital diaphragmatic hernia; ECMO, extracorporeal membrane oxygenation; O/E LHR, observed/expected lung-to-head ratio; PPROM, preterm prelabor rupture of membranes; LHR, lung-to-head ratio.

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significantly improve survival in severe CDH to more than 40%, based on feasibility studies as well as a recently published international, multicenter randomized trial [4,5]. To date, all published FETO studies have been carried out in a standardized prenatal setting with a primary focus on management aspects of tracheal occlusion. However, neither the transition to neonatal care nor the postnatal management setting has been standardized after FETO to the same degree [4–16]. This aspect may not be trivial since individual centers may differ significantly in postnatal management approaches, and it is well recognized that outcomes in CDH may be influenced by center experience and case volume [17]. Whereas many FETO centers offer functional integration of prenatal and postnatal CDH management within the same health care system, some FETO centers subsequently refer fetuses for delivery at neonatal CDH programs that are not formally integrated with prenatal care and may not employ extracorporeal membrane oxygenation (ECMO) and other adjunctive therapies as a means of support [5–16]. Accordingly, there remains little information on the extent to which postnatal care integration may independently impact survival.

Our objective was to perform a systematic review, meta-analysis, and investigation of individual participant data to determine the potential impact of the prenatal and postnatal care integration on infant survival after FETO. We distinguished between an integrated care setting where prenatal and postnatal CDH care occurred at the same program from a nonintegrated setting where this was not the case. Our group hypothesized that children with severe CDH managed by integrated care programs may have increased access to ECMO and other advanced therapies and are therefore more likely to survive compared to those managed at nonintegrated programs.

Methods

We performed a systematic review and meta-analysis according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) and MOOSE (Meta-analyses of Observational Studies in Epidemiology) guidelines [18,19] The protocol for this systematic review is submitted for registration on PROSPERO (ID 301,273) [20].

Search strategy and selection criteria

Research studies that provided information on patient outcomes after undergoing FETO for CDH were identified. Using the MeSH search terms 'FETO' or 'fetoscopic endoluminal tracheal occlusion,' we searched PubMed, MEDLINE, the Cochrane Central Register of Controlled Trials, and ClinicalTrials.gov. The search was restricted to human subject studies in the English language published between January 2004-December 2021. The last search was performed on December 7, 2021.

Articles were considered for inclusion if in hospital mortality was provided for patients with isolated, left- or right-sided CDH. The meta-analysis provided a comparison of patients who underwent FETO versus expectant prenatal care. The participant analysis provided a comparison of individual patients who underwent FETO in an integrated versus nonintegrated care setting (Supplemental Fig. 1). Patients in both analyses were confirmed to have severe CDH, as defined by an ultrasound measured O/E LHR of 20–30% and/or an LHR $<$1.0. Missing data were requested from corresponding authors if not reported in the publication. Studies that performed FETO on patients with O/E LHR$<$20% were not considered to eliminate compassionate FETO patients with almost certain lethal disease. Studies were also excluded if the FETO technique was experimental [21] or if the postnatal care details were not specified. We included randomized and non randomized controlled studies, as well as observational studies in the meta-analysis and individual analysis. Ongoing trials, case reports of initial attempts at FETO, and studies with duplicated data were excluded.

Data collection and study outcomes

Two independent reviewers (SRS and AAB) reviewed all titles and abstracts for the systematic review and meta-analysis, as well as extracted data, at two separate time points. Disputes regarding included studies were resolved by a third reviewer (SMK). The primary outcome measure was in hospital survival after FETO in comparison to those who received expectant prenatal care.

An individual analysis was performed on studies that included individual data points in addition to aggregated data. The primary outcome was in hospital mortality rate (range, 0–450 days) following FETO, stratified by the care setting. Details on the FETO procedure, change in O/E LHR after tracheal occlusion, access to ECMO at the institutional level, and ECMO use were extracted. The care setting was defined as "integrated" for cases where FETO and postnatal management occurred at a single institution (reviewers JLM and AAB). All integrated centers were confirmed to provide neonatal CDH care with preestablished ventilation guidelines, hemodynamic parameters, imaging criteria, and advanced therapeutic adjuncts [5–10]. In contrast, a "nonintegrated" care setting was determined in cases where FETO and postnatal care did not occur within the same institution or health care system [11–16].

Data analysis

Statistical analyses were performed with STATA 16.1. A p-value $\leq$0.05 was considered statistically significant. Treatment effect sizes were calculated as a log odds ratio with 95% confidence intervals (CI). A forest plot was generated using a random-effects model to account for the small sample size of the FETO studies. Heterogeneity was analyzed with a chi square test and I^2 test. Publication bias was assessed with the creation of a funnel plot and a risk of bias assessment tool [22]. Continuous variables were evaluated for normality using the Shapiro-Wilks test and compared using parametric or non parametric testing as appropriate. Proportional distribution of categorical variables was evaluated by chi square. Survival trends were compared using a Mann-Whitney U test and a Kaplan-Meier curve. Multilevel logistic regression was utilized to identify variables between care settings that accounted for significant differences in survival.

Results

Study strategy and selection

Overall, the systematic review identified 8002 studies reporting on in hospital survival in CDH. Of these, 5005 were excluded based on publication date, language, and experimental setup (Fig. 1). Among the remaining 2947 titles and abstracts and 67 full text articles, 11 studies were eligible for inclusion in this report. Five articles reporting on FETO and an expectant management control group were included in the meta-analysis, while nine studies provided individual FETO participant data for analysis. Three studies with 70 participants enrolled for FETO were utilized in both the meta- and individual participant analysis. Following completion of the data extraction, 192 CDH patients were included in the meta-analysis with 109 managed in an integrated program and 83 managed in a nonintegrated care setting. The individual participant analysis consisted of 150 FETO patients, with 58 pa-

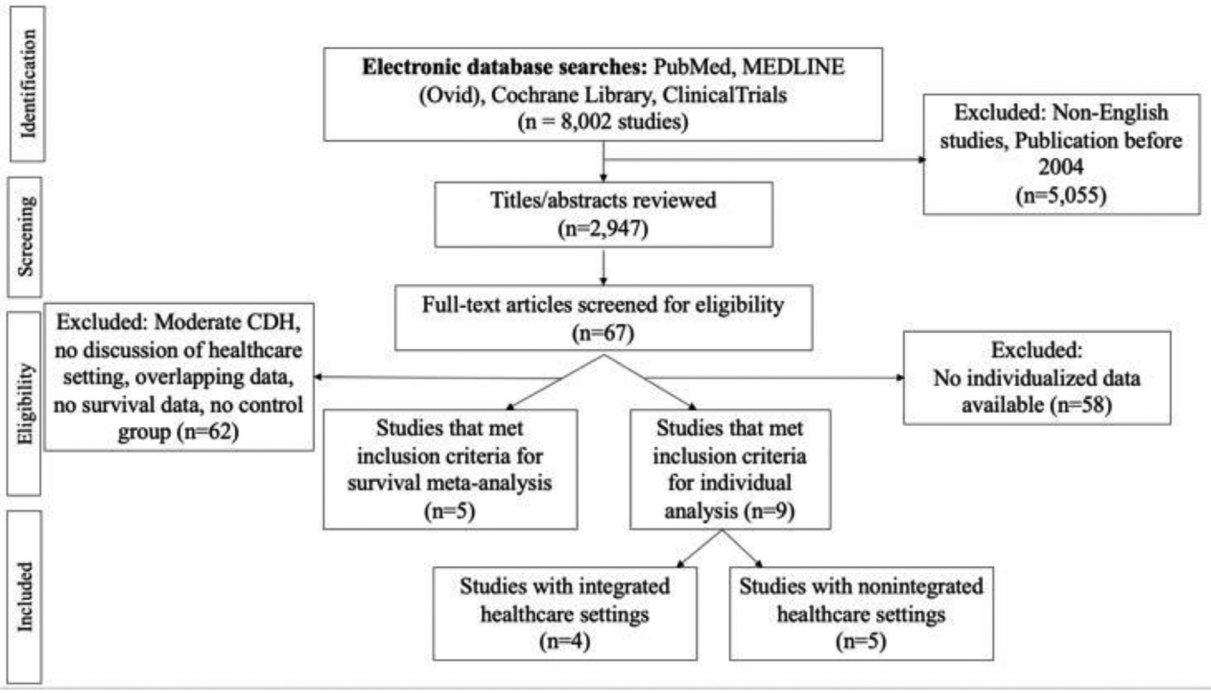

Fig. 1. Flowchart of studies for systematic review, meta-analysis, and individual analysis.

tients in the integrated cohort and 92 patients in the nonintegrated cohort.

Study characteristics and risk of bias

Six studies (54.5%) described a dedicated perinatal care transition plan at the same institution and were considered to represent an integrated care setting. The countries of origin for these studies were Brazil ($n = 2$), Spain ($n = 1$), and the United States ($n = 2$). In the remaining five studies, there was more than one delivery institution as pregnant mothers were not required to deliver at the FETO center and were thus described as nonintegrated settings. The countries of origin for these studies included Mexico, Spain, Japan, Germany, Belgium, and the United Kingdom. All participants were singletons without chromosomal or additional anatomic abnormalities. Patients had varying degrees of intrathoracic liver or stomach herniation, as determined by their individual study protocols (Table 1).

In the meta-analysis, four studies were prospective controlled studies, and one study was a randomized controlled trial. A funnel plot showed small sample size and similar standard of errors but did not demonstrate asymmetry. A Risk of Bias in Non Randomized Studies of Interventions (ROBINS-I) tool was used to determine the risk of bias to be moderate (Supplemental Fig. 2) [22]. The studies were homogenous with an I^2=0%.

Impact of FETO on postnatal survival rates

The meta-analysis of pooled data based on 192 participants revealed a significant increased in hospital survival after FETO when compared to patients with similar disease severity who underwent expectant fetal management (50.4% vs. 4.7%; Odds ratio=2.86; 95% CI: 1.82 to 3.89, $p < 0.001$)(Fig. 2). A subgroup analysis showed a significant survival benefit for FETO patients managed in an integrated care setting (OR=2.97; 95% CI: 1.69 to 4.26), but not for those managed in a nonintegrated care setting (OR=2.64; 95% CI: 0.87 to 4.4).

Prenatal characteristics of FETO participants

Clinical characteristics of the 150 patients receiving undergoing FETO were stratified based on institutional care setting (Table 2). Those managed in an integrated postnatal care setting had a significantly higher pre FETO O/E LHR (25.6 ± 5.8 vs. 23.3 ± 7.3; $p = 0.04$) and earlier gestational age at FETO (27.8 ± 1.1 vs. 28.5 ± 1.9 weeks, $p = 0.01$). There was a subsequent trend towards a longer period of tracheal occlusion among integrated programs (38.4 ± 11.0 vs. 33.9 ± 15.4 days, $p = 0.05$) but similar growth of fetal lung post occlusion between fetuses treated in integrated and nonintegrated programs (post FETO O/E LHR of 51.9 ± 25.3 vs. 49.1 ± 23.2, $p = 0.57$). The management of balloon removal was comparable between care settings.

Preterm prelabor rupture of membranes (PPROM) at less than 37 weeks developed with similar frequency in both cohorts but occurred at a later gestational age in those managed in an integrated care setting (34.1 ± 2.2 vs. 32.1 ± 2.9 weeks; $p = 0.004$). Similarly, gestational age at delivery (36.0 ± 2.2 vs. 34.9 ± 2.8 weeks, $p < 0.001$) and infant birthweights (2.67 ± 0.6 vs. 2.42 ± 0.5 kg, $p = 0.04$) were significantly higher for participants in integrated care settings (Table 2).

Postnatal outcomes after FETO

Table 2 shows the postnatal characteristics of 150 FETO patients managed within integrated and nonintegrated care settings. At delivery, infants born in an integrated program had lower 1 min Apgar scores (4.0 ± 2.0 vs. 6.0 ± 2.3, respectively; p=<0.01) but nearly identical 5 min Apgar scores (7.0 ± 1.6 vs. 7.2 ± 2.2, respectively; $p = 0.73$) when compared to those in a nonintegrated care program. Patients in integrated programs had ECMO available at their institution at a significantly higher rate than those in nonintegrated programs [$n = 47$ (74.0%) vs. $n = 8$ (7.0%), $p < 0.001$]. Accordingly, as access to ECMO was higher in integrated settings, ECMO utilization was also significantly higher after FETO in the integrated care setting compared to the nonintegrated setting [$n = 17$ (39.5%) vs. $n = 1$ (12.5%), respectively; $p < 0.001$].

Table 1
Systematic review of studies evaluating survival after FETO for severe congenital diaphragmatic hernia.

First author	Study years	Country	Type of study	Total FETO cases	CDH Inclusion Criteria	ECMO access	Healthcare setting
Belfort	2012–2017	USA	Prospective, non-randomized	24	Isolated left or right sided; O/E LHR <30%	Yes	Integrated
Baschat	2018–2021	USA	Prospective non-randomized	19	Isolated left or right sided; O/E LHR <30%	Yes	Integrated
Cruz-Martinez	2012- 2019	Mexico	Prospective non-randomized	25	Isolated left sided; O/E LHR <26%; ILH*	No	Non-integrated
Deprest	2002- 2003	UK, Belgium, Spain	Multicenter prospective non-randomized	21	Isolated left or right sided; LHR<1; ILH	No	Non-integrated
Enriquez	2003–2010	Spain	Retrospective case control	7	Isolated left or right sided; LHR <1	Yes	Integrated
Kohl	–	Germany	Prospective non-randomized	8	Isolated left or right sided; LHR ≤ 1 in right and ≤ 0.9 in left hernias; ILH	Yes	Non-integrated
Kosinski	2014–2016	Poland	Prospective non-randomized	27	Isolated left sided; O/E LHR <25%; LHR <1	No	Non-integrated
Peralta	2007–2009	Brazil	Prospective non-randomized	8	Isolated left sided; LHR<1; ILH	No	Integrated
Ruano	2006–2008	Brazil	Prospective non-randomized	17	Isolated; LHR<*l*; ILH	No	Integrated
Ruano	2008–2010	Brazil	Prospective randomized	20	Isolated left or right sided; O/E LHR <25%; ILH	No	Integrated
Wada	2014–2016	Japan	Prospective non-randomized	11	Isolated left sided; ILH; >50% stomach herniation	No	Non-integrated

ILH; intrathoracic liver herniation; LHR; lung-to-head ratio; O/E LHR; observed/expected lung-to-head ratio.

The in hospital survival rate following FETO was significantly higher for infants managed in an integrated care setting (70.7% vs. 45.7%, $p = 0.003$, Table 2). Neonates died later in integrated care programs (median day of death: 18 vs. 2 days, respectively; $p < 0.001$). The majority of deaths in those managed in the integrated cohort occurred after the first two weeks of life (late death: 70.6% vs. 14.0%, $p < 0.001$). The Kaplan-Meier curve revealed that differences in the mortality during within the first three weeks of life largely accounted for the survival differences at hospital discharge (Fig. 3).

Postnatal predictors of survival after FETO

Multilevel regression was used to assess the survival difference between CDH infants managed within integrated and nonintegrated care settings. This analysis identified access to ECMO as a significant predictor of survival (OR 18.8, $p = 0.049$). Gestational age at PPROM (OR=2.5, $p = 0.045$) and higher 5 min Apgar scores (OR=2.6, $p = 0.049$) were also independent and significant cofactors for increased survival. Although there were significant differences in pre FETO O/E LHR, occlusion time, gestational age at delivery, and birthweight on univariate analysis, these variables did not maintain significance in multivariate analysis (Table 3). Among participants managed in an integrated care setting, 9 of 17 (52.9%) infants on ECMO and 25 of 31 (80.7%) infants not requiring ECMO survived to discharge. In contrast, only one infant receiving ECMO survived, and 41 of 90 (45.6%) infants managed without ECMO were alive in nonintegrated programs.

Discussion

FETO in severe CDH is unique when compared to many other prenatal pediatric surgical interventions because achieving optimal survival relies heavily on the success of postnatal management, including aggressive neonatal resuscitation as well as operative repair of the diaphragm defect. In this systematic review with analysis of individual participant data, we evaluated whether the perinatal care setting used to transition the FETO patient to definitive postnatal care might impact survival. Our study showed that an integrated care setting, where the transition from fetal to neonatal therapy is offered at the same institution, is associated with significantly higher in hospital survival rates when compared to those of infants managed in care settings where these resources are not integrated in the same manner.

These data suggest the importance of the postnatal healthcare setting where the fetal surgical therapy is intended to be used. Although patients managed in integrated programs did have slightly higher pre FETO O/E LHRs and later gestational ages at delivery, our multivariable analysis revealed that institutional access to ECMO was the most important factor associated with increased survival after FETO. Accordingly, infants managed in an integrated care setting had increased access to ECMO and were more likely to survive the first weeks of life. These observations suggest that FETO in combination with a standardized and aggressive postnatal care management strategy may offer the greatest opportunity for improved survival in fetuses diagnosed with severe CDH.

Thus far, most of the published work to date on severe CDH management have almost exclusively focused on the effects of specific prenatal or postnatal interventions [22–25]. For example, the recently published, landmark study from Tracheal Occlusion To Accelerate Lung Growth (TOTAL) trial demonstrated survival rates of nearly 40% in severe CDH following standardized prenatal assessment and management with FETO compared to the expectant fetal management rates of 5–15% [4,5]. However, there have been concerns about the external validity of this European-based trial based on a number of factors, including the very low rate of ECMO utilization (5%) when compared to the experience at most large North American centers. While some of the lower ECMO utilization rates may be attributable to ineligibility following preterm birth after FETO as ECMO cannulation for premature neonates is typically offered for those who are more than 32–34 weeks gestation. Thus, the majority of infants born in nonintegrated centers would be eligible for ECMO cannulation, with a mean gestational age at birth of 34.9 weeks (IQR, 33.6–37 weeks) and a mean birthweight of 2.4 kg

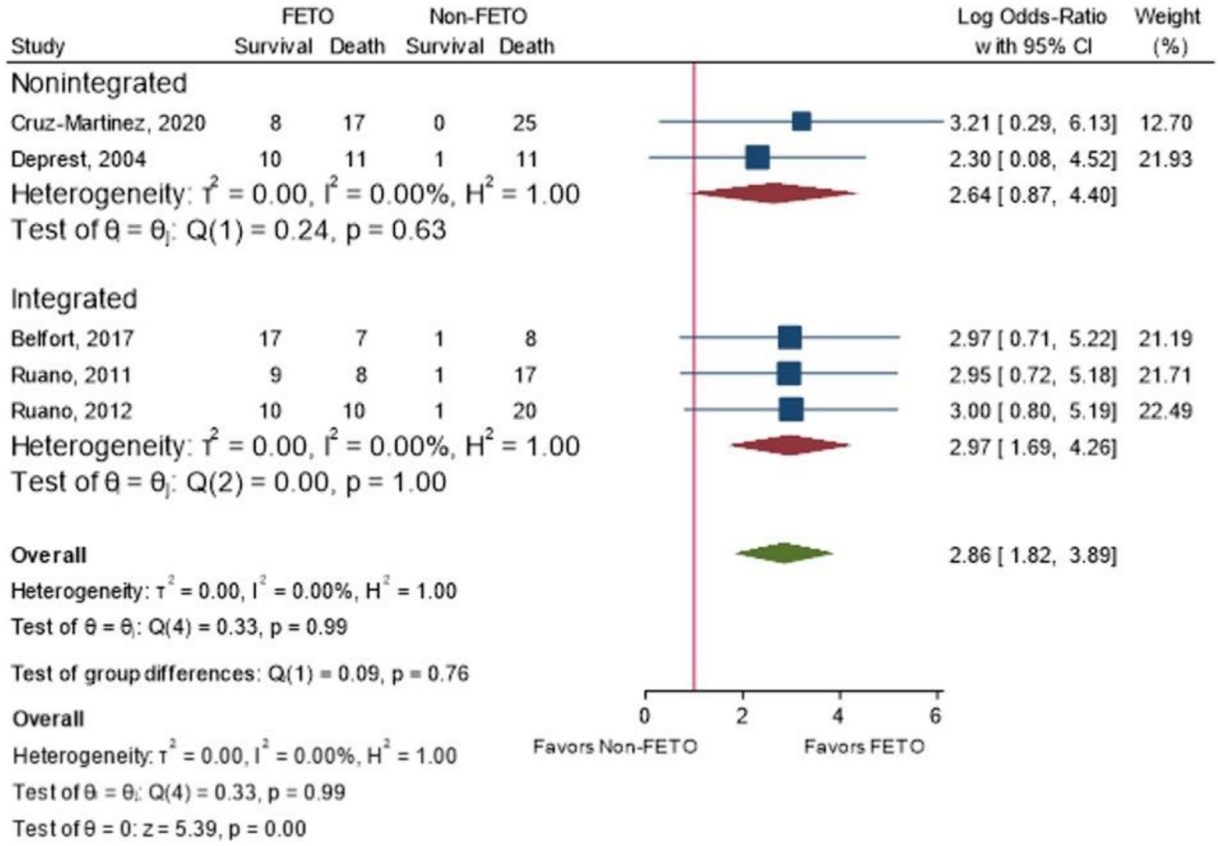

Fig. 2. Forest plot of survival in FETO and non-FETO patients in integrated and non-integrated healthcare settings.

Table 2
Prenatal and postnatal characteristics of FETO patients in integrated and nonintegrated care settings.

	Integrated programs $n = 58$	Non-integrated programs$n = 92$	*p-value*
Prenatal			
Pre-FETO O/E LHR	25.6 +/- 5.8	23.3 +/- 7.3	0.04
Balloon placement GA (weeks)	27.8 +/- 1.1	28.5 +/- 1.9	0.01
FETO placement time (minutes)	20.8 +/- 23.6	16.8 +/- 12.6	0.22
Post-FETO O/E LHR	51.9 +/- 25.3	49.1 +/- 23.2	0.57
Difference in pre- and post-FETO O/E LHR	25.8 +/- 15.9	26.3 +/- 19.4	0.89
Balloon removal GA (weeks)	33.5 +/- 1.3	33.4 +/- 2.0	0.77
Occlusion days (days)	38.4 +/- 11.0	33.9 +/- 15.4	0.05
Balloon removal type			0.30
Fetoscopy	36 (62.1)	53 (58.2)	
EXIT	5 (8.6)	11 (12.1)	
Needle	17 (29.3)	22 (24.2)	
Postnatal	0 (0.0)	5 (5.5)	
Cesarean delivery*	13 (39.4)	32 (88.9)	<0.0001
PPROM rate (< 37 weeks)	26 (44.8)	32 (38.1)	0.42
PPROM GA (weeks)	34.1 +/- 2.2	32.1 +/- 2.9	0.004
Delivery GA (weeks)	36.0 +/- 2.2	34.9 +/- 2.8	0.009
Gender*			0.67
Male	20 (60.6)	20 (55.6)	
Female	13 (39.4)	16 (44.4)	
Postnatal			
Birth weight (grams)	2674 +/- 555.1	2420 +/- 474.6	0.04
Apgar score at 1 min	4.0 +/- 2.0	6.0 +/- 2.3	0.0009
Apgar score at 5 min	7.0 +/- 1.6	7.2 +/- 2.2	0.73
Hernia side			
Left	53 (91.4)	83 (90.2)	0.81
Right	5 (8.6)	9 (9.8)	
ECMO	17 (35.4)	1 (1.1)	<0.0001
In-hospital survival	41 (70.7)	42 (45.7)	0.003
Late mortality+	12 (70.6)	7 (14.0)	<0.001

Data are mean±SD or n (%).

EXIT, ex utero intrapartum treatment; FETO, fetoscopic endoluminal tracheal occlusion; GA, gestational age; O/E LHR, observed/expected lung-to-head ratio; PPROM, preterm prelabor rupture of membranes; ECMO, extracorporeal membrane oxygenation.

* Smaller sample size used in analysis.

+ Defined as mortality after 2 weeks of life.

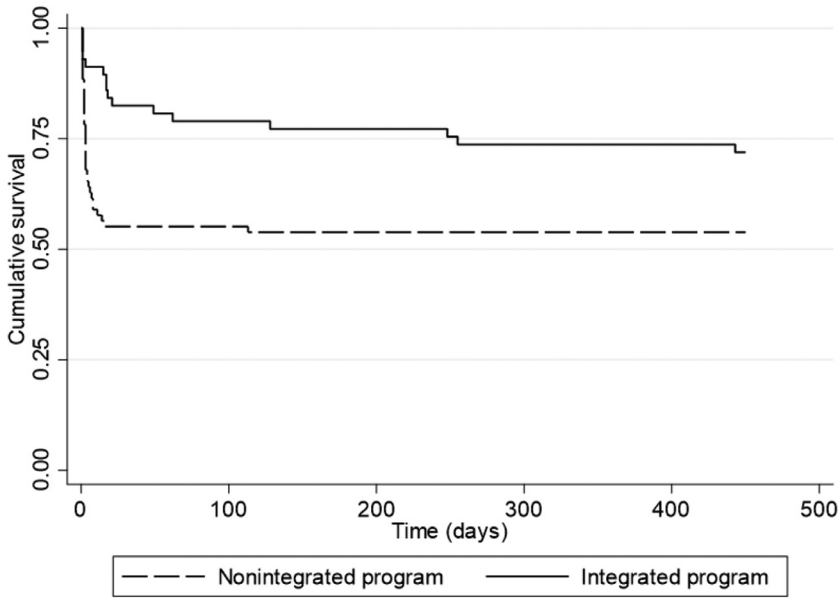

Fig. 3. Kaplan-Meier survival curve of patients in integrated and nonintegrated healthcare settings.

Table 3
Multilevel regression assessing odds of survival after fetoscopic tracheal occlusion.

	Unadjusted		Adjusted	
Variables	OR	*p-value*	OR	*p-value*
Pre-FETO O/E LHR	1.1	0.01	1.2	0.59
Balloon placement GA	0.9	0.55	0.1	0.75
Occlusion days	1.0	0.12	0.8	0.78
PPROM GA	1.2	0.08	2.5	0.045
Delivery GA	1.1	0.08	0.4	0.20
Birthweight	1.0	0.07	1.0	0.59
Apgar at 1 min	1.1	0.56	0.8	0.84
Apgar at 5 min	1.5	0.06	2.6	0.049
Access to ECMO	3.4	<0.01	18.8	0.049

(IQR, 2.0–2.8 kg).Moreover, as revealed by the increased survival without ECMO in children managed in integrated programs, ECMO access may simply be a surrogate marker of additional advanced neonatal therapies that are available to manage these critically ill infants, including non conventional ventilator management strategies and pulmonary hypertension pharmacotherapy[17]. The predominance of early neonatal deaths for patients managed outside an integrated care setting suggests that the lack of availability of these advanced therapies to address early respiratory compromise may be the key contributor to lower infant survival following FETO. Additional concerns about the generalizability of the TOTAL trial results are related to the presumed absence of early surgical repair after FETO because of hemodynamic instability as well as the observation that patients managed expectantly outside of the trial had a 31% survival rate compared to a 39% survival rate after FETO [26].

This systematic review has several limitations. First, most of the studies included in our analysis were small, non randomized feasibility studies which is not surprising given the limited number of FETO studies to date. This may increase the possibility that our results are subject to issues related to patient heterogeneity, chance, and publication bias since unsuccessful FETO outcomes are less likely to be published. We were unable to incorporate any data from the TOTAL trial itself since the published results were presented as pooled data from many institutions (of which some are integrated and some are nonintegrated), and we were not given access to individual participant data. A second limitation of our analysis is its reliance on studies that were not specifically designed to answer our question regarding the healthcare setting. As such, there were likely a subset of patients in the nonintegrated cohort who may have received care at the same institution as their fetoscopic procedure. However, as the survival difference between the integrated and nonintegrated cohort was so large, it is doubtful that potential misclassification of the postnatal care site would substantially affect the overall findings in this paper. Third, the studies included in this review spanned a period of 17 years, with the earliest study from a nonintegrated program published in 2004. Although our survival data are comparable to results published in the recently TOTAL trial, we acknowledge that the effect of time may be a confounder in our analysis as both FETO techniques and postnatal management have continued to be refined with small, incremental improvements in clinical outcomes in the last decade. Lastly, as we obtained our individual analysis data from published studies, we were unable to account for all possible patient-specific markers (e.g., defect size, concomitant cardiac anomalies, timing of repair in relation to ECMO) and institution-specific factors (e.g., CDH case volume, non FETO survival rates) which may have differed between integrated and nonintegrated settings. These factors remain highly debated among the pediatric surgical community [27–30], and elucidating the relative importance of these covariates is complex and beyond the scope of our work. However, the focus of this study was on the integration of care for FETO patients and thus these factors are beyond the scope of this study.

Conclusions

This study addresses the impact of an integrated postnatal healthcare setting in the context of severe CDH. We were able to utilize existing data to evaluate a facet of FETO that has been underemphasized in the current literature to show that survival after FETO for severe CDH is significantly dependent on postnatal care integration. A multi-disciplinary care model, in which there is coordinated involvement of neonatal and surgical teams working closely with maternal fetal medicine specialists and other fetal surgeons, is likely to be complementary for producing the highest survival rates in these complex patients. Future studies in the United States and elsewhere should focus on conducting well designed trials from experienced FETO centers with more collaboration with

pediatric surgeons and neonatologists aimed at better standardization of postnatal treatment algorithms.

Type study

Systematic Review and Meta-Analysis

Level of evidence

Level III

Financial support

None

Declarations of Competing Interest

None

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jpedsurg.2022.05.011.

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