

Intrapartum surgical treatment of congenital diaphragmatic hernia: A review of 10 cases and literature review

Abstract

Congenital Diaphragmatic Hernia (CDH) poses significant respiratory challenges at birth due to lung hypoplasia and pulmonary hypertension. The Ex-utero Intrapartum Treatment (EXIT) procedure offers a potential strategy to secure the airway while maintaining uteroplacental circulation in selected severe cases. Through literature review and case analysis, the therapeutic indicators, clinical effects and challenges faced by this technology were studied and evaluated. Studies have shown that a standardized EXIT operation process combined with multidisciplinary collaborative perioperative management can significantly increase the survival rate of children and reduce the risk of complications. With the advancement of fetoscopy technology and imaging assessment, the application scope of EXIT will be further expanded. The conclusion indicates that EXIT is an important component of the individualized treatment system for CDH. In the future, larger-sample studies and long-term follow-up are needed to optimize the treatment plan.

Keywords: Congenital diaphragmatic hernia; Perioperative management; Clinical efficacy.

Introduction

Congenital Diaphragmatic Hernia (CDH) is a severe congenital malformation caused by developmental defects of the diaphragm, whose pathogenesis is closely associated with fusion disorders during the embryonic development of the diaphragm [1]. The diaphragm originates from four embryonic components, and its normal development relies on the precise fusion of the transverse septum, bilateral pleuroperitoneal membranes, dorsal mesentery of the esophagus, and body wall muscles within a specific time window [1]. The developmental abnormalities of the Pleuroperitoneal Folds (PPF) are considered a key early event leading to diaphragmatic defects, while the “mesenchymal hit” hypothesis and genetic mutations of transcription factors such as GATA-4 and FOG-2 have been

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confirmed to be associated with the occurrence of CDH in animal models [1]. The incidence of CDH in live births is approximately 0.8–5 per 10,000, with Bochdalek hernia (posterolateral hernia) being the most common type, accounting for 70–75% of cases, and its incidence on the left side (about 85%) is significantly higher than that on the right side [1]. The clinical manifestations of this disease mainly depend on the type and severity of abdominal viscera herniated into the thoracic cavity, which can cause severe respiratory distress, pulmonary hypertension and pulmonary hypoplasia, and it is a life-threatening emergency in the neonatal period [2,3]. Historically, the mortality rate of neonates with CDH without surgical intervention was extremely high. A 1925 survey by Carl Hedblom showed that the mortality rate of 44 neonates with congenital diaphragmatic hernia who did not receive surgery reached as high as 75% [1].

Traditionally, the treatment of CDH has relied on postnatal surgical repair. However, for fetuses prenatally diagnosed with severe CDH, especially those with hepatic herniation and an extremely low predicted Lung-to-Head Ratio (LHR), the severe respiratory insufficiency that develops immediately after birth renders conventional postnatal surgery extremely high-risk and results in a persistently high mortality rate [4]. This clinical dilemma has spurred the need for fetal intervention, aiming to improve fetal lung development or create conditions for a smooth transition after birth. Against this backdrop, Ex utero Intrapartum Treatment (EXIT) has emerged as an innovative perinatal surgical strategy. Although first reported in 1981 [5,6], the term “ex-utero intrapartum treatment (EXIT)” was introduced in 1997 by a team that had successfully performed fetal surgery [7]. Also described as “operation on placental support” or “airway management on placental support, EXIT allows surgical procedures or airway management in the fetus by maintaining uteroplacental circulation outside the uterus. Cesarean section is completed only after ensuring the neonate’s safety. It was first successfully applied to safely “unplug” fetuses reated using the PLUG (Plug the Lung Until it Grows) technique due to Congenital Diaphragmatic Hernia (CDH) [7]. Mychaliska et al. [7] reported a series of six successful cases where EXIT was applied for the “unplug” phase, and two cases where EXIT was performed in fetuses diagnosed with neck masses. After identifying patients in need of EXIT, patient management begins with the creation of a multidisciplinary team that includes obstetricians, radiologists, obstetric anesthesiologists, pediatric surgeons, anesthesiologists, and neonatologists. Based on

Magnetic Resonance Imaging (MRI) findings Akhtar S, Khan MA, Ali S, et al, [1] a multidisciplinary team must develop a plan before surgery to minimize confusion and prepare for multiple scenarios. The final decision regarding the direction of further treatment of the fetus or whether EXIT is necessary should be made by the multidisciplinary team. It is essential to plan and prepare the procedures. Although fetal management under EXIT can be performed for a considerable duration (150 min) [9], procedures should be performed quickly to avoid maternal infection. This article describes 10 cases of EXIT surgery diagnosed prenatally as congenital diaphragmatic hernia and conducts a literature review on the surgical management of such cases.

Case report

This study has obtained the patient’s authorization for the disclosure of their case details for research purposes.

General information

Among the 10 infants, there were 7 males and 3 females. The gestational age ranged from 37 to 39 weeks with an average of (38.2±1.5) weeks. The birth weight was between 2700 and 3800 grams, with an average of (3150±250) grams. Prenatal evaluation: The ultrasound - measured O/E LHR was (1.5±0.3). Among them, there were 5 cases of severe CDH (O/E LHR <25%) and 5 cases of moderate CDH (O/E LHR 26% - 45%). Prenatal examination indicated that 3 infants were complicated with congenital heart disease, including 2 cases of atrial septal defect and 1 case of ventricular septal defect (Table 1).

Table 1: Prenatal clinical data of neonates with congenital diaphragmatic hernia.

Case	Gender	Gestational age at initial diagnosis	Gestational age at birth and surgery	Birth weight	LHR and O/E LHR
1	Male	About 24w	38w+5	3100 g	1.08; 22.6%
2	Male	About 22w	37w	3500 g	1.13; 24.6%
3	Female	About 28w	39w+3	3780 g	1.72; 35.2%
4	Male	unknown	39w+1	3850 g	1.223; 25.2%
5	Female	28w	39w+5	3700 g	1.56; 31.5%
6	Male	23w	39w+5	3600 g	1.244; 25.7%
7	Male	26+4w	38w	2700 g	1.74; 35.5%
8	Female	32w	38w+3	3120 g	1.18; 23.8%
9	Male	23w	39w+5	3600 g	1.99; 38.5%
10	Male	29w	38w	3150 g	1.93; 37.8%

All 10 infants were delivered by cesarean section following umbilical cord clamping, and the newborns were immediately transferred to the adjacent operating room for endotracheal intubation, venous access establishment, as well as nasogastric tube and urinary catheter indwelling. Vital signs were closely monitored intraoperatively. Among them, thoracoscopic diaphragmatic hernia repair was performed in 8 cases, and open repair via a 3-4 cm small incision was conducted in 2 cases. Intraoperative findings revealed that parts of the liver, gastric bubble, colon and small intestine had herniated into the left thoracic cavity in all 8 thoracoscopic cases; 2 cases were complicated with congenital intestinal malrotation, 1 case with pulmonary sequestration, and 1 case with Poland syndrome. The estimated diameter of the hernial sac was approximately 2-5 cm intraoperatively. After reduction of the hernial sac contents, significant expansion of the previously compressed

lung tissue was observed due to ventilation. The defect was closed with interrupted sutures using non-absorbable sutures (Prolene) intraoperatively, and a closed thoracic drainage tube was placed.

Results

All 10 surgeries were successfully completed, with a surgical success rate of 100%. The average operation time was (25.3±10.5) minutes. During the perioperative period, 9 infants survived, with a survival rate of 90.0%. One infant with severe CDH complicated with bilateral pulmonary hypoplasia developed severe pneumothorax on the 2nd day after the operation. The chest X - ray showed that the right lung tissue was compressed by approximately 40%. Compared with the chest X - ray on the day after the operation, the condition was worse. At the same time, the infant was complicated with neonatal heart

failure, neonatal hypoproteinemia and other conditions, which increased the difficulty and duration of treatment. Finally, the parents gave up further treatment. The remaining 9 infants were discharged healthily, with no recurrence within 1-4 years after the operation and a good prognosis. The postoperative follow-up lasted for 6-12 months, with an average of (8.5±2.1)

months. The chest X-rays of 9 infants (90%) basically returned to normal after the operation. Neurodevelopmental evaluation showed that the developmental quotients of gross motor, fine motor, language and social skills of all surviving infants were ≥ 85, and there was no obvious neurodevelopmental delay (Table 2).

Table 2: Surgical conditions and clinical outcomes of infants with congenital diaphragmatic hernia.

No.	Surgical duration (min)	Ventilator duration (h)	Side	Surgical method	Feeding status	Hospital stay (days)	Prognosis
1	30	168.5	Left	Open abdominal	on the 4 th day	26	good
2	20	335.5	Left	Laparoscope	No feeding	14	bad
3	20	189.5	Right	Laparoscope	the 2 nd day	16	good
4	30	139.5	Left	Laparoscope	the 3 rd day	16	good
5	15	190	Left	Open abdominal	the 2 nd day	20	good
6	25	149.5	Left	Laparoscope	the 2 nd day	15	good
7	30	164.5	Right	Laparoscope	the 6 th day	13	good
8	20	130	Left	Laparoscope	the 3 rd day	18	good
9	20	144	Left	Laparoscope	the 2 nd day	18	good
10	25	146	Left	Laparoscope	the 2 nd day	28	good

Discussion and literature review

The Ex-utero Intrapartum Treatment (EXIT) procedure represents a pivotal advancement in fetal surgery, conceived to manage life-threatening congenital anomalies that compromise immediate neonatal resuscitation. Its core principle is the maintenance of uteroplacental circulation during partial delivery of the fetus, thereby providing a critical window to perform lifesaving interventions while the fetus remains oxygenated via placental support [5]. This technique was initially developed and successfully applied for the management of airway obstruction in cases of severe Congenital Diaphragmatic Hernia (CDH) [5]. The historical trajectory of fetal surgery, with CDH as a focal point, can be traced to pioneering work at institutions like the University of California, San Francisco, where the disappointing outcomes of postnatal repair for CDH due to pulmonary hypoplasia inspired the concept of prenatal intervention [6].

As experience grew, the indications for the EXIT procedure expanded beyond CDH to encompass any congenital anomaly that impedes immediate neonatal resuscitation, leading to various procedural “declinations” based on the therapeutic objective [5]. These include EXIT-to-airway for securing airway patency in cases of cervical masses or intrinsic obstruction, EXIT-to-resection for debulking large tumors, and EXIT-to-separation for conjoined twins [5]. The procedure is particularly indicated for suspected or confirmed extrinsic or intrinsic airway obstruction where airway access cannot be rapidly established after delivery, such as in congenital high airway obstruction syndrome (CHAOS) or large cervical teratomas [5,6]. The successful execution of an EXIT procedure is fundamentally dependent on meticulous prenatal planning and a coordinated multidisciplinary team approach involving obstetricians, fetal surgeons, neonatologists, pediatric surgeons, otolaryngologists, and anesthesiologists [5,6]. This team is responsible for comprehensive preoperative imaging, development of a specific surgical and airway management algorithm, and even simulation training to ensure preparedness [5].

The surgical execution of an EXIT procedure is a meticulously orchestrated sequence that hinges on maintaining uteroplacental circulation to provide a stable, oxygenated environment for fetal intervention. The core principle involves achieving profound uterine relaxation through deep maternal inhalational anesthesia to prevent placental separation and ensure continuous fetal gas exchange [10]. Following a maternal laparotomy, typically via a low transverse abdominal incision, intraoperative ultrasound is employed to map the placenta and determine the optimal site for hysterotomy, maintaining a safe margin from the placental edge [11]. The hysterotomy is then performed using specialized atraumatic techniques, such as a uterine stapling device, to minimize bleeding and maintain amniotic fluid volume [11,12].

Once the hysterotomy is established, only the fetal head, neck, and one upper extremity are delivered; the remainder of the fetal body and the umbilical cord are retained within the uterine cavity to preserve heat, minimize fluid loss, and, most critically, sustain fetoplacental circulation [10]. Fetal anesthesia and immobilization are often achieved via the transplacental passage of maternal agents, supplemented, if necessary, by a direct intramuscular fetal cocktail containing medications such as fentanyl, rocuronium, and atropine [13,14]. The specific surgical intervention then proceeds based on the prenatal diagnosis. For Congenital Diaphragmatic Hernia (CDH), the historical and foundational indication for EXIT was the reversal of tracheal occlusion (e.g., removal of a balloon or clip) performed as a prior fetal intervention [10,11]. This role has become increasingly central with the advent of fetoscopic Tracheal Occlusion (FETO), as detailed in the preceding section. In contemporary practice, EXIT for CDH may also encompass securing the airway via intubation, administering surfactant, and establishing vascular access, including cannulation for Extracorporeal Membrane Oxygenation (ECMO), a strategy known as EXIT-to-ECMO [11].

The management of the fetal airway is the most critical technical component and follows a structured, stepwise algorithm. The initial approach is direct laryngoscopy for

endotracheal intubation. If this is not feasible due to anatomical distortion from a mass or obstruction, the next step is rigid bronchoscopy, which can be used both diagnostically and therapeutically to visualize the obstruction and guide intubation [10,13]. In cases of severe obstruction, such as laryngeal atresia or a large cervical teratoma, a surgical tracheostomy may be required as the definitive procedure to secure the airway while on placental support [10,14]. For other pathologies, the EXIT procedure can be adapted to perform resection of cervical or mediastinal masses (EXIT-to-resection) or to provide other life-supporting interventions [11,13].

A successful EXIT procedure is fundamentally dependent on a highly coordinated multidisciplinary team. This team typically includes maternal-fetal medicine specialists, fetal and pediatric surgeons, pediatric otolaryngologists, neonatologists, anesthesiologists for both the mother and fetus, specialized nurses, and perfusionists if ECMO is anticipated [12,13]. The complexity is magnified in twin pregnancies, where the team must balance the needs of the affected fetus with the safety of the unaffected co-twin, requiring extreme coordination and careful monitoring of both fetuses throughout the procedure [11]. Following the completion of the planned fetal intervention and confirmation of a secured airway, the umbilical cord is clamped and cut, and the neonate is fully delivered to the awaiting neonatal resuscitation team. Uterotonic agents are then administered to the mother to stimulate uterine contraction and prevent postpartum hemorrhage [12]. This procedural framework provides the essential platform upon which the innovations in prenatal therapy, such as novel FETO devices and combined surgical strategies, are ultimately delivered and transitioned to postnatal care.

The clinical efficacy of Ex-utero Intrapartum Treatment (EXIT) for Congenital Diaphragmatic Hernia (CDH) is primarily evaluated through survival rates and long-term outcomes, which are significantly influenced by the severity of pulmonary hypoplasia, the presence of associated anomalies, and the quality of postnatal management. Historically, the prognosis for CDH was dismal, with mortality rates approaching 100% before the era of prenatal diagnosis [15]. Contemporary data from specialized centers demonstrate improved but variable survival, highlighting the critical role of standardized, multidisciplinary care protocols. A single-center retrospective analysis from Kepler University Hospital Linz reported an overall survival rate of 75% among 67 newborns treated between 2005 and 2020, which increased to 80% following the implementation of an Extracorporeal Membrane Oxygenation (ECMO) program in 2009 [16]. This aligns with broader literature suggesting survival rates of 70-80%, and up to 90% in some reports, for isolated CDH managed in high-volume tertiary centers [16]. The presence of concomitant congenital malformations is a major determinant of outcome. In the Brazilian series, the overall mortality was 92% (35/38), with all cases involving chromosomal abnormalities resulting in death [15]. Even among cases with isolated CDH (no associated malformations or abnormal karyotype), the mortality rate in that series was 88%, which is higher than the 40-75% typically reported from developed countries, a discrepancy attributed to differences in prenatal selection, termination of pregnancy rates, and the level of specialized neonatal care [15]. The Linz cohort reported a 45% rate of concomitant malformations, with 67% of those requiring additional surgery, underscoring the complexity of care [16].

The EXIT procedure for CDH, while a life-saving intervention, is associated with a spectrum of maternal and neonatal complications that require meticulous perioperative management. Maternal complications primarily stem from the need for profound uterine relaxation and the risk of hemorrhage. The administration of high-dose inhalational anesthetics, such as sevoflurane, to achieve uterine atony can lead to significant maternal hypotension, which must be aggressively managed with vasopressors to maintain adequate placental perfusion and maternal hemodynamic stability [17]. Uterine atony post-delivery is a major concern, potentially resulting in severe postpartum hemorrhage. Prophylactic administration of uterotonic agents like oxytocin is standard upon completion of the fetal procedure and prior to uterine closure to counteract this effect [17]. The surgical incision itself, often a low transverse hysterotomy, carries risks of extension, adjacent organ injury, and future uterine complications such as dehiscence or rupture in subsequent pregnancies.

Neonatal complications are predominantly related to the underlying severe CDH pathophysiology and the challenges of establishing adequate ventilation and circulation during the transition to extrauterine life. The most critical immediate complication is the inability to achieve effective gas exchange due to pulmonary hypoplasia and Persistent Pulmonary Hypertension of the Newborn (PPHN). Management during the EXIT window focuses on securing the airway, often via endotracheal intubation or tracheostomy, and initiating High-Frequency Oscillatory Ventilation (HFOV) or other advanced respiratory support before umbilical cord clamping [17]. Hemodynamic instability is common, necessitating prompt vascular access for inotropic support and management of PPHN, which may include Inhaled Nitric Oxide (iNO) and other pulmonary vasodilators. The procedure's success is critically dependent on maintaining fetal-placental circulation until the neonatal airway is secured and ventilation is stabilized, a period that must be carefully monitored to prevent fetal acidosis.

Postoperative care for the neonate is a direct continuation of the management initiated during the EXIT procedure. This involves ongoing sophisticated respiratory support, often with HFOV and iNO, to manage severe respiratory failure and PPHN [17]. Hemodynamic monitoring and support remain paramount, with a focus on maintaining systemic perfusion while reducing pulmonary vascular resistance. Throughout the perioperative period, a multidisciplinary team comprising maternal-fetal medicine specialists, pediatric surgeons, neonatologists, anesthesiologists, and specialized nursing staff is essential for coordinated decision-making and the implementation of these complex management strategies to mitigate the inherent risks of the EXIT procedure for CDH.

The Ex-Utero Intrapartum Treatment (EXIT) procedure has emerged as a critical component in the management of severe Congenital Diaphragmatic Hernia (CDH), particularly for fetuses who have undergone Fetal Endoscopic Tracheal Occlusion (FETO). In these cases, EXIT is indicated as part of the delivery strategy to maintain uteroplacental circulation while the tracheal occlusion balloon is removed and the airway is secured, a process essential for transitioning to postnatal ventilation [10]. This controlled delivery and resuscitation platform directly addresses the profound pulmonary hypoplasia and hypertension that are the primary causes of mortality in CDH by facilitating a controlled transition from fetal to neonatal life, allowing for the establishment of a secure airway and

initiation of advanced respiratory support before umbilical cord clamping.

The clinical impact of this approach is supported by a propensity score-matched analysis, which demonstrated that the application of EXIT was associated with specific perinatal benefits for infants with CDH [24]. These findings underscore that EXIT is not a standalone intervention but a pivotal link between prenatal fetal therapy and intensive postnatal management. Its impact is most significant in a carefully selected cohort of severe CDH cases, where traditional delivery methods would likely result in immediate cardiorespiratory collapse upon cord clamping due to unaddressed airway obstruction or insufficient lung function.

Consequently, the integration of EXIT into clinical practice has refined patient selection criteria and perioperative management protocols. Optimal candidates are typically fetuses with severe, isolated CDH, often with intrathoracic liver herniation and a low Lung-to-Head Ratio (LHR), who have undergone FETO to promote lung growth [10]. The procedure demands a highly coordinated multidisciplinary team involving fetal surgeons, neonatologists, pediatric anesthesiologists, and obstetricians. This team-based approach, centralized in specialized perinatal centers, is a direct consequence of adopting EXIT and has elevated the standard of care for complex fetal conditions. The literature confirms that outcomes for CDH are directly related to the level of neonatal care and the implementation of standardized management guidelines, within which EXIT serves a specialized but vital role. Building on this established role, future research must now focus on refining its application and integrating novel strategies to further improve outcomes.

Conclusion

Intrapartum surgery for congenital diaphragmatic hernia is a safe and effective early intervention method that can rapidly improve the respiratory and circulatory functions of the infant, shorten the duration of mechanical ventilation and hospital stay, and has good surgical safety. Strictly adhering to surgical indications (LHR>1.0, relatively stable hemodynamics) and standardizing perioperative management can significantly improve survival rates and long-term prognosis. In well-established CDH treatment centers, intrapartum surgery is safe and feasible, with good clinical outcomes, rapid relief of compression, relatively easy surgery, and quick recovery for the child. It also reduces the anxiety and waiting time for the mother. In the future, it is necessary to further expand the sample size, conduct in-depth research on the impact of different surgical methods, and combine prenatal intervention measures to further improve the treatment effect of congenital diaphragmatic hernia.

Declarations

Conflicts of interest: No other potential conflicts of interest relevant to this article were reported.

Data availability statement: The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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