

Repair of congenital diaphragmatic hernia under high-frequency oscillatory ventilation in high-risk patients: an opportunity for earlier repair while minimizing lung injury

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BACKGROUND: Repair of congenital diaphragmatic hernia (CDH) is ideally delayed until ventilatory parameters are stabilized and patients are switched to conventional ventilation. However, in selected high-risk patients, repair can be performed earlier while they are still on high-frequency oscillatory ventilation (HFOV).

DESIGN AND SETTINGS: A retrospective review of all CDH cases treated in our tertiary referral center between 1997 and 2013.

METHODS: In 1997, we started repairing selected high-risk CDH cases under HFOV with or without inhaled nitric oxide (iNO). All repairs were performed once the infants' blood gas levels were acceptable. The infants were gradually weaned to conventional ventilation followed by extubation as their ventilatory parameters improved. Their records were reviewed to determine the group-wide outcomes.

RESULTS: Between 1997 and 2013, 55 infants with CDH were treated in our institute; of these 12 high-risk cases were repaired under HFOV/iNO combinations and 1 was repaired without iNO. All patients had significant pulmonary hypertension and 8 had herniated livers. The mean age at repair was 9.1 (6.3) days. Two mortalities occurred at the first and tenth postoperative days. Among the remaining 11 survivors, the median ventilation and hospitalization days were 29.5 (11–84) and 45.5 (25–107), respectively, and the median duration under HFOV and conventional ventilation days were 15 (9–40) and 12 (3–47), respectively.

CONCLUSION: CDH repair can be performed earlier under HFOV and iNO. The possible advantages are earlier restoration of normal anatomy and earlier start of enteral feeding while minimizing the risk of lung injury.

Management of congenital diaphragmatic hernia (CDH) remains challenging and is associated with high mortality despite recent advances in perioperative care.^{1,2} Patients who suffer from significant lung hypoplasia and persistent pulmonary hypertension (PPH) are at high risk and difficult to treat. Barotrauma caused by aggressive high-pressure ventilation is recognized as one of the leading causes of morbidity and mortality in these cases.³ Recently developed management strategies focus on gentle ventilation to protect against ventilator-induced lung injury using permissive hypercapnia and high-frequency oscillatory ventilation (HFOV)⁴ and attempt to reduce pulmonary vascular

resistance using selective vasodilators such as inhaled nitric oxide (iNO).^{5,7}

While the timing of surgical repair for CDH has not been well defined, most surgeons agree on delaying repair until patient ventilatory parameters are stabilized and they are switched to conventional mechanical ventilation (CMV).⁸⁻¹¹ However, we think that repairing CDH once the patient is stabilized while under HFOV can offer an opportunity for earlier repair and the subsequent advantages of earlier enteral feeding and the possibility of earlier recovery.

In this study, we reviewed our preliminary experience and the feasibility of our practice of earlier CDH repair while patients were under HFOV.

METHODS

In 1997, we started repairing selective high-risk CDH cases under HFOV with the aim of minimizing ventilator time and the duration of total parenteral nutrition (TPN) and enhancing the overall recovery of these challenging patients. The target population included patients with significant PPH and lung hypoplasia that caused failure of the initial conventional ventilation. To minimize barotrauma, we adopted a liberal definition of CMV failure. CMV failure was defined as follows: the need for peak inspiratory pressure >25 cm H₂O or mean arterial pressure >12 cmH₂O to maintain a partial pressure of carbon dioxide (PCO₂) <65 mm Hg; and/or fraction of inspired oxygen (FiO₂) >0.9 to achieve post-ductal blood oxygen saturation (SO₂) $>88\%$. We do not offer extracorporeal membrane oxygenation (ECMO) for CDH cases in our center, but the use of iNO is encouraged in all high-risk patients. However, due to the lack of strong evidence supporting its positive impact on CDH outcomes, the decision to use iNO is typically left to the individual neonatologist's discretion.

Patients were considered ready for surgical repair when they remained stable for at least 24 hours under HFOV. Stability required to undergo surgery was defined as maintaining a PCO₂ <60 mm Hg and requiring FiO₂ <0.65 to achieve a post-ductal SO₂ $>88\%$. Surgical repair was performed at the bedside for all cases after field isolation using artificial mobile barriers. A complete operating room team was present in addition to an active neonatal intensive care unit (NICU) staff support. As we previously reported, CDH repair is among the procedures we routinely perform at the bedside for selective NICU cases.¹²

Enteral orogastric feeding was started 1 to 2 days after repair and gradually increased up to full feeds while weaning off of TPN.

After receiving institutional review board approval for this study, we reviewed the records of all CDH cases admitted to our hospital between December 1997 and January 2014. Only high-risk cases that underwent repair under HFOV with or without iNO were included. High-risk cases were excluded if they died before the repair was performed. Collected data included demographics, related clinical findings, ventilatory parameters, operative details, and outcomes.

RESULTS

During the study period, 55 infants with CDH were treated in our institute; among these, 13 high-risk cases were repaired under HFOV (7 boys and 6 girls). Concurrent iNO was used in all but 1 case. The mean

gestational age was 38.1 (1.0) weeks, and the mean birth weight was 2.9 (0.5) kg (Table 1). Apart from the substantial PPH and patent ductus arteriosus, echocardiography did not identify any significant associated congenital heart anomalies in the study group. Herniated liver was identified in 8 cases.

The mean age at repair was 9.1 (6.3) days. HFOV settings immediately before repair showed a mean airway pressure of 14.2 (2.1) cmH₂O, frequency of 10.0 (1.9) Hz, amplitude of 25.0 (5.5), and FiO₂ of 42.0 (8.4) (Table 2). Preoperative blood gas values were pH of 7.4 (0.1), PCO₂ of 46.7 (8.7), and mean SO₂ of 95.7 (2.0). The subcostal abdominal approach was used in all but 3 cases, in which a thoracoscopic approach was used. Prosthetic patches were required to close the diaphragmatic defects in 4 cases. The mean operative time was 144 (60) minutes. Blood gas taken within 1 hour postoperatively showed a pH of 7.4 (1.0) and PCO₂ of 44.3 (11.0) mm Hg.

Two mortalities occurred at the first and tenth postoperative days. The first baby had complete left diaphragm agenesis, experienced quick postoperative respiratory and hemodynamic deterioration, and died within 24 hours. The second case died of respiratory failure on the tenth postoperative day. No postoperative wound or patch infection was reported. Among the remaining 11 survivors, the median ventilation and hospitalization days were 29.5 (11-78) and 45.5 (25-107) days, respectively, while the median time under HFOV and conventional ventilation days were 15 (9-40) and 12 (3-47) days, respectively.

DISCUSSION

HFOV has been used to protect against barotrauma in neonates with PPH who are difficult to ventilate. Consequently, the earlier use of HFOV has become an essential element in all recent CDH protocols for managing high-risk patients who suffer from persistent poor ventilatory parameters.^{6,7} Another tool, iNO, is often used to manage PPH due to its ability to cause selective pulmonary vasodilatation and improve pulmonary blood flow.¹³ A randomized trial demonstrated the beneficial effect of iNO in improving oxygenation in neonates with PPH;¹⁴ however, in cases of CDH, this improvement failed to translate into improved mortality rates or decreased ECMO needs.¹²

This preliminary report highlights the feasibility and outcomes of early repair of high-risk CDH while patients are under HFOV. Surgical repair was traditionally performed during the first 48 hours ("honeymoon period"), but later evidence has demonstrated that surgical timing is less important compared to physiologi-

cal parameters^{1,2,10}, and repair can be delayed until the patient is stabilized and shifted to conventional ventilation.^{9,10} However, in most of these studies, the impact of timing of surgery has not been studied exclusively in high-risk patients who might require prolonged ventilation periods of days or even weeks before achieving the physiological stability required to switch them to conventional ventilation and shift them to the operating room.⁵ We think such a delay might not be necessary but may lead to undesirable effects.

In addition to the theoretical advantages of restoring the thoracic anatomy and providing the needed space for lung expansion, other overlooked advantages of earlier CDH repair include the opportunities to start enteral feeding and wean the patient from TPN. Earlier enteral feeding plays an important role in avoiding TPN-related complications, particularly liver injury that could lead to portal hypertension and splenomegaly¹⁴ and further complicate the reduction of herniated contents. Moreover, in premature neonates, enteral trophic feeding has been shown to decrease sepsis and promote growth and was associated with shorter hospitalization duration.¹⁵ In adults, a nutritional protocol that implements earlier enteral feeding for critically ill patients was shown to decrease the duration of mechanical ventilation¹⁶ and shorten the intensive care unit stay.¹⁷

We previously reported that minimally invasive repair of CDH is becoming easier and more feasible, even in high-risk patients once they are stabilized.¹⁸ Consequently, some of the patients in our group had their CDH repair thoracoscopically while under HFOV. HFOV during thoracoscopy could offer further pulmonary protection from the higher intraoperative ventilatory pressures required to compensate for the induced pneumothorax and CO₂ adsorption. Moreover, avoiding larger tidal volume by using HFOV could facilitate thoracoscopic repair by minimizing intraoperative lung expansion, which can lead to poor visualization and possible lung trauma from the repeated introduction of thoracoscopic instruments into an already limited space filled with an expanded lung.

In high-risk CDH patients, many centers have similarly adopted earlier CDH repair once patients are stabilized on ECMO.¹⁹ In a recent study, Fallon et al. compared early versus late repair in high-risk patients on ECMO and concluded that the earlier repair group had shorter ECMO duration and fewer circuit complications and trends toward better survival.²⁰ Another study by Dassinger et al. reported similar findings of better survival rates (71% vs. 49%; $P=.016$) of their ECOMO patients who underwent earlier repair com-

Table 1. Patient and surgical characteristics.

Characteristic (n=13)	Value
Patient characteristics	
Gestational age (wk)	38.1 (1.0)
Birth weight (kg)	2.9 (0.5)
Herniated liver (n)	8
Major cardiac anomalies (n)	0
Surgical details	
Age at repair (d)	9.1 (6.3)
Laparotomy (n)	10
Thoracoscopy (n)	3
Patch repair (n)	4
Surgical time (min)	144 (60)

Table 2. Ventilatory parameters.

Parameter	Value
Preoperative HFOV parameters	
Mean arterial pressure (cmH ₂ O)	14.2 (2.1)
Frequency (Hz)	10.0 (1.9)
Amplitude	25.0 (5.5)
FiO ₂	42.0 (2.1)
Preoperative blood gas^a	
pH	7.4 (0.05)
PCO ₂ (mm Hg)	46.7 (8.7)
Postoperative blood gas^a	
pH	7.4 (1.0)
PCO ₂ (mm Hg)	44.3 (11.0)
Ventilation time	
HFOV (d)	15 (9–40), ^b 18.9 (9.6)
Conventional (d)	12 (3–47), ^b 19.0 (16.7)

^aBlood gas collected within 1 hour before and after the procedure; ^bmedian and range. HFOV: High-frequency oscillatory ventilation; FiO₂: fraction of inspired oxygen; PCO₂: partial pressure of carbon dioxide.

pared to ECMO registry patients who underwent delayed repair.²¹

In our opinion, the major barriers facing CDH repair under HFOV and iNO are their availability in operating rooms and anesthesiologists' lack of experience in handling such modes of ventilation. These barriers can be overcome by performing the repair at the bedside with a joint team from anesthesia and neonatology.

Migliazza et al.²² described bedside repair of all of their CDH cases; however, we think that their routine repair of all CDH cases at the bedside may add unnecessary obstacles to an already difficult management.

Despite admitting 55 CDH cases during the study period, our study was still limited in number due to the selective nature of case recruitment. This was because only cases of failed conventional ventilation were considered study candidates. Patients with poor prognostic features who suffered from congenital heart diseases, low birth weight, and prematurity might have been excluded either before their referral to our center or before becoming stable enough to undergo surgical repair. This could explain the low mortality rate of our cohort.

There might be an element of bias toward performing earlier repair under HFOV at the bedside for patients who are stable enough to be switched to CMV. This could originate from the general belief in the neonatologists' superior skill and experience in handling

HFOV compared to anesthesiologists, who are often uncomfortable managing critically ill neonates under unfamiliar ventilation modes in the operating room. However, in our study, the mean duration under HFOV (18.9 days) was significantly greater than the age at repair (9.1 days), which indicates that our patients were not stable enough to be switched off of HFOV.

In conclusion, this preliminary experience demonstrates that CDH repair of high-risk patients under HFOV with or without iNO can be safely performed and may even be beneficial. We are hopeful that evidence will continue to accumulate as more surgeons, neonatologists, and anesthesiologists become more comfortable exploring this modality for managing such a challenging diagnosis.

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