Impact of Objective Echocardiographic Criteria for Timing of Congenital Diaphragmatic Hernia Repair

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Objective To assess the impact of specific echocardiographic criteria for timing of congenital diaphragmatic hernia repair on the incidence of acute postoperative clinical decompensation from pulmonary hypertensive crisis and/or acute respiratory decompensation, with secondary outcomes including survival to discharge, duration of ventilator support, and length of hospitalization.

Study design The multidisciplinary congenital diaphragmatic hernia management team instituted a protocol in 2012 requiring the specific criterion of echocardiogram-estimated pulmonary artery pressure ≤80% systemic blood pressure before repairing congenital diaphragmatic hernias. A retrospective review of 77 neonatal patients with Bochdalek hernias repaired between 2008 and 2015 were reviewed: group 1 included patients repaired before protocol implementation (n = 25) and group 2 included patients repaired after implementation (n = 52).

Results The groups had similar baseline characteristics. Postoperative decompensation occurred less often in group 2 compared with group 1 (17% vs 48%, $P = .01$). Adjusted analysis accounting for repair type, liver herniation, and prematurity yielded similar results (15% vs 37%, $P = .04$). Group 2 displayed a trend toward improved survival to 30 days postoperatively, though this did not reach statistical significance (94% vs 80%, $P = .06$). Patient survival to discharge, duration of ventilator support, and length of hospitalization were not different between groups.

Conclusions The implementation of a protocol requiring echocardiogram-estimated pulmonary arterial pressure ≤80% of systemic pressure before congenital diaphragmatic hernia repair may reduce the incidence of acute postoperative decompensation, although there was no difference in longer-term secondary outcomes, including survival to discharge. *(J Pediatr 2017;■■:■■-■■).*

Congenital diaphragmatic hernia is a severe birth defect characterized by herniation of abdominal contents into the thorax caused by a defect in the diaphragm. It occurs in 2 in 10 000 births[1] and presents with a wide range of severity. Historically, congenital diaphragmatic hernia was considered a surgical emergency, until a study in the late 1980s revealed that repair after a period of stabilization of 1-5 days did not worsen outcomes.[2] Since that time, several studies have attempted to identify the optimal timing of congenital diaphragmatic hernia repair, but clear objective criteria for repair are still not defined.

The severity of pulmonary hypertension in congenital diaphragmatic hernia is a major determinant of patient survival.[3] Cardiac catheterization, the gold standard for hemodynamic monitoring of pulmonary hypertension, is difficult and fraught with risk. Pulmonary hypertension can be estimated noninvasively using Doppler echocardiogram, a frequently used alternative in clinical practice.[3-7] Although the limitations of echocardiography in accurately predicting pulmonary hypertension are well known, a composite of tricuspid regurgitant jet, interventricular septal configuration, and ductal and atrial shunt allow bedside estimation of pulmonary pressures with reasonable accuracy to guide clinical decision making. Clinical experience has led to the observation that congenital diaphragmatic hernia repair during the phase when pulmonary hypertension is severe and the pulmonary vascular bed most reactive may precipitate an acute postoperative decompensation.[8,9] Acute changes in pulmonary compliance following congenital diaphragmatic hernia repair may also contribute to cardiopulmonary interactions during acute postoperative decompensation.[8-10] Acute pulmonary decompensation and pulmonary hypertensive crisis often requires an escalation in care and even the need for extracorporeal membrane oxygenation (ECMO) support.

These observations led our multidisciplinary congenital diaphragmatic hernia management team to institute objective criteria for the timing of congenital diaphragmatic hernia repair based on echocardiogram-estimated pulmonary arterial pressure. We reviewed our experience with the use of these criteria for timing of congenital diaphragmatic hernia repair with respect to their effect on the incidence of postoperative decompensation and secondary patient outcomes. Our aim was to test the hypothesis that the institution of echocardiogram-based criteria

ECMO	Extracorporeal membrane oxygenation
PAP	Pulmonary artery pressure
SBP	Systolic blood pressure

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to determine timing of congenital diaphragmatic hernia repair led to a reduction in acute postoperative clinical decompensation in our patients with congenital diaphragmatic hernias.

Methods

In 2012, the multidisciplinary congenital diaphragmatic hernia management team at Children's Hospital Colorado implemented a protocol requiring the specific criterion of echocardiogram-estimated pulmonary artery pressure (PAP) of less than or equal to 80% of systemic systolic blood pressure (SBP) (PAP/SBP ≤80%) be met before operative repair of the defect. For patients who were already on veno-arterial ECMO prior to congenital diaphragmatic hernia repair, the recommendation was to perform the repair shortly after ECMO cannulation as soon as coagulation measures stabilized to reduce the incidence of circuit-related complications.[11] Serial echocardiograms were performed daily, with rare exception, on each infant with congenital diaphragmatic hernia before repair, throughout the entire study period. Members of the designated congenital diaphragmatic hernia team reviewed these echocardiograms to ensure quality and consistency. For the purpose of this study, the echocardiogram of each patient performed just prior to surgery was independently over-read by a single blinded pediatric cardiologist.

Standard clinical echocardiographic views were used to estimate PAP compared with SBP at the time of the scan. The following rubric was used for estimating the ratio of systolic PAP to SBP, considering each factor in order of priority and incorporating the modified Bernoulli equation when applicable: (1) estimating PAP by direction and velocity of ductus arteriosus flow, if present; (2) estimating PAP from a peak tricuspid regurgitant jet velocity, if present; (3) estimating PAP via direction and velocity of flow through a ventricular septal defect, if present; and (4) estimating PAP using changes in ventricular septal geometry (**Table I**).[3,5,12-18] As estimates of right atrial (RA) pressure were not consistently available for all studies, the RA pressure was defined to be 0 mm Hg for all patients.[19] Systolic systemic pressures were measured at the same time as the echocardiogram using an indwelling arterial blood pressure catheter.

At Children's Hospital Colorado, a multidisciplinary congenital diaphragmatic hernia management team is comprised of 3 pediatric surgeons, 2 neonatologists, and 1 cardiologist who use standardized protocols and treatment algorithms, which were in place during the entire study period (**Appendix**; available at www.jpeds.com). These treatment algorithms include minimizing tidal volume delivery, peak inspiratory pressure, and fraction of inspired oxygen. Pressure-limited synchronized intermittent mandatory ventilation settings (peak inspiratory pressure ≤25 cm H_2O) are transitioned to airway pressure release ventilation and subsequently to high frequency oscillatory ventilation (mean airway pressure ≤16 cm H_2O, ΔP ≤40 cm H_2O) as needed to maintain pCO_2 35-65 mm Hg as long as pH is ≥7.25. Systemic blood pressure is maintained (normotensive for age plus 10 mm Hg) with a single bolus of 20 mL/kg normal saline after which steroids are administered. If the blood pressure target is not consistently attained, an epinephrine infusion is started and if further pressure support is required, dopamine, then vasopressin infusions are added. If there is evidence of right ventricular dysfunction, milrinone infusion is administered. Once normal left ventricular function is confirmed by echocardiogram, pulmonary hypertension is managed by inhaled nitric oxide. If pulmonary pressure remains elevated, intravenous sildenafil may be added. Veno-arterial ECMO cannulation is initiated only in cases of severe cardiac dysfunction or when sufficient oxygenation and ventilation cannot be achieved despite maximum medical therapy. Once on ECMO, congenital diaphragmatic hernia is usually repaired within 24-36 hours, after anticoagulation status has been stabilized. When repairing on ECMO, aminocaproic acid is given for up to 48 hours postoperatively to reduce bleeding complications.

Table I. Equations for measurements of PAP

Equations for measurements of PAP	
For neonates with a PDA, the following equation was used:	Systolic PAP = SBP − 4(PDA Vmax)^2 (for left to right shunts) Systolic PAP = SBP + 4(PDA Vmax)^2 (for right to left shunts)
For neonates with tricuspid regurgitation, the following equation was used:	RVSP = Systolic PAP = 4(TR Vmax)^2
For neonates with a VSD, the following equation was used:	Systolic PAP = SBP − 4(VSD Vmax)^2 (for left to right shunts) Systolic PAP = SBP + 4(VSD Vmax)^2 (for right to left shunts)

PDA, patent ductus arteriosus; *RSVP*, right ventricular systemic pressure; *TR*, tricuspid regurgitation; *Vmax*, maximum velocity of flow; *VSD*, ventricular septal defect.
The following rubric was used for estimating the ratio of systolic PAP to SBP, considering each factor in order of priority (1) direction and velocity of ductus arteriosus flow, if present; (2) peak tricuspid regurgitant jet velocity, if present; (3) estimating PAP via direction and velocity of flow through a ventricular septal defect, if present; and (4) estimating PAP using changes in ventricular septal geometry.
When no other variables were available, septal geometry categorized "normal" to "mild" septal deviation were considered PAP/SBP ≤80% equivalency, whereas "moderate" to "severe" septal deviation were considered PAP/SBP >80% equivalency. These data were not used to estimate specific values for PAP/SBP, but rather to simply categorize them as PAP/SBP either ≤ or >80%.

Data from patients who had undergone congenital diaphragmatic hernia repair at Children's Hospital Colorado from January 1, 2008 through December 31, 2015 were retrospectively collected. Patients with right- or left-sided Bochdalek hernias were included, and patients with Morgagni hernias, bilateral hernias, hiatal hernias, and diaphragmatic eventration were excluded. Other exclusion criteria included delayed presentation >48 hours from birth, severe genetic anomalies not including Trisomy 21, additional multiple major anomalies deemed within 24 hours of birth to be incompatible with life, and having undergone fetal intervention.

The primary study outcome was acute postoperative decompensation within the first 24 hours, defined as an overall sustained escalation in care for >12 hours compared with the immediate preoperative period, and which included initiation of or increase in pulmonary vasodilators, paralytics, pressor requirements, ventilator requirements including respiratory rate, positive end expiratory pressure, fraction of inhaled oxygen, or change to high frequency ventilation, or placement on

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