Journal of Pediatric Surgery xxx (2018) xxx–xxx

Contents lists available at ScienceDirect

Journal of Pediatric Surgery

journal homepage: www.elsevier.com/locate/jpedsurg

Predictive value of oxygenation index for outcomes in left-sided congenital diaphragmatic hernia

Ashley S. Bruns [a,*], Patricio E. Lau [b], Gurpreet S. Dhillon [c], Joseph Hagan [d], Joshua A. Kailin [c], George B. Mallory [e], Pablo Lohmann [a], Oluyinka O. Olutoye [b], Rodrigo Ruano [f], Caraciolo J. Fernandes [a]

[a] Section of Neonatology, Baylor College of Medicine/Texas Children's Hospital, Houston, TX, USA
[b] Department of Pediatric Surgery, Baylor College of Medicine/Texas Children's Hospital, Houston, TX, USA
[c] Section of Pediatric Cardiology, Baylor College of Medicine/Texas Children's Hospital, Houston, TX, USA
[d] Center for Research & Evidence Based Practice, Texas Children's Hospital, Houston, TX, USA
[e] Department of Pediatric Pulmonary Medicine, Baylor College of Medicine/Texas Children's Hospital, Houston, TX, USA
[f] Department of Obstetrics and Gynecology, Mayo Clinic School of Medicine, Rochester, MN, USA

ARTICLE INFO

Article history:
Received 21 June 2017
Received in revised form 1 December 2017
Accepted 20 December 2017
Available online xxxx

Key words:
Congenital diaphragmatic hernia
Oxygenation index
Pulmonary hypertension
Hypoxemic respiratory failure
Survival
Outcome

ABSTRACT

Background & objectives: Congenital Diaphragmatic Hernia (CDH) is associated with significant morbidity and mortality. This study compares the efficacy of the highest oxygenation index in the first 48 h (HiOI) versus current prenatal indices to predict survival and morbidity.

Methods: Medical records of 50 prenatally diagnosed, isolated, left-sided CDH patients treated from January 2011 to April 2016 were reviewed. Data abstracted included HiOI, lung to head ratio (LHR), observed to expected total fetal lung volume (O/E TFLV), percent liver herniation (%LH), 6 month survival, respiratory support at discharge, ventilator days and length of stay. Data were analyzed using parametric and nonparametric tests and regression analyses as appropriate.

Results: HiOI was associated with significantly increased LOS ($p<0.001$), respiratory support at discharge ($p<0.001$), greater ventilator days ($p=0.001$) and higher odds of death ($p=0.004$) with risk of death increasing by 5% for every one-unit increase in OI. HiOI was statistically a better predictor of LOS than O/E TFLV ($p=0.007$) and %LH ($p=0.02$).

Conclusions: In isolated, left-sided CDH patients, HiOI is associated with higher mortality, greater length of stay, more ventilator days and increased respiratory support at discharge. HiOI is a better predictor of length of stay than O/E TFLV and %LH.

Type of study: Retrospective Study

Level of evidence: II

Despite improvement in supportive therapies for congenital diaphragmatic hernia (CDH), morbidity and mortality remain significant with mortality ranging from 20% to 40% [1]. Morbidity and mortality are largely consequences of the degree of pulmonary hypoplasia and associated pulmonary hypertension present in the developing lung [2–4]. Currently, prenatal evaluation with fetal magnetic resonance imaging (MRI) and ultrasonography (US) is used to predict clinical severity of CDH. Key indices are based on anatomic measurements including observed-to-expected total fetal lung volume (O/E TFLV), percentage of liver herniation (%LH) and observed-to-expected lung-to-head ratio (LHR) [5–9]. Reports have shown significant correlation of these imaging tools with survival and need for extracorporeal membrane oxygenation (ECMO) use, but only to a certain extent as these findings address anatomic effects only and do not consider functional effects on cardiac and pulmonary vascular development. Analyses with receiver-operating characteristic (ROC) curves have shown accuracy of prediction using these measurements to be 70%–83% [10–12]. Accuracy in this range, at times, yields a clinical course quite different than the prenatally predicted clinical course. Fetal MRI and US measure the anatomic severity of CDH secondary to the degree of pulmonary

Abbreviations: CDH, congenital diaphragmatic hernia; MRI, magnetic resonance imaging; US, ultrasonography; O/E TFLV, observed to expected total fetal lung volume; %LH, percent liver herniation; LHR, lung to head ratio; O/E LHR, observed to expected lung to head ratio; ROC, receiver operating characteristic; RACHS-1, risk adjustment for congenital heart surgery; GA, gestational age; OI, oxygenation index; ECMO, extracorporeal membrane oxygenation; FiO2, fraction of inspired oxygen; M_{PAW}, mean airway pressure; PaO2, partial pressure of oxygen in arterial blood; SCC, Spearman's Correlation Coefficient; LOS, length of stay; RSS, respiratory support score at discharge; OR, odds ratio; CI, confidence interval; AUC, area under the curve; Cont-VI, contralateral velocity index; BOId1, best oxygenation index for day of life 1.

* Corresponding author at: Section of Neonatology, Texas Children's Hospital, 6621 Fannin Street, WT-6104, Houston, Texas 77030. Tel.: +1 832 826 1380.
E-mail address: bruns@bcm.edu (A.S. Bruns).

https://doi.org/10.1016/j.jpedsurg.2017.12.023
0022-3468/© 2018 Elsevier Inc. All rights reserved.

hypoplasia, so it has been theorized that better predictive models of CDH are obscured by the limitations of predicting postnatal pulmonary hypertension, which is largely a function of lung vascular development.

Oxygenation index (OI) is a calculated value used in the neonatal literature to estimate the severity of hypoxemic respiratory failure. The best OI in the first 24 h of life in CDH patients has been shown to predict survival [13]. However, use of the best OI may not reflect accurately the severity of dysfunction present. We hypothesized that the highest OI in the first 48 h of life (HiOI) would be associated with mortality and respiratory morbidity. In addition, as OI is a marker for postnatal cardiopulmonary function, we further hypothesized that OI would be more closely associated with morbidity and mortality than fetal imaging measurements currently used.

1. Methods

1.1. Study cohort

Approval was obtained from the Institutional Review Board for the Baylor College of Medicine and Affiliated Hospitals. A retrospective, observational study was conducted in patients with CDH referred for general surgery consultation between January 2011 and April 2016. A total of 118 patients had postnatal surgical consultation for suspected CDH. Of these, 87 had a prenatal diagnosis of left-sided CDH during the study period. Patients with significant cardiac malformations (defined as a Risk Adjustment for Congenital Heart Surgery (RACHS-1) score greater than or equal to 2), those who received fetal intervention, patients with chromosomal anomalies, right-sided, bilateral or ventral CDH patients, or patients treated with comfort care only were excluded [14–16] (Fig. 1). Medical records of the remaining 50 patients with isolated, left-sided, prenatally diagnosed CDH were reviewed.

1.2. Measured outcomes

The primary outcome was survival to 6 months chronologic age. This endpoint was chosen for consistency in reporting as 6 month survival has previously been used in our institution as a primary outcome for CDH research when assessing prenatal & postnatal predictors of outcome [9,12,17–19]. Patient demographics and clinical parameters in the first 48 h included: race, ethnicity, sex, gestational age (GA), birth weight, Apgar scores at 1 and 5 min, mode of delivery, prenatal US measurements of LHR, MRI measurements of TFLV and %LH, postnatal age of repair, HiOI, use of ECMO, ventilator parameters, arterial blood gases, length of hospital stay, discharge medications and discharge respiratory support.

Calculation of the OI was performed using the following formula: $OI = (FiO_2 \times M_{PAW} \times 100)/PaO_2$, where FiO_2 is fraction of inspired oxygen, M_{PAW} is mean airway pressure (mmHg), and PaO_2 is partial pressure of oxygen in arterial blood (mmHg). If a subject was on high frequency oscillatory ventilation, the delivered M_{PAW} was used; whereas if on conventional mechanical ventilator, the recorded M_{PAW} from the device was used for calculation of OI. The HiOI was rounded to the nearest whole number and used for statistical analysis.

1.3. Neonatal protocol

Institutional guidelines are used for patient care. Furthermore, our CDH patients are cared for by a core group of neonatologists, thus ensuring consistency of care delivered. Management in our institution begins with conventional mechanical ventilation with escalation to high frequency oscillator if peak pressures required are greater than 28 cm of H_2O. Nitric oxide is initiated if OI exceeds 25 on two separate measurements. Umbilical arterial and venous catheters are placed and the patient is stabilized prior to surgical repair. If OI exceeds 40 on two separate measurements, ECMO management is considered. Once on ECMO, surgical repair of the defect is typically undertaken within 48–72 h. Timing of subsequent extubation from ventilator support is determined by clinical stability. Timing of discharge is determined by clinical stability and family preparedness.

1.4. Statistical analysis

Logistic regression analysis was used to examine the association of OI with death and respiratory medication at discharge (both bivariate associations and after adjusting for the 5-min Apgar score and gestational age). The 5-min Apgar score and EGA were collected on all infants, thus these were included in the regression model to determine what effects, if any, they may have on the outcomes. Parameters including highest PaO2, lowest PaO2, highest lactate and highest PCO2 were also analyzed in bivariate analyses. Highest OI, highest lactate and

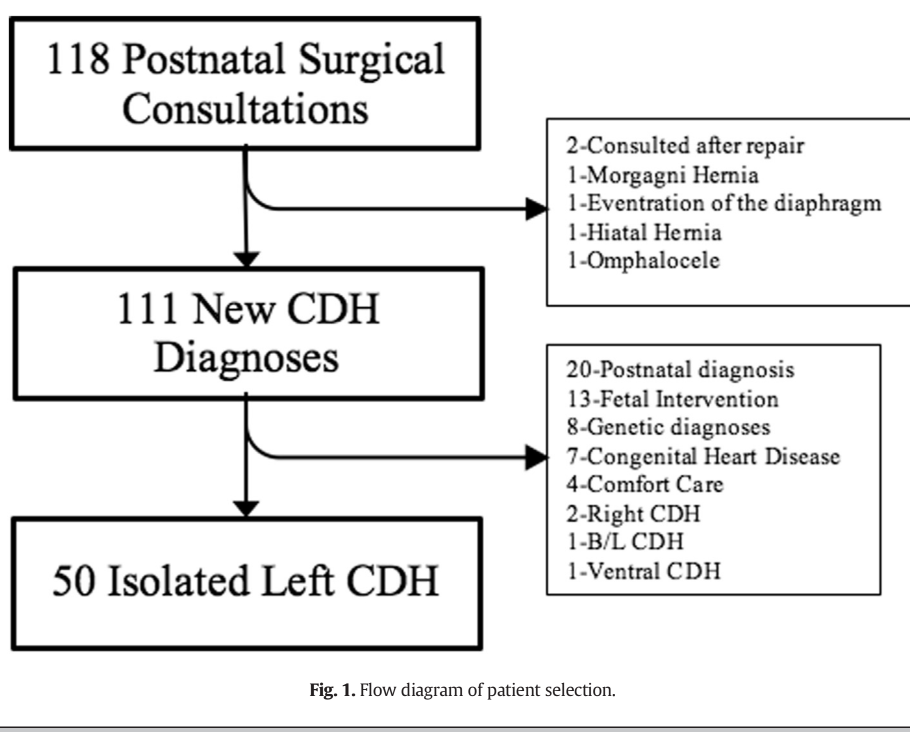

Fig. 1. Flow diagram of patient selection.