Journal of Pediatric Surgery 52 (2017) 928–932

Contents lists available at ScienceDirect

Journal of Pediatric Surgery

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

Factors associated with early recurrence after congenital diaphragmatic hernia repair☆

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ARTICLE INFO

Article history:
Received 27 February 2017
Accepted 9 March 2017

Key words:
Congenital diaphragmatic hernia
Recurrence
Minimally-invasive surgery
Defect size
Extracorporeal membrane oxygenation

ABSTRACT

Background: The purpose of this study was to identify patient and treatment characteristics associated with early (in hospital) hernia recurrence after congenital diaphragmatic hernia (CDH) repair.
Methods: Data from the Congenital Diaphragmatic Hernia Study Group registry were queried from 2007 to 2015. Recurrence of the diaphragmatic hernia after initial repair and prior to death or discharge was determined at the time of reoperation. Minimally invasive surgery (MIS) approaches included laparoscopy or thoracoscopy, and open approaches consisted of laparotomy or thoracotomy. Multivariate regression analysis was performed.
Results: Of 3984 patients, 3332 (84%) underwent CDH repair. 76 (2.3%) patients had an early recurrence. The rate of recurrence was less variable over time for patients undergoing laparotomy vs thoracoscopy (range: 1.1–3.7% vs 1.7–8.9% annually). Timing of repair, whether performed after, during, or before ECMO did not significantly alter recurrence rates (0% vs 4.2% vs 3.0%, $p = 0.116$). Larger defect size (C: OR 4.3, 95% CI 1.2–15.4; D: OR 7.1, 95% CI 1.7–29.1) and an MIS approach (OR 3.2, 95% CI 1.7–6.0) were the only independent predictors of recurrence.
Conclusion: Larger defect size and an MIS approach were associated with higher rates of early recurrence, while ECMO use and timing of repair with ECMO were not.
Type of study: Treatment study.
Level of evidence: II.

Survivors of congenital diaphragmatic hernia (CDH) face significant morbidity. Ongoing pulmonary, neurodevelopmental, and/or gastrointestinal pathophysiology affect 50%–90% of CDH patients [1–3]. Often, CDH patients have a prolonged initial hospital course, during which they experience significant morbidity. While some of the morbidity is a result of the natural history of the disease, some components of morbidity are the result of treatment. Postoperative hemorrhage, ventilator associated lung injury, surgical site infection, and adhesive bowel obstruction are a few of the early complications seen in the management of CDH [4,5]. One of the more common sources of potentially preventable morbidity is diaphragmatic hernia recurrence.

The incidence of CDH recurrence ranges from 3% to approximately 50%, depending upon the specific patient population and individual publication [6–9]. More specifically, an early or "in-hospital" recurrence rate of approximately 3% has been reported [8]. Previous publications have identified multiple factors associated with diaphragmatic recurrence including patient variables such as liver herniation [8], length of stay [7], and treatment variables including need for ECMO [10], operative approach [11], diaphragmatic patch repair [9], or abdominal patch requirement [7]. These rates and associations are highly variable given reporting challenges and lack of structured long-term follow-up. Further, most of these studies draw conclusions from small cohorts or single center studies, severely limiting the validity and translatability of the findings.

Factors associated with early recurrence are incompletely understood. Recently, the CDHSG staging system was developed and its strong association with morbidity and mortality reported [12,13]. The purpose of this study was to identify patient and treatment characteristics, including CDHSG stage, associated with early CDH recurrence. In addition, we evaluated recurrence rates over time.

1. Materials and methods

1.1. Study design and setting

The international Congenital Diaphragmatic Hernia Study Group (CDHSG) registry was queried for live-born neonates undergoing CDH repair from 2007 to 2015. The CDHSG is a voluntary consortium of children's hospitals committed to studying key clinical questions related to CDH through prospective data collection and analysis. Data collection

☆ Source of support: Center for Clinical and Translational Sciences Training Award, University of Texas McGovern Medical School (5KL2-TR000370-10).

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http://dx.doi.org/10.1016/j.jpedsurg.2017.03.011
0022-3468/

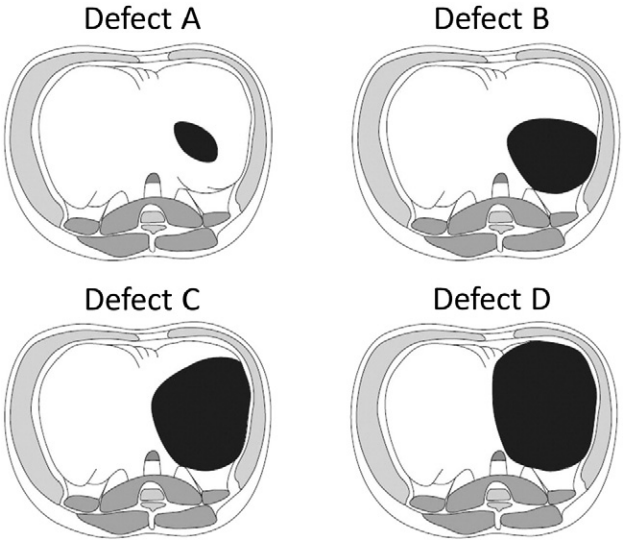

Fig. 1. CDHSG staging system. Defects are classified as: A: mallest defect, usually "intramuscular" defect with >90% of the hemi-diaphragm present; this defect involves <10% of the circumference of the chest wall, B: approximately 50%–75% of the hemi-diaphragm is present and less than 50% of the thoracic wall is involved in the defect, C: less than 50% of the diaphragm is present and greater than 50% of the thoracic wall is involved in the defect, and D: largest defect, minimal or no diaphragm is present – also known as "agenesis". All "A" and some "B" defects are closed primarily, while large "B", and all "C" or "D" defects require a patch (or a muscle flap).

forms are intermittently updated to include additional variables of interest. In 2007, the CDHSG Staging System was established which classifies defect size into one of four letters (A–D) whereby "A" defects are the smallest and "D" defects are the largest (Fig. 1) [12]. The CDHSG registry has been approved for use by the Institutional Review Board of the University of Texas Medical School at Houston (HSC-MS-03-223).

1.2. Outcomes

The primary outcome was early recurrence of the diaphragmatic hernia after initial repair and prior to death or discharge. This outcome was determined at the time of reoperation. The secondary outcome was initial hospital length of stay (LOS) for patients who survived to discharge or transfer.

1.3. Patient and operative characteristics

Patient and operative characteristics including gestational age, birth weight, Apgar score at 5 min, major cardiac and chromosomal anomalies, defect side and size (A–D), age at repair, liver herniation at time of repair, surgical approach, patch use, and extracorporeal membrane oxygenation (ECMO) for patients with posterolateral defects were reviewed. Minimally invasive surgery (MIS) included laparoscopic or thoracoscopic repairs, and open approaches consisted of laparotomy or thoracotomy.

1.4. Statistical analysis

Data are described based on their distribution. Medians (interquartile range) and means ± standard deviations are reported. Binary and continuous parametric data were assessed using chi-squared, Fisher's exact or Student's *t*-tests, and continuous nonparametric data were assessed with Mann–Whitney *U* tests. Multivariable logistic and linear regression models were developed using a stepwise approach incorporating variables found to have *p*-values <0.2 on univariate analysis. Missing data are described in Table 1, and patients with incomplete data were excluded from the regression models. Statistical analyses were performed with Stata/IC 13.1 (Stata Corp LP, College Station, TX).

2. Results

2.1. Cohort characteristics

A total of 3984 patients were entered into the CDHSG registry from 2007 to 2015, and 3332 (84%) underwent CDH repair. A median of

Table 1
Baseline patient characteristics and treatment details.

Pt/Rx characteristics	Missing data	All patients	Patients without recurrence ($n = 3256$)	Patients with recurrence ($n = 76$)	*p*-Value
Premature	0 (0)	641 (19.2)	623 (19.1)	18 (23.7)	0.32
Mean birth weight, kg	6 (0.2)	3.02 ± 0.59	3.02 ± 0.59	2.93 ± 0.73	0.186
Median Apgar at 5 min	213 (6.4)	7 (6–8)	7 (6–8)	7 (5–8)	0.043
Major cardiac anomaly	0 (0)	190 (5.7)	183 (5.6)	7 (9.2)	0.202
Chromosomal anomaly	0 (0)	148 (4.4)	143 (4.4)	5 (6.6)	0.388
Defect side, left	3 (0.1)	2821 (84.7)	2753 (84.6)	68 (89.5)	0.246
Median age at repair, day	4 (0.1)	5 (3–9)	5 (3–9)	5.5 (3–13)	0.318
Liver herniation	84 (2.5)	1481 (45.6)	1436 (45.2)	45 (60.8)	0.008
Defect size	19 (0.6)				<0.001
A		456 (13.8)	451 (13.9)	5 (6.6)	
B		1342 (40.5)	1325 (40.9)	17 (22.4)	
C		1079 (32.6)	1044 (32.3)	35 (46)	
D		436 (13.1)	417 (12.9)	19 (25)	
Approach	265 (8.0)				0.053
Open		2579 (84.1)	2526 (84.3)	53 (75.7)	
MIS		488 (15.9)	471 (15.7)	17 (24.3)	
ECMO	0 (0)	965 (29.0)	933 (28.7)	32 (42.1)	0.011[a]
No ECMO		2367 (71.0)	2323 (71.4)	44 (57.9)	
ECMO before repair		90 (2.7)	90 (9.6)	0 (0)	
ECMO during repair		506 (15.2)	485 (52)	21 (65.6)	
ECMO after repair		369 (11.1)	358 (38.4)	11 (34.4)	
Patch	7 (0.2)				0.001
Primary		1579 (47.5)	1557 (47.9)	22 (29)	
Patch		1746 (52.5)	1692 (52.1)	54 (71)	

Data are presented as *n* (%) unless otherwise indicated.
[a] Chi-square test comparing ECMO yes/no for the two patient groups.